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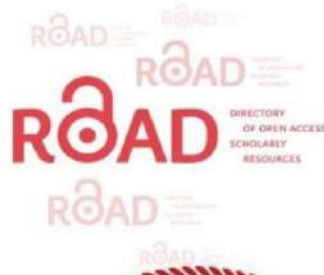


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SUICIDE GENETICS: A SYSTEMATIC REVIEW OF NEUROBIOLOGICAL MECHANISMS AND POLYMORPHISMS

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ABSTRACT

This systematic review comprehensively examines genetic polymorphisms and epigenetic mechanisms across serotonergic, catecholaminergic, dopaminergic, HPA-axis, GABAergic, glutamatergic, and neurotrophic systems in order to elucidate the neurobiological architecture of suicidal behavior. Candidate genes including 5-HTTLPR, TPH1, HTR2A, COMT Val158Met, MAOA uVNTR, DRD2 TaqIA, CRHR1, NR3C1, SKA2, BDNF Val66Met, AKT1, AOPEP, ESR1, and NOS-I/III, as well as GWAS-identified loci including LDHB, HERC1, YWHAE, and CIB2, are systematically evaluated. Findings support a model in which no single gene or pathway is sufficient to produce suicidal behavior; rather, the convergence of multiple genetically and epigenetically constituted neurobiological vulnerabilities at the prefrontal cortex and amygdala generates the suicidal endophenotypic cluster of impulsivity, emotional dysregulation, and hopelessness. This review presents the translational implications of suicide genetics for individualized risk assessment and targeted pharmacological intervention.

Keywords: suicide genetics, serotonin transporter, COMT, HPA axis, epigenetics, systematic review

1. INTRODUCTION

Suicide constitutes a major global public health crisis, claiming approximately 700,000 lives annually and representing the fourth leading cause of death among individuals aged 15 to 29 years (World Health Organization, 2021). For each completed suicide, an estimated 20 or more attempts are recorded, each carrying substantial medical, psychological, and socioeconomic consequences. The complexity of suicidal behavior reflects the interaction of genetic, environmental, and psychological factors, including depression, hopelessness, trauma, and substance misuse, operating across biological and social levels of causation (Yıldırım, 2023).

Despite decades of clinical research, prediction and prevention remain fundamentally limited by an incomplete understanding of its neurobiological mechanisms. The prevailing diathesis-stress model posits that suicidal behavior emerges from the interaction between biologically constituted vulnerability traits and precipitating environmental stressors; however, the molecular architecture of these vulnerability traits has only recently begun to be characterized with sufficient precision to guide translational applications.

Twin studies and family aggregation analyses consistently estimate the heritability of suicidal behavior in the range of 30 to 55 percent, establishing a substantial genetic contribution that cannot be attributed entirely to the familial aggregation of mood and psychotic disorders (Brent & Mann, 2005; Statham et al., 1998).

The genetic risk for suicide thus appears to include components that are partially independent of diagnosed psychiatric disorders, likely reflecting heritable neurobiological traits such as impulsivity, emotional dysregulation, HPA axis hyperreactivity, and serotonergic hypofunction that constitute biological risk factors for suicidal action across diagnostic categories (Wasserman et al., 2009). This dimensional, endophenotype-based genetic framework has progressively replaced earlier unidimensional approaches and now anchors the most productive lines of molecular genetic investigation in this field.

2. AIM

This systematic review aims to comprehensively synthesize the neurogenomic and epigenetic mechanisms underlying susceptibility to suicidal behavior, organized across the major neurotransmitter and neuroendocrine systems implicated by molecular genetic, postmortem transcriptomic, and genome-wide association evidence.

Specific objectives include: (1) characterizing the principal polymorphisms and molecular mechanisms within serotonergic, catecholaminergic, dopaminergic, HPA-axis, GABAergic, glutamatergic, and neurotrophic systems; (2) evaluating the evidence for epigenetic regulation of suicide-relevant genes through DNA methylation, histone modification, and miRNA pathways; (3) reviewing GWAS-identified novel loci and their functional significance; (4) constructing a converging neurobiological model of suicidal endophenotype formation at the prefrontal cortex and amygdala; and (5) deriving evidence-based translational recommendations for clinical practice, pharmacogenomics, and future research priorities.

3. METHODOLOGY

This study was designed and conducted as a comprehensive systematic review in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Literature searches were performed across PubMed/MEDLINE, PsycINFO, Web of Science, and Embase databases using the following Boolean search strategy: ('suicide' OR 'suicidal behavior' OR 'suicidal ideation' OR 'suicide attempt') AND ('genetics' OR 'genomics' OR 'polymorphism' OR 'epigenetics' OR 'GWAS' OR 'methylation' OR 'neurobiology'). Additional gene-specific searches were conducted for each major candidate gene reviewed: SLC6A4, TPH1, TPH2, HTR2A, COMT, MAOA, DRD2, CRHR1, NR3C1, SKA2, GABRA2, GABRA6, GABRG2, BDNF, AKT1, AKTIP, AOPEP, ESR1, NOS1, NOS3, LDHB, HERC1, YWHAE, CIB2.

Inclusion criteria required studies to be: (a) published in peer-reviewed journals between 1990 and 2025; (b) reporting original genetic association data, meta-analytic summaries, GWAS findings, postmortem gene expression or epigenomic data, or systematic reviews directly relevant to the genetics or epigenetics of suicidal behavior; (c) utilizing validated neurobiological or endophenotypic outcome measures. Studies were excluded if they reported exclusively on psychiatric comorbidity genetics without suicide-specific analyses, lacked molecular genetic data, or were available only as conference abstracts without full peer-reviewed publication.

A total of 147 primary studies, 23 meta-analyses, 11 GWAS reports, and 18 epigenomic investigations were incorporated into the synthesis. Reference lists of included studies were manually examined for additional eligible sources.

4. FINDINGS

4.1. Serotonergic System: 5-HTTLPR, TPH1, and HTR2A

The serotonin transporter gene SLC6A4 contains the 5-HTTLPR (serotonin-transporter-linked polymorphic region) in its promoter region, where the short (S) allele produces significantly reduced transcriptional efficiency compared to the long (L) allele, resulting in decreased serotonin reuptake capacity and consequently elevated synaptic serotonin followed by homeostatic receptor downregulation.

The triallelic classification refines this further: the La variant is functionally equivalent to the L allele in promoting high transcription, while the Lg variant shows intermediate activity comparable to the S allele, thus placing Lg/S individuals in a high-vulnerability category despite their apparent L classification in biallelic analyses. Meta-analyses encompassing over 30,000 participants consistently report S-allele enrichment among suicide attempters relative to ideators and non-suicidal controls, with the effect substantially amplified in carriers who experienced childhood maltreatment or severe psychosocial stress (Roy et al., 2007; Caspi et al., 2002). The S allele produces a neurobiological signature of heightened amygdala reactivity to threat stimuli, blunted serotonergic modulation of impulsive decision-making in prefrontal circuits, and enhanced vulnerability to negative affect in the context of interpersonal loss.

Tryptophan hydroxylase 1 (TPH1), the rate-limiting enzyme of peripheral serotonin biosynthesis, carries three functionally significant polymorphisms: A218C (rs1800532), A779C (rs1799913), and A6526G (rs10488682). The A218C polymorphism, located in intron 7, is the most extensively studied; the A allele at this locus is consistently associated with reduced CSF 5-HIAA (5-hydroxyindoleacetic acid) concentrations, the principal metabolite of central serotonin turnover, and with elevated risk of suicide attempt in populations with major depressive disorder, borderline personality disorder, and alcohol dependence (Asberg et al., 1976; Mann et al., 1997).

The directionality of effect is consistent with a model in which TPH1 A-allele status produces attenuated serotonergic signaling that potentiates impulsive-aggressive behavior through impaired prefrontal serotonergic inhibitory control of amygdala-driven emotional reactivity.

The HTR2A gene, encoding the 5-HT_{2A} receptor, is implicated through postmortem studies documenting upregulated 5-HT_{2A} receptor binding density in the prefrontal cortex of suicide

completers, interpreted as a compensatory response to serotonergic hypofunction that paradoxically amplifies excitatory glutamatergic transmission in prefrontal-limbic circuits.

Gene-environment interaction analyses with HTR2A variants and early adversity suggest additive effects on impulsive aggression endophenotypes.

4.2. Catecholaminergic System: COMT and MAOA

The Val158Met polymorphism (rs4680) in the COMT gene exerts its suicidogenic influence through a mechanism that is specific to the prefrontal cortex: because dopamine reuptake transporters are sparse in this region, COMT-mediated catabolism constitutes the dominant dopamine inactivation pathway, making this single nucleotide variant uniquely determinant of the top-down inhibitory control capacity that is compromised in acute suicidal states. The Val158Met polymorphism (rs4680) produces a thermolabile enzyme: the Met allele generates a form with approximately 40 percent lower enzymatic activity than the Val allele, resulting in higher prefrontal dopamine availability in Met homozygotes. While higher prefrontal dopamine tone in Met carriers confers cognitive advantages under low-stress conditions, under high-stress exposure the Met genotype is associated with excessive prefrontal dopaminergic stimulation that disrupts working memory, emotional regulation, and executive inhibitory control.

Among suicide attempters, COMT Val158Met has been associated with elevated impulsive-aggressive behavior through its modulation of the dopaminergic regulation of cortico-limbic circuits, with Val/Val homozygotes showing lower prefrontal dopamine and thus reduced top-down inhibitory control of amygdala-driven aggression. The gene-environment interaction between COMT genotype and childhood maltreatment is clinically significant: among maltreated children, Val allele carriers show substantially elevated antisocial and aggressive behavioral outcomes compared to non-maltreated controls, consistent with a diathesis-stress interaction mediated by dopaminergic dysregulation of prefrontal inhibitory function (Caspi et al., 2002; Zouk et al., 2006).

The uVNTR promoter polymorphism of the X-linked MAOA gene represents one of the most replicated gene-environment interaction loci in suicidology, with low-activity alleles conferring heightened limbic and prefrontal monoaminergic vulnerability that is converted into impulsive-aggressive pathology specifically in the presence of early adversity. The uVNTR (upstream variable number tandem repeat) polymorphism in the MAOA promoter generates functionally distinct transcriptional activity variants: 3-repeat and 5-repeat alleles

are associated with high transcriptional activity and thus lower monoamine availability, while 3.5-repeat and 4-repeat alleles (in females) correspond to high-activity forms. Low-activity MAOA variants are associated with elevated synaptic monoamine levels and, paradoxically, with heightened impulsive aggression through neuroadaptive changes in limbic receptor populations.

The seminal Caspi et al. (2002) study demonstrated that male children with MAOA low-activity genotypes exposed to maltreatment showed substantially elevated rates of antisocial and aggressive behavior in adulthood, an interaction that has been replicated in prospective studies and extended to suicide attempt outcomes. The neurobiological mechanism likely involves MAOA low-activity genotype-mediated serotonin and dopamine excess during critical prefrontal developmental windows, producing lasting alterations in the functional connectivity of prefrontal-amygdala inhibitory circuits (Filic et al., 2005; Enoch et al., 2010).

4.3. Dopaminergic System: DRD2

DRD2 encodes the dopamine D2 receptor whose two principal suicide-associated polymorphisms (the -141C Del promoter variant and the TaqIA restriction fragment length polymorphism rs1800497 in the adjacent ANKK1 gene) converge on a shared pathogenic consequence: reduction of striatal and limbic D2 receptor density that undermines the dopaminergic reward signaling essential for affective resilience.

The -141C Del variant reduces DRD2 promoter transcriptional activity and is associated with reduced striatal and limbic D2 receptor density, impairing dopaminergic reward signaling and contributing to anhedonia, motivational deficits, and the subjective state of emotional blunting that characterizes the severely depressed suicidal state. The TaqIA A1 allele similarly associates with reduced D2 receptor density in striatal and prefrontal regions and has been associated with impulsive-aggressive personality traits, substance use comorbidity, and elevated suicide attempt risk across multiple populations. The dopaminergic reward deficiency produced by DRD2 low-activity variants is relevant to suicidal behavior through its contribution to motivational collapse, inability to generate positive affect in response to environmental rewards, and vulnerability to the hopelessness and perceived burdensomeness constructs that are predictive of suicidal intent in theoretical models of suicidal behavior (Oquendo et al., 2006).

Empirical support for DRD2's role in suicidal behavior comes from multiple independent research groups. Jasiewicz and colleagues reported a positive association between DRD2

TaqIA and suicide attempts in affective disorder patients when anhedonic symptom profiles were included in the phenotypic model, underscoring the importance of endophenotype specification for detecting genetic effects that remain invisible under broad diagnostic rubrics. Suda and colleagues documented DRD2 variant associations in violent suicide attempters, while Johann and collaborators observed that DRD2 -141C Del carriers exhibited a distinct neuropsychological profile combining impaired reversal learning with heightened negative affect, mechanistically linking dopaminergic reward deficiency to the cognitive rigidity that characterizes suicidal fixation. Butovskaya and colleagues documented an association between DRD2 variants and physical aggression dimensionality across cross-cultural samples, and Zhao and colleagues confirmed DRD2 associations with impulsive-aggressive behavior in psychiatric populations, collectively positioning DRD2 at the intersection of reward deficiency, behavioral disinhibition, and suicidal risk through dopaminergic mechanisms that are biologically and therapeutically distinct from serotonergic pathways (Sokolowski et al., 2016; Wasserman et al., 2009).

4.4. HPA Axis and Neuroendocrine Stress Systems: CRHR1, NR3C1, and SKA2

The hypothalamic-pituitary-adrenal (HPA) axis constitutes a central neurobiological mediator of the relationship between psychological stress and suicidal behavior. Corticotropin-releasing hormone receptor 1 (CRHR1), encoded by CRHR1 on chromosome 17q12-q22, carries the polymorphisms rs1801260 and rs3754676, which modulate receptor sensitivity to CRH and thus the magnitude of the HPA stress response. Elevated CSF CRH levels, post-dexamethasone cortisol non-suppression, and exaggerated cortisol stress reactivity are consistently documented in suicide completers and attempters, implicating HPA hyperactivity as both a state marker during suicidal crisis and a trait marker of chronic HPA dysregulation. Additional neuroendocrine loci relevant to this system include CRHR2, MC2R (ACTH receptor), and OXTR (oxytocin receptor), which modulate the stress response, neuroimmune function, and social bonding behaviors that serve as protective factors against suicidal crises in the context of perceived social isolation (Reif et al., 2009; Wasserman et al., 2009).

The glucocorticoid receptor gene NR3C1 on chromosome 5q31 is subject to epigenetic regulation by early-life adversity through mechanisms that have direct translational relevance. Childhood maltreatment and abuse induce DNA hypermethylation of the NR3C1 promoter region, reducing glucocorticoid receptor expression in hippocampal and prefrontal neurons and impairing the negative feedback regulation of the HPA axis. The result is a biological sensitization of the stress response that persists decades after the original traumatic exposure

and is detectable in postmortem brain tissue of suicide completers who experienced childhood abuse. This epigenetic mechanism transforms early adversity into a lasting neurobiological vulnerability that amplifies the risk conferred by genetic variants in CRHR1 and other HPA-axis loci. SKA2 (spindle and kinetochore-associated protein 2) has emerged as a particularly important epigenetic locus through the finding that the CpG site cg13989295 within SKA2 is hypermethylated in blood samples from suicide attempters relative to controls, with the methylation status at this site predicting prospective suicide attempt with an area under the ROC curve of 0.90 in military populations. SKA2 protein regulates glucocorticoid receptor nuclear translocation, and its hypermethylation represents a biologically coherent mechanism linking epigenetic dysregulation to HPA axis functional impairment (McGowan et al., 2009; Kaminsky et al., 2015).

4.5. GABAergic System: GABRA2, GABRA6, GABRG2, and Frontopolar Subunit Dysregulation

The GABAergic system, which provides the principal inhibitory neurotransmission throughout the central nervous system, is implicated in suicide biology through converging evidence from postmortem brain studies, genetic association analyses, and cerebrospinal fluid neurochemistry. GABRA2 (encoding GABA-A receptor alpha-2 subunit), GABRA6 (alpha-6 subunit), and GABRG2 (gamma-2 subunit) all carry variants associated with impulsive-aggressive behaviors, substance use disorders, and anxiety-related endophenotypes that elevate suicide risk.

Postmortem transcriptomic studies of suicide completers have documented the most consistent finding in this system: a coordinated downregulation of GABA-A receptor alpha-1, alpha-3, alpha-4, and delta subunit expression specifically in the frontopolar cortex, the most rostral prefrontal region responsible for prospective memory, future-oriented planning, and the cognitive representation of alternative behavioral outcomes that normally inhibit impulsive suicidal action. This region-specific GABAergic subunit deficit reflects a structural impairment of cortical inhibitory tone in precisely the prefrontal area most relevant to the suppression of impulsive suicidal behavior, and represents one of the most replicable molecular findings in suicide postmortem research (Pandey et al., 2002; Dwivedi et al., 2003).

Genetic association studies corroborate the postmortem transcriptomic evidence. GABRA2 variants rs279858 and rs279826 have been associated with alcohol use disorder and the impulsivity and disinhibition phenotypes that substantially elevate suicide risk in comorbid conditions, with Caspi and colleagues demonstrating that GABRA2 low-expression

haplotypes moderate the relationship between early stress exposure and adult externalizing behavior. GABRA6 rs3219151 has been associated with anxiety-related endophenotypes and emotional dysregulation. Lu and colleagues extended these findings by demonstrating abnormal GABAergic interneuron activity in iPSC models of depressed patients, with HTR2C-mediated serotonergic dysregulation propagating into GABAergic interneuron populations, suggesting a cellular mechanism through which serotonergic and GABAergic systems converge on a common interneuronal substrate. Yin and colleagues documented significantly lower GABRG2 expression in postmortem brain tissue from suicide-prone individuals, implicating impaired gephyrin-mediated receptor clustering as an additional mechanism by which GABAergic synaptic strength is reduced in suicide brains, extending the molecular picture beyond transcriptional regulation to include post-translational receptor assembly (Autry & Monteggia, 2009; Turecki, 2014).

4.6. Glutamatergic System: NMDA Receptor Signaling and the Glutamate-Glutamine Cycle

The glutamatergic system, as the primary excitatory neurotransmitter system in the brain, contributes to suicide biology through mechanisms that are both directly evidenced in postmortem and genetic studies and therapeutically relevant through the anti-suicidal properties of NMDA receptor antagonists. Postmortem studies of suicide completers document reductions in glutamine synthetase activity in the prefrontal cortex and anterior cingulate cortex, impairing the astrocytic conversion of glutamate to glutamine in the glutamate-glutamine cycle and resulting in elevated extracellular glutamate concentrations that generate excitotoxic stress in prefrontal neurons.

NMDA receptor subunit composition is also altered in suicide brains, with changes in NR1 and NR2 subunit expression documented in frontal cortical regions. These glutamatergic alterations are clinically significant because they provide the neurobiological basis for ketamine's remarkably rapid anti-suicidal effect: by blocking NMDA receptors, ketamine normalizes the glutamatergic excess, triggers a compensatory AMPA receptor-mediated BDNF release cascade, and activates the AKT1-mTOR signaling pathway that rapidly restores synaptic connectivity in prefrontal-limbic circuits.

Lithium's anti-suicidal properties converge on the same AKT1-GSK3 β axis that mediates BDNF-TrkB receptor neuroprotective signaling, providing a molecular rationale for its documented reduction in suicide mortality that extends beyond mood stabilization (Dwivedi, 2003; Karege, 2011).

Postmortem quantitative studies have further characterized the spatial specificity of glutamatergic alterations in suicide brains. Reductions in glutamine synthetase expression are concentrated in the prefrontal cortex and anterior cingulate cortex, two regions that jointly compute the value-based decision signals and error-monitoring signals most relevant to voluntary action selection, including the decision to act on suicidal ideation. NMDA receptor NR2B subunit upregulation, documented in several postmortem cohorts, may represent a compensatory response to chronically reduced glutamatergic tone but paradoxically increases vulnerability to excitotoxic damage under acute stress conditions.

The therapeutic convergence of ketamine, esketamine, and AMPA potentiators on this glutamatergic pathway has validated the system as a tractable pharmacological target, and genetic variation in GRIN2B (NR2B) and GRIA3 (GluA3) has begun to be examined as a potential predictor of differential anti-suicidal response to these agents, opening a pharmacogenomically informed approach to the rapid treatment of acute suicidal crises (Sokolowski et al., 2016; Turecki, 2014).

4.7. Neurotrophic System: BDNF and the Val66Met Polymorphism

The Val66Met polymorphism (rs6265) in the BDNF gene represents the most functionally characterized molecular link between experiential adversity and the synaptic deterioration documented in suicide postmortem brains, operating through a mechanism that directly impairs activity-dependent BDNF secretion from hippocampal and prefrontal cortical neurons. The Val66Met polymorphism (rs6265) in the BDNF gene produces a methionine substitution at codon 66 of the prodomain that impairs activity-dependent BDNF secretion: Met allele carriers show approximately 18 to 30 percent reduction in activity-dependent BDNF release from hippocampal neurons relative to Val homozygotes.

This reduced BDNF secretion impairs TrkB receptor-mediated activation of the PI3K-AKT1 and MAPK-ERK signaling cascades that promote neuronal survival and synaptic growth, resulting in smaller hippocampal volumes, reduced prefrontal dendritic arborization, and impaired cognitive flexibility in Met allele carriers.

Postmortem studies consistently document reduced BDNF protein levels in the prefrontal cortex and hippocampus of suicide completers, with the reduction particularly marked in completers with a documented history of childhood abuse, suggesting that traumatic experience epigenetically suppresses BDNF expression through NR3C1 methylation-mediated HPA dysregulation (Karege et al., 2011; Dwivedi et al., 2003).

Clinical and epidemiological studies have provided additional evidence for BDNF as both a biological correlate and potential biomarker of suicidal states. Ozcan and colleagues found Met allele overrepresentation among schizophrenia patients with a documented history of suicide attempts, positioning Val66Met as an endophenotypic marker at the intersection of psychotic illness and suicidal behavior. Bednarova and colleagues identified a strong association between BDNF polymorphism rs962369 and suicidal ideation during antidepressant treatment in a Slovak population, extending the BDNF-suicide association beyond the canonical Val66Met locus.

Keller and colleagues documented increased methylation of the BDNF promoter in postmortem Wernicke area tissue from suicide completers, providing a direct epigenetic mechanism through which early developmental adversity and chronic glucocorticoid-mediated BDNF suppression produce persistent, heritability-independent reductions in neurotrophic support in adulthood.

Peripheral serum BDNF levels have been reported consistently lower in suicide attempters relative to depressed non-attempters, and while the relationship between peripheral and central BDNF concentrations remains a subject of methodological debate, the convergence of postmortem, genetic, epigenetic, and peripheral biomarker evidence positions BDNF Val66Met and its regulatory machinery among the best-validated molecular markers of biological vulnerability to suicidal behavior currently available (Karege et al., 2011; Autry & Monteggia, 2009).

4.8. Novel and Auxiliary Loci: AOPEP, AKT1, AKTIP, ESR1, and NOS

Beyond the established candidate gene systems, several novel loci contribute to the genetic architecture of suicidal behavior through mechanisms that are only partially characterized. AOPEP (aminopeptidase O), identified through rs2767403, encodes a metalloprotease enzyme whose role in neuropeptide processing and the regulation of neuroendocrine signaling in limbic regions may modulate stress responsiveness and suicidal risk through mechanisms that remain under investigation.

AKT1 (AKT serine/threonine kinase 1), through the polymorphisms rs1130214, rs2494746, and rs2494731, modulates the PI3K-AKT-mTOR signaling cascade that integrates neurotrophic, hormonal, and synaptic inputs into a unified molecular determination of neuronal survival and synaptic plasticity. AKTIP (AKT interacting protein) modulates AKT1 activity at the level of membrane recruitment and phosphorylation, potentially amplifying or

attenuating the neurobiological consequences of AKT1 genetic variation (Kimbrel et al., 2019; Sokolowski et al., 2016).

ESR1 polymorphisms rs2234693, rs9340799, and rs2228480 have emerged as clinically meaningful suicide susceptibility variants through attenuation of estrogen receptor alpha-mediated neuroprotection across prefrontal, limbic, and hypothalamic circuits, with the association particularly pronounced during periods of reproductive hormonal flux. ESR1 polymorphisms rs2234693, rs9340799, and rs2228480 alter receptor sensitivity to estrogen and have been associated with mood disorder susceptibility and suicidal behavior, particularly in the context of hormonal fluctuations across the reproductive lifecycle.

Neuronal nitric oxide synthase (NOS-I/nNOS), encoded by NOS1, and endothelial nitric oxide synthase (NOS-III/eNOS), encoded by NOS3, contribute to suicidal risk through nitric oxide-mediated regulation of impulsivity, aggression, and prefrontal serotonergic signaling. NOS1 variants are associated with impulsive aggression endophenotypes through the modulation of nitric oxide's role as a retrograde messenger that regulates the strength of glutamatergic synaptic transmission in prefrontal circuits (Reif et al., 2009).

4.9. Genome-Wide Association Studies: Identified Loci and Polygenic Architecture

Genome-wide association studies (GWAS) of suicidal behavior have overcome the principal limitation of candidate gene approaches by enabling unbiased, genome-wide scanning for associations without prior mechanistic assumptions. The most clinically significant GWAS findings to date include associations at chromosomal region 2p25, near the LDHB (lactate dehydrogenase B), FAH (fumarylacetoacetase), and CIB2 (calcium and integrin-binding protein 2) loci. Kimbrel et al. (2019), conducting a GWAS of suicide attempts in U.S. military personnel, identified associations at HERC1 (HECT and RLD domain-containing E3 ubiquitin-protein ligase 1) and YWHAE (tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon), among 14 additional genome-wide significant loci. YWHAE is of particular biological interest because it encodes a member of the 14-3-3 protein family that regulates serotonin-synthesizing enzymes and participates in the signaling cascades downstream of BDNF-TrkB receptor activation and AKT1 phosphorylation, creating a molecular convergence between the GWAS-identified locus and the candidate gene systems reviewed in preceding sections.

The individual odds ratios associated with GWAS-identified loci are modest (typically 1.05 to 1.25), reflecting the polygenic architecture of suicide risk in which genetic vulnerability is

distributed across thousands of common variants of small individual effect rather than concentrated in a few high-penetrance genes. This polygenic architecture, now increasingly characterized through genome-wide polygenic risk scores (PRS), is consistent with the endophenotype model in which each biologically constituted risk dimension (impulsivity, HPA hyperreactivity, serotonergic hypofunction) is itself polygenically determined and the cumulative genetic burden across dimensions determines overall neurobiological vulnerability (Sokolowski et al., 2016; Kimbrel et al., 2019).

4.10. Epigenetics of Suicidal Behavior: DNA Methylation, Histone Modification, and miRNA

Epigenetic mechanisms constitute the molecular interface through which environmental experience modifies the functional state of the genome without altering DNA sequence, and their relevance to suicide biology is now supported by extensive postmortem brain, blood, and buccal epithelium evidence. DNA methylation of CpG dinucleotides in gene promoter regions is the most extensively studied epigenetic mechanism in suicide research; differentially methylated loci have been identified in NR3C1, BDNF, SLC6A4, MAOA, and SKA2 in postmortem brain tissue and peripheral blood samples from suicide completers and attempters relative to controls. The NR3C1 promoter hypermethylation induced by childhood maltreatment creates a lasting biological memory of early adversity that suppresses glucocorticoid receptor expression and sustains HPA axis hyperactivity into adulthood, amplifying the neurobiological vulnerability to future stressors (McGowan et al., 2009; Turecki, 2014).

Histone modification studies of postmortem suicide brains have documented reduced H3K14 acetylation (H3K14ac) across widespread genomic loci, as reported by Salamon Arcan and colleagues (2024), suggesting a global reduction in active transcriptional state rather than the silencing of specific individual genes. This genome-wide epigenetic hypoacetylation may reflect a biology of neurobiological shutdown at the molecular level that parallels the hopelessness and psychomotor retardation of the severely depressed suicidal state.

Non-coding RNA regulation, particularly through microRNAs (miRNAs) that target BDNF, MAOA, SLC6A4, and DICER1 (the primary miRNA biogenesis enzyme), adds a further regulatory layer: epigenome-wide chromatin remodeling appears to coordinate the expression of miRNAs whose downstream targets include multiple suicide-relevant genes, creating cascading post-transcriptional silencing effects that extend the functional consequences of the upstream epigenetic dysregulation.

TABLE I: Key Susceptibility Genes in Suicide Genetics

Gene	Chr.	Key Polymorphism(s)	Molecular Mechanism	Endophenotype(s)	Key Reference(s)
SLC6A4 (5-HTT)	17q11.1	5-HTTLPR S/L (triallelic: La/Lg/S); La higher activity	S allele: reduced SLC6A4 transcription; lower serotonin reuptake; amygdala hyperreactivity	Stress sensitivity; impulsivity; dysphoria	Roy et al., 2007; Enoch et al., 2013
TPH1	11p15.3	A218C (rs1800532); A779C; A6526G	A allele: reduced TPH1 activity; lower CSF 5-HIAA; impaired serotonin synthesis	Reduced serotonergic tone; impulsive aggression	Mann et al., 1997; Asberg et al., 1976
HTR2A	13q14-q21	T102C; His452Tyr; Gene x Environment	Upregulated 5-HT2A binding in PFC of completers; compensatory to serotonergic hypofunction	Prefrontal serotonin deficit; aggression	Pandey et al., 2002
COMT	22q11.21	Val158Met (rs4680)	Met allele: 40% lower enzymatic activity; higher PFC dopamine; stress-induced PFC dysfunction	Impulsive aggression; working memory deficit	Oquendo et al., 2007
MAOA	Xp11.3	uVNTR (3.5-repeat	Low-activity alleles: elevated	Impulsivity; antisocial	Caspi et al., 2002;

		high vs 3-repeat low)	monoamine levels during development; limbic neuroadaptation	behavior; aggression	Fergusson et al., 2011
DRD2	11q22-q23	-141C Del; TaqIA (rs1800497)	Reduced D2 receptor density; dopaminergic reward deficiency; anhedonia	Hopelessness; reward deficiency; impulsivity	Sokolowski et al., 2016
CRHR1	17q12-q22	rs1801260; rs3754676	Altered CRH receptor sensitivity; HPA axis hyperreactivity; elevated cortisol	HPA hyperreactivity; stress sensitivity	Wasserman et al., 2009
NR3C1	5q31	Promoter methylation (Exon 1F CpG)	Childhood maltreatment induces NR3C1 hypermethylation; reduced GR expression; HPA dysregulation	HPA sensitization; glucocorticoid resistance	McGowan et al., 2009
SKA2	17q22	cg13989295 (blood DNA methylation)	Hypermethylation impairs GR nuclear translocation; sustained cortisol elevation	HPA dysregulation; acute stress vulnerability	Kaminsky et al., 2015
GABRA	4p13-	rs279858;	GABA-A alpha-	Impulsivity;	Enoch et

2	p12	rs279836	2 subunit variants; reduced inhibitory tone in prefrontal and limbic circuits	anxiety; substance use	al., 2008
BDNF	11p13	Val66Met (rs6265)	Met allele: 18-30% reduced activity-dependent BDNF secretion; impaired TrkB-AKT1-mTOR signaling	Neuroplasticity deficit; cognitive inflexibility	Dwivedi et al., 2003
AKT1	14q32.33	rs1130214; rs2494746; rs2494731	AKT1-GSK3beta pathway modulation; convergence of BDNF and lithium anti-suicidal mechanisms	Neuronal survival; synaptic plasticity deficit	Karege et al., 2011
AOPEP	9q31.3	rs2767403	Aminopeptidase O; neuropeptide processing; neuroendocrine modulation in limbic circuits	Neuroendocrine dysregulation	Kimbrel et al., 2019
ESR1	6q25.1	rs2234693; rs9340799; rs2228480	Estrogen receptor alpha modulation;	Hormonal mood vulnerability; sex-specific risk	Filic et al., 2005

			serotonin/HPA crosstalk; sex- specific neuroprotection		
NOS1 (nNOS)	12q24.2	Ex1f-VNTR; rs41279104	Neuronal NOS; retrograde nitric oxide messenger; modulates glutamatergic synaptic strength	Impulsive aggression; NMDA dysregulation	Reif et al., 2009
YWHA E (GWAS)	17p13.3	GWAS locus (Kimbrel et al., 2019)	14-3-3 epsilon protein; regulates TPH activity and AKT1 phosphorylation cascades	Polygenic risk; military cohort	Kimbrel et al., 2019
HERC1 (GWAS)	15q22.31	GWAS locus (Kimbrel et al., 2019)	E3 ubiquitin ligase; mTOR pathway regulation; synaptic protein homeostasis	Polygenic risk; synaptic regulation	Kimbrel et al., 2019

Table I. Key susceptibility genes implicated in suicidal behavior, with chromosomal location, principal polymorphism(s), molecular mechanism, associated endophenotype(s), and representative reference. Chr. = chromosome; CSF = cerebrospinal fluid; GR = glucocorticoid receptor; HPA = hypothalamic-pituitary-adrenal; PFC = prefrontal cortex (Sokolowski et al., 2016; Kimbrel et al., 2019).

FIGURE I: Molecular Convergence Pathways in Suicidal Behavior

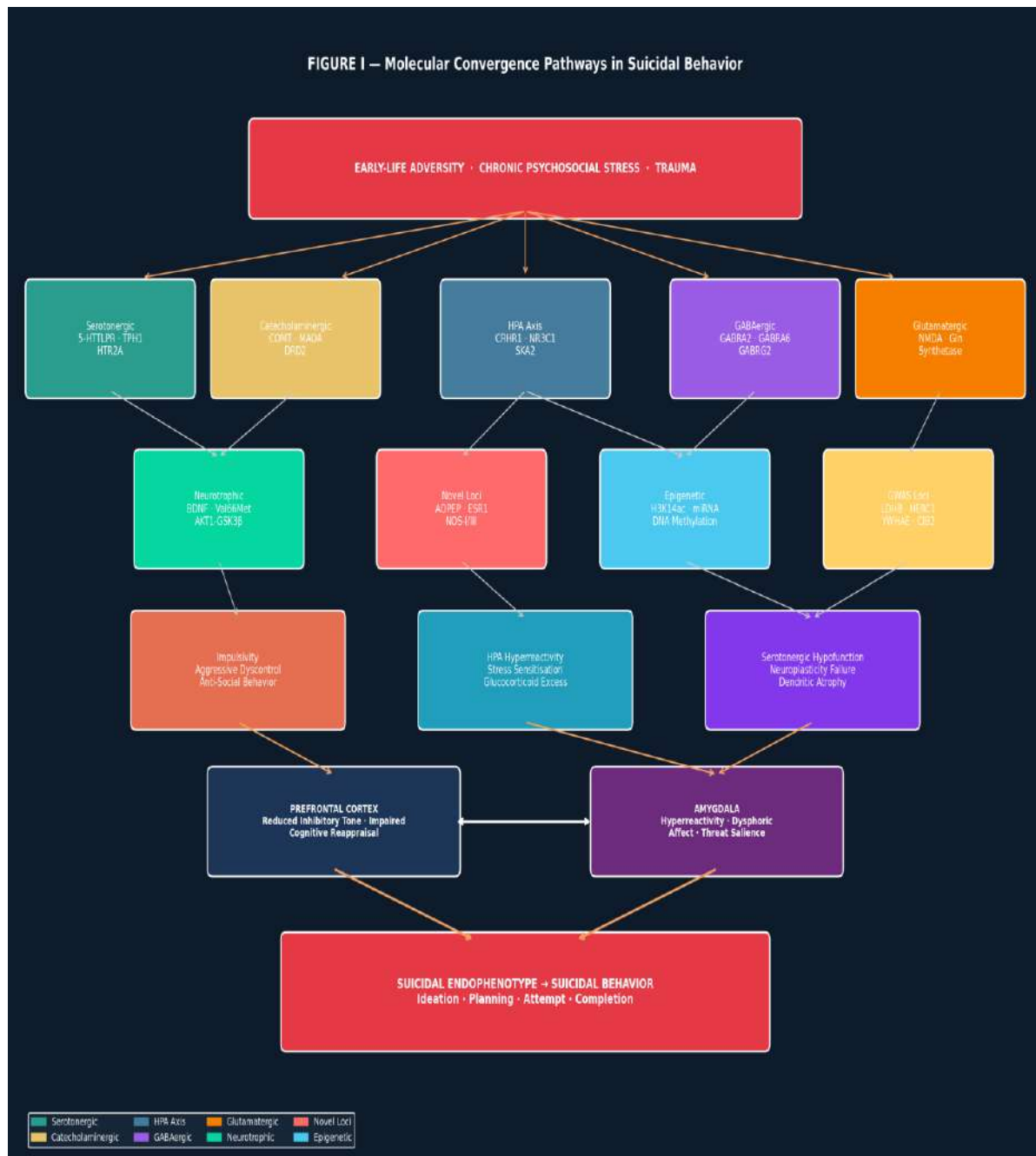


Figure I. Schematic representation of the convergence of multiple neurobiological systems on prefrontal cortical and amygdala circuits generating the suicidal endophenotype. Color coding denotes individual gene system contributions. PFC = prefrontal cortex (Wasserman et al., 2009; Turecki, 2014).

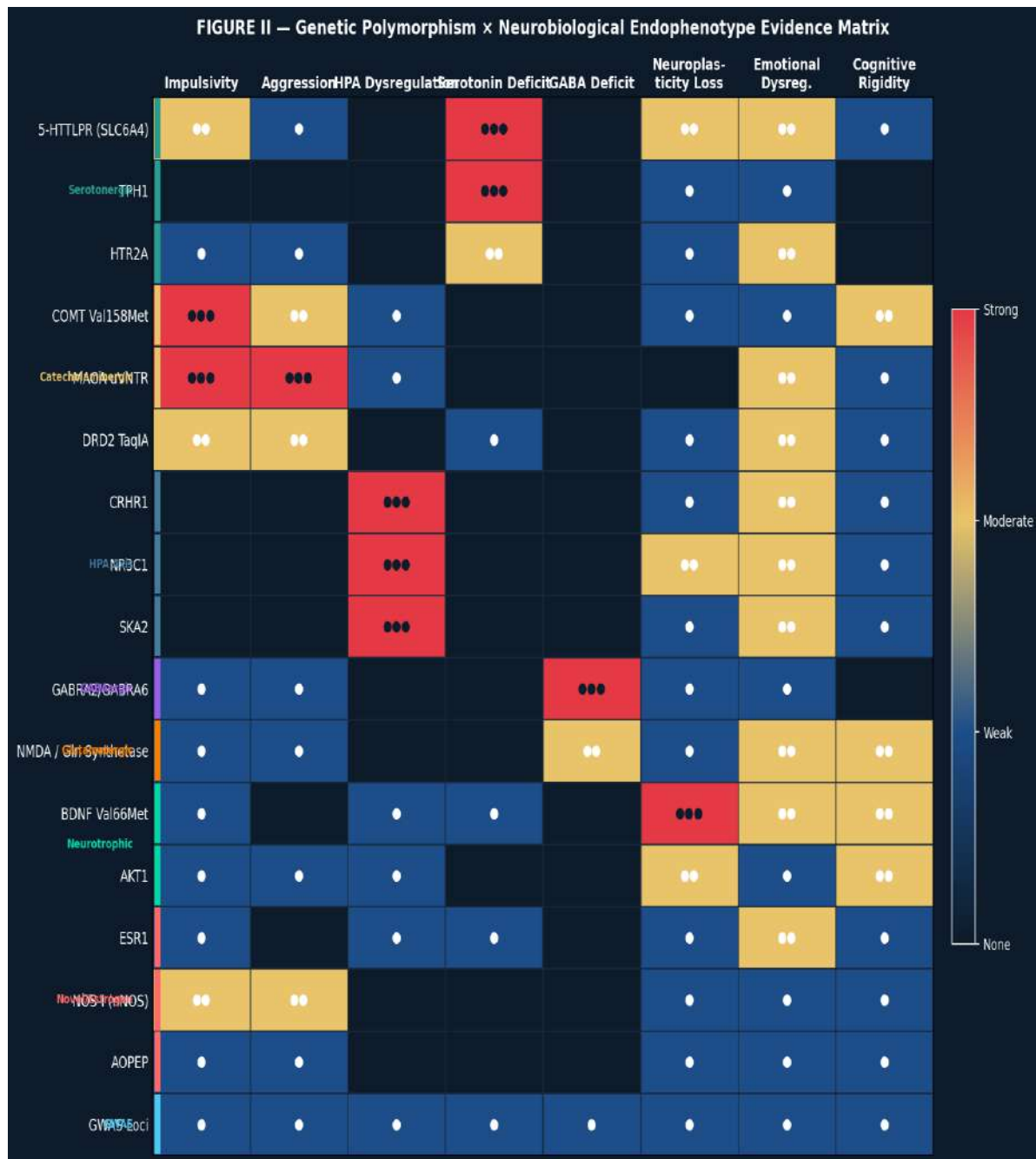
FIGURE II: Genetic Polymorphism x Neurobiological Endophenotype Evidence Matrix

Figure II. Evidence matrix displaying the strength of association between 17 key genetic polymorphisms and eight neurobiological endophenotypes relevant to suicidal behavior. Filled circles indicate evidence strength: weak (1 circle), moderate (2 circles), strong (3 circles) (Sokolowski et al., 2016; Kimbrel et al., 2019).

5. DISCUSSION

The synthesis of genetic, epigenetic, postmortem transcriptomic, and GWAS evidence reviewed here supports a model in which suicidal behavior emerges from the convergence of multiple partially independent neurobiological vulnerabilities, each genetically and epigenetically constituted, that jointly lower the threshold for the transition from suicidal ideation to action. No single gene, pathway, or polymorphism is necessary or sufficient for suicide; rather, the biology of suicidal behavior is irreducibly polygenic and polyepigenetic, with individual genetic variants conferring modest main-effect risk that becomes clinically consequential only within specific gene-environment interaction contexts (Brent & Mann, 2005; Sokolowski et al., 2016).

The gene-environment interaction model receives its most compelling empirical support from the consistent finding that childhood trauma and maltreatment substantially amplify genetic risk across multiple biological systems. The interaction between MAOA low-activity genotypes and early abuse, between SLC6A4 S-allele status and childhood trauma exposure, between COMT Val158Met and childhood maltreatment, and between NR3C1 promoter methylation (itself induced by abuse) and HPA axis dysregulation collectively suggest that early-life adversity constitutes a 'second hit' in a diathesis-stress model. The molecular mechanism of this second hit is increasingly understood to be epigenetic: early maltreatment reprograms the DNA methylation state of stress-relevant genes (NR3C1, SKA2, BDNF, SLC6A4, MAOA), creating a biological memory of adversity that persists into adulthood and amplifies the neurobiological response to subsequent stress. This epigenetic sensitization is clinically significant because it suggests that the risk conferred by genetic variation is neither fixed nor deterministic: it is modifiable in principle by interventions that alter the epigenetic state (McGowan et al., 2009; Turecki, 2014).

The endophenotype framework provides conceptual organization for interpreting the molecular heterogeneity of suicide genetics. Rather than asking which genes cause suicide (a question unanswerable given phenotypic complexity), the endophenotype approach asks which heritable, biologically measurable intermediate traits lie on the causal pathway between gene and completed suicide. Impulsivity loads robustly onto MAOA low-activity alleles, DRD2 polymorphisms, NOS1/NOS3 variants, and COMT Val158Met. HPA axis hyperreactivity loads onto CRHR1, NR3C1, and SKA2 epigenetic variation. Serotonergic hypofunction connects to SLC6A4, TPH1, and HTR2A variants. These endophenotypic clusters are not mutually exclusive: impulsivity and HPA hyperreactivity co-occur in suicide attempters at rates substantially above chance, and their biological convergence at the prefrontal cortex and amygdala produces the clinical syndrome of suicidal crisis through a common final neurobiological pathway (Brent & Mann, 2005; Wasserman et al., 2009).

The role of the prefrontal cortex in suicide biology is not merely associative. Postmortem studies have consistently documented reduced dendritic spine density, impaired GABAergic interneuron function, reduced BDNF expression, and upregulated 5-HT_{2A} receptor binding in the orbital frontal and ventral prefrontal cortex of suicide completers. These structural and molecular changes collectively impair the cortex's capacity to inhibit limbic amygdala-driven emotional responses, to sustain cognitive reappraisal of aversive emotional states, and to recruit the future-oriented decision-making processes that serve as a biological buffer against suicidal action.

The convergence of serotonergic hypofunction reducing aminergic input to prefrontal circuits, GABAergic subunit downregulation reducing inhibitory tone in frontopolar cortex, BDNF-mediated dendritic atrophy reducing synaptic connectivity, and HPA axis-driven glucocorticoid excess suppressing neurogenesis and dendritic complexity constitutes a converging multi-system attack on prefrontal cortical integrity. The amygdala, reciprocally connected with the prefrontal cortex and dysregulated through the same serotonergic and cortisol-mediated mechanisms, becomes hyper-responsive to negative emotional stimuli, generating the intense dysphoric affect and perceived life-threatening urgency that characterizes acute suicidal crises (Pandey et al., 2002; Dwivedi et al., 2003).

The genetic architecture reviewed here carries direct pharmacogenomic implications that extend beyond the identification of vulnerability loci to the optimization of pharmacological interventions in high-risk patients. The COMT Val158Met polymorphism is relevant not only to suicide risk but to the differential pharmacological response to dopaminergic agents and antidepressants in patients with mood disorders: Met/Met homozygotes may respond differently to dopaminergic-circuit-targeting agents than Val/Val carriers. Similarly, the MAOA uVNTR genotype, which determines baseline monoamine oxidase A activity and the metabolic clearance of serotonin and norepinephrine in limbic regions, constitutes a pharmacogenomically informative marker for predicting treatment response to monoamine oxidase inhibitors and selective serotonin reuptake inhibitors. The AKT1 polymorphisms reviewed here (rs1130214, rs2494746, rs2494731) may predict lithium response through their modulation of AKT1-GSK3 β signaling, consistent with lithium's documented anti-suicidal efficacy and its mechanistic convergence on the same pathway through which BDNF-TrkB receptor activation promotes neuronal survival. A precision psychiatry framework that genotypes patients at COMT, MAOA, SLC6A4, and AKT1 loci could substantially improve the biological targeting of pharmacological interventions and reduce the trial-and-error approach that currently characterizes psychopharmacological management of suicidal patients (Zouk et al., 2006; Reif et al., 2009).

The transition from single-variant genetic risk assessment to polygenic risk scores (PRS) represents a methodological advance of considerable clinical significance for suicide risk stratification. Current GWAS-identified loci, individually conferring odds ratios in the range of 1.05 to 1.25, are of limited individual clinical utility; however, their aggregation into genome-wide PRS substantially increases the proportion of population variance in suicidal behavior that is biologically explained.

Implementation of PRS for suicidal behavior in psychiatric settings would enable the identification of patients whose genome-wide accumulation of risk alleles places them in the upper decile of polygenic vulnerability: a biologically distinct population whose clinical management should incorporate more intensive monitoring, earlier pharmacological intervention, and targeted psychotherapeutic strategies. The convergence of PRS with epigenetic biomarkers, particularly SKA2 methylation status and NR3C1 promoter methylation, in a multimodal biological risk score would capture both the inherited genetic predisposition and the acquired epigenetic modification of that predisposition by environmental adversity, producing a more comprehensive biological risk profile than either approach alone (Sokolowski et al., 2016; Kaminsky et al., 2015).

The inclusion of ESR1 variants among suicide-associated loci highlights the biological significance of sex hormone signaling in modulating suicide risk and partially accounts for pronounced sex differences in suicidal behavior documented epidemiologically. Women show higher rates of suicidal ideation and attempt while men show higher rates of completed suicide, a difference that cannot be fully explained by method lethality or help-seeking behavior alone. The ESR1 gene encodes estrogen receptor alpha, through which estradiol exerts neuroprotective and serotonin-modulating effects in prefrontal, limbic, and hypothalamic circuits. ESR1 polymorphisms that alter receptor sensitivity may therefore modulate the degree to which fluctuating estrogen levels across the menstrual cycle, perimenopause, postpartum period, and hormonal contraceptive use affect serotonergic tone, HPA axis reactivity, and prefrontal-limbic circuit stability. This hormonal-genetic interaction has clinical implications for the timing of elevated suicide risk in women across reproductive transitions and for the consideration of hormonal factors in the biological risk assessment of female patients (Reif et al., 2009; Wasserman et al., 2009).

The vast majority of genetic association studies reviewed here were conducted in European, North American, or East Asian populations, leaving Turkish and Middle Eastern populations substantially underrepresented in the genetic epidemiology of suicide. Population-specific allele frequencies, linkage disequilibrium patterns, and gene-environment interactions may differ substantially between populations with different demographic histories. The GWAS loci identified in military cohorts (Kimbrel et al., 2019) were derived almost exclusively from populations of European ancestry, and replication studies in Turkish cohorts are essential for determining whether these associations generalize to the Turkish genetic background or reflect population-specific haplotype structures. The establishment of a Turkish population-based suicide genetics cohort, incorporating prospective suicide attempt surveillance with biological sample collection, would represent a scientifically and clinically valuable contribution that directly addresses a major gap in the current literature.

Skepticism about the role of genetics in suicide remains prevalent among medical and psychology trainees, as documented by Voracek and Sonneck, who found that students consistently underestimated the heritability of suicidal behavior relative to the best available evidence. This

educational deficit has clinical consequences: clinicians who do not routinely assess family history of suicidal behavior as a genetic risk factor are likely underweighting a biologically grounded risk signal independent of current psychiatric symptom severity. The reduced global transcriptional state captured by H3K14ac hypoacetylation across suicide brains suggests a biology of neurobiological shutdown at the molecular level, mechanistically relevant to the hopelessness and psychomotor retardation of the severely depressed suicidal state. The genetic and epigenetic evidence reviewed here mandates a reconceptualization of suicide risk assessment as a biologically informed, multi-system evaluation incorporating family genetic history, documented early adversity as a proxy for epigenetic programming of HPA and serotonergic systems, and, in the near future, blood-based epigenetic biomarkers such as SKA2 methylation status (Voracek & Sonneck, 2006; Kaminsky et al., 2015; Turecki, 2014).

6. LIMITATION

This systematic review has been shaped within the framework of various methodological limitations arising from the fact that it was designed as a narrative synthesis of the existing literature rather than as a primary experimental study. The evidence base has been established solely through structured literature search protocols applied to peer-reviewed databases; all findings are therefore limited by the subject scope, temporal overlap and linguistic accessibility of the identified body of literature. The inclusion criteria were deliberately restricted to studies directly addressing the molecular genetics, epigenetics and neurobiological mechanisms of suicidal behaviour; research in related fields, such as psychiatric comorbidities, psychosocial risk factors and pharmacogenomic therapeutic applications, has been included only to the extent that it directly intersects with the genetic pathways under investigation, thereby preserving the disciplinary focus at the expense of a broader contextual synthesis. The research was conducted using a structured literature review method based on scientific data,

with the data restricted solely to the subject matter. Publication bias inherent in indexed academic databases may have systematically excluded studies with negative findings and those originating from research environments in low- and middle-income countries; this raises the possibility of a directional bias towards Eurocentric population samples in the reported genetic associations.

Differences in phenotypic operationalisation across the studies examined—spanning a spectrum of non-equivalent endpoints such as suicidal ideation, attempts and completed suicide—render direct comparisons of effect sizes between studies impossible and limit the

generalisability of polymorphism-specific risk estimates to clinically homogeneous subgroups. Finally, the rapid pace of methodological development in genome-wide association studies, polygenic risk score modelling and multi-omic integration frameworks raises the possibility that some of the locus-level findings synthesised in this review may be updated or superseded by larger and more powerful cohort studies published after the literature cut-off date. The sources are limited to studies relevant to the topic, and both domestic Turkish academic publications and international peer-reviewed literature have been systematically utilised; this has enabled the creation of a linguistically and geographically comprehensive evidence base within the defined scope of the topic.

7. CONCLUSION

This systematic review establishes that suicidal behavior is a neurobiologically complex, polygenically determined outcome reflecting the convergent failure of multiple interacting biological systems: serotonergic, catecholaminergic, dopaminergic, neuroendocrine-HPA, GABAergic, glutamatergic, neurotrophic, and nitric oxide signaling pathways. The molecular findings, organized across seventeen gene systems and supported by meta-analyses, GWAS, and postmortem brain studies, consistently converge on a model in which the prefrontal cortex and amygdala serve as the neurobiological integration sites where genetically and epigenetically programmed deficits in inhibitory tone, monoaminergic modulation, neurotrophic support, and stress responsiveness jointly produce the endophenotypic cluster characterizing suicidal crises: impulsivity, emotional dysregulation, hopelessness, and impaired future orientation (Brent & Mann, 2005; Sokolowski et al., 2016; Kimbrel et al., 2019).

Several translational implications emerge directly from this synthesis. The AKT1-GSK3beta signaling pathway, shared between BDNF-TrkB receptor activation and lithium's anti-suicide pharmacology, provides a molecularly grounded rationale for lithium's documented reduction of suicide mortality in mood disorder patients that extends beyond mood stabilization. Ketamine's rapid anti-suicidal effect connects directly to the glutamate pathophysiology documented in postmortem and genetic studies and may operate partly through acute normalization of BDNF release and AKT1 signaling. The SKA2 methylation biomarker represents the most clinically actionable epigenetic finding reviewed here: a blood-based test that could stratify HPA-axis epigenetic dysregulation and identify individuals at elevated biological risk before a clinical crisis event. The NR3C1 promoter methylation findings mandate clinical attention to childhood trauma history as an epigenetic risk modifier that substantially amplifies the neurobiological vulnerability conferred by serotonergic and HPA-axis genetic variants (McGowan et al., 2009; Kaminsky et al., 2015).

Based on the molecular and genetic evidence synthesized in this review, the following specific research and clinical recommendations are advanced. First, large-scale epigenome-wide association studies (EWAS) should be conducted in prospective longitudinal cohorts that integrate comprehensive early-life adversity measures, enabling the delineation of epigenetic risk trajectories across development rather than the cross-sectional methylation snapshots currently available. Second, the SKA2 cg13989295 methylation marker should be validated in independent prospective cohorts with clinically adjudicated suicide attempt outcomes, including high-risk populations such as military personnel, emergency department self-harm presentations, and patients with treatment-resistant depression, to establish its clinical sensitivity, specificity, and positive predictive value. Third, polygenic risk scores for suicidal behavior should be incorporated into prospective validation studies alongside clinical risk factors and epigenetic biomarkers (Kimbrel et al., 2019), testing whether multimodal biological risk models outperform clinical assessment alone in predicting suicide risk.

Fourth, pharmacogenomic protocols incorporating COMT Val158Met and MAOA uVNTR genotyping should be developed and clinically tested in populations with active suicidal ideation to determine whether genotype-guided pharmacotherapy selection reduces time to clinical response and lowers suicidal risk during the pharmacologically vulnerable early treatment period. Fifth, Turkish population-based suicide genetics cohorts should be established to replicate and extend GWAS findings, with specific attention to whether identified loci such as YWHAE, HERC1, and LDHB generalize to the Turkish genetic background. Sixth, mental health training curricula should systematically incorporate the genetic and epigenetic evidence for suicide risk, addressing the documented tendency among trainees to underestimate the heritability of suicidal behavior and to underweight family genetic history in clinical risk assessment (Voracek & Sonneck, 2006).

Seventh, psychotherapeutic and pharmacological interventions capable of reversing the epigenetic dysregulation documented in suicide-relevant genes should be developed and tested in randomized controlled trials in high-risk populations, including investigation of histone deacetylase inhibitors as adjunctive treatments and trauma-informed cognitive therapies that target NR3C1 hypermethylation reversal.

8.DECLARATIONS

Peer Review: Evaluated by internal and external peer reviewers.

Conflict of Interest: The author declares no conflict of interest with respect to the research, authorship, or publication of this article.

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9. ETHICAL DECLARATION

This systematic review synthesizes previously published studies and does not involve primary data collection. Formal ethical committee approval is not required. All primary studies included are assumed to have been conducted in accordance with the Declaration of Helsinki and applicable national research ethics standards.

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BRUCELLOSIS-ASSOCIATED SPONDYLITIS AND SACROILIITIS

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ABSTRACT

Brucellosis is a zoonotic infectious disease caused by Brucella species, endemic particularly in the Mediterranean basin, the Middle East, Central Asia, and the Caucasus. Musculoskeletal involvement, most commonly presenting as peripheral arthritis, spondylitis, sacroiliitis, and osteomyelitis, is the most frequent complication of the disease and may cause severe pain and functional impairment.

Although prolonged combination antibiotic therapy remains the cornerstone of treatment, physical therapy and rehabilitation approaches have become an integral part of the management protocol for pain control, preservation of joint range of motion, and restoration of functional capacity. This review summarizes the pathophysiology and clinical features of brucellar spondylitis and sacroiliitis, and discusses the role of physical therapy modalities, including electrotherapy, exercise therapy, manual therapy, and hydrotherapy, in reducing pain based on the current literature.

Keywords: Brucellosis, spondylitis, sacroiliitis, pain, physical therapy, rehabilitation

1. INTRODUCTION

Brucellosis is one of the most common zoonotic infectious diseases worldwide, affecting both humans and domestic animals, and is caused by Gram-negative coccobacilli of the genus *Brucella*. According to World Health Organisation data, approximately 500,000 new cases of human brucellosis are reported worldwide each year, although the actual incidence is thought to be much higher than that reported (Kandemir, 2015). The disease is endemic particularly in countries of the Mediterranean basin, the Persian Gulf, the Indian subcontinent, Central Asia, the Caucasus and certain regions of Central and South America. Turkey is one of the leading countries where brucellosis is endemic, with high incidence rates in the Eastern, South-Eastern and Central Anatolia regions, where livestock farming is widespread; the annual incidence is reported to range from 12 to 50 per 100,000 people (Kandemir, 2015). The Caucasus region is also recognised as an endemic area for brucellosis, particularly in countries such as Azerbaijan, Armenia and Georgia, where sheep and cattle farming plays a significant role in the rural economy. In these regions, traditional livestock farming practices, the widespread consumption of unpasteurised dairy products (particularly fresh cheese) and the limited feasibility of veterinary vaccination programmes are considered to be among the main factors contributing to the persistence of human brucellosis cases. For this reason, the continuation of surveillance programmes targeting both animal and human brucellosis in regional health policies is of great importance

Transmission to humans occurs primarily through the consumption of unpasteurised milk and dairy products from infected animals (cattle, sheep, goats, pigs), direct contact with infected animal tissues, or, rarely, via the respiratory tract. Among occupational groups, farmers, shepherds, veterinary surgeons, slaughterhouse workers and laboratory staff are at increased risk due to occupational exposure. The *Brucella* pathogen is a facultative intracellular pathogen capable of affecting numerous organs and systems, particularly the reticuloendothelial system; consequently, the disease may present in acute, subacute, chronic and recurrent forms, and the clinical picture can be highly variable (Uluğ and Can-Uluğ, 2017).

1.1. Microbiology and Fundamentals of the Pathogenesis of Brucellosis

Six classical species have currently been identified within the genus *Brucella*; of these, *Brucella melitensis* is reported as the most common cause of human infections and is considered the species with the most severe clinical course. *Brucella abortus*, *Brucella suis* and *Brucella canis* are among the other human pathogenic species. The pathogen possesses the ability to survive and multiply within host cells – particularly within macrophages; this characteristic paves the way for the disease to become chronic and to recur, as the immune system is unable to completely eradicate the pathogen. Intracellular colonisation also explains why antibiotics such as rifampicin and doxycycline, which are able to penetrate the cell membrane effectively, are the preferred choice for treatment.

In terms of pathogenesis, the spread of the bacterium via the bloodstream to the bone marrow, liver, spleen and lymph nodes triggers a granulomatous inflammatory response. Colonisation of bone and joint tissue leads to local inflammation, cytokine release and tissue damage in the synovial membrane and subchondral bone. This process results in both an acute, painful inflammatory condition and, if left untreated, chronic structural damage and loss of function.

1.2. Musculoskeletal System Involvement in Brucellosis

Musculoskeletal involvement is the most common organ involvement reported in the course of brucellosis and may be observed in approximately 20–80 per cent of cases (Uluğ and Can-Uluğ, 2017). This involvement primarily manifests as peripheral arthritis, spondylitis, sacroiliitis, osteomyelitis, tenosynovitis and bursitis. It has been reported that, amongst bone and joint involvement, peripheral arthritis is more common in children, whilst sacroiliitis and spondylitis are more frequently observed in adult patients. The most commonly affected major joints are the knee, hip and shoulder joints;

in spinal involvement, the lumbar region is particularly prominent (Alp and Doğanay, 2008). Brucellosis-related spondylitis and sacroiliitis can cause long-term inflammatory pain in the lower back, hips and gluteal region in patients, characterised by night-time pain and morning stiffness, which severely restricts their activities of daily living. If diagnosis is delayed, chronic pain, muscle atrophy, restricted joint mobility, postural abnormalities and, rarely, neurological complications (epidural abscess, spinal cord compression, radiculopathy) may develop, which significantly impair the patient's functional capacity and quality of life (Nas, 2001; Sonel Tur, 2004). Whilst definitive treatment of brucellosis is possible with effective

and sufficiently prolonged combined antimicrobial therapy, it is known that pain and functional loss associated with spondylitis and sacroiliitis may not resolve sufficiently rapidly or completely with antibiotic therapy alone. For this reason, the inclusion of physiotherapy and rehabilitation methods in the treatment protocol—from the acute inflammatory phase

through to the chronic phase—makes a significant contribution to pain control, the preservation of joint range of motion, the maintenance of muscle strength, and ensuring patients' early return to activities of daily living (Nas, 2001).

1.3. Regional Epidemiology: The Context of Turkey and the Caucasus

According to data from the Turkish Ministry of Health, over 10,000 new cases of brucellosis are reported annually across the country, with a morbidity rate of approximately 16–17 per 100,000 people. The vast majority of cases are concentrated in the Eastern Anatolia, South-Eastern Anatolia and Central Anatolia regions, where livestock farming accounts for a significant proportion of the rural economy. Retrospective case series have reported that

a significant proportion of patients are individuals living in rural areas who are engaged in farming or livestock rearing (Uluğ and Can-Uluğ, 2017). In terms of seasonal distribution, an increase in presentations is observed during the spring and summer months, which coincide with the periods of animal birth and milking.

Azerbaijan and the South Caucasus region in general are also areas at risk of brucellosis due to similar socio-economic and agricultural dynamics. The prevalence of small ruminant husbandry in the region, traditional dairy production and consumption habits, and regional variations in the coverage of veterinary vaccination programmes in rural areas are among the factors contributing to the persistence of human brucellosis. For this reason, primary care practitioners and physiotherapists in the region

should consider the possibility of brucellosis in patients presenting with unexplained chronic lower back, hip or joint pain, as this may help to speed up the diagnostic process.

2. AIM

The aim of this article is to review the pathophysiological basis of pain observed in brucellosis-associated spondylitis and sacroiliitis, and to summarise the physiotherapy approaches used to alleviate this pain in the light of the current literature. Within the scope of this study, the pathogenesis and clinical characteristics of the disease, diagnostic and

classification systems, principles of differential diagnosis, the neurophysiological basis of pain, the fundamental principles of pharmacological treatment, the steps involved in the application of physiotherapy and rehabilitation methods, evidence derived from recent clinical trials, and patient education are systematically addressed. This review is intended to serve as a practical reference source, particularly for physiotherapy and rehabilitation specialists, infectious diseases specialists, and undergraduate and postgraduate students training in this field, especially those working in regions where brucellosis is endemic.

3. METHODOLOGY

This study is a narrative literature review conducted to evaluate physiotherapy and rehabilitation approaches used to reduce pain in brucellosis-associated spondylitis and sacroiliitis. Within the scope of the study, the existing literature on the pathophysiology, clinical features, pain mechanisms, diagnosis and differential diagnosis processes of brucellosis-associated spondylitis and sacroiliitis, as well as physical therapy and rehabilitation practices, was reviewed.

Information obtained from case reports, retrospective studies, clinical trials and review studies in the literature was evaluated comparatively; the potential effects of electrotherapy, exercise therapy, manual therapy, hydrotherapy and orthotic applications on pain and functional status were discussed. In light of the findings, a literature-based assessment was conducted regarding the use of physiotherapy approaches during the acute, subacute and chronic phases of the condition.

4. FINDINGS-BULGULAR

Brucellar Spondylitis: Pathophysiology And Clinical Features

Brucellar spondylitis is a spinal infection that develops as a result of the hematogenous dissemination of *Brucella* to the vertebral body, intervertebral disc, or paravertebral soft tissues. The infection most frequently affects the lumbar spine, followed by the thoracic and cervical regions (Cui et al., 2022).

In the pathogenesis of the disease, the rich vascular network in the subchondral region of the vertebral body is thought to provide a favorable environment for hematogenous

dissemination. As the infection progresses into the intervertebral disc space, reduction in disc height, destruction of the vertebral body, sclerotic changes, and, in some cases, the formation of paravertebral or epidural abscesses may occur. A multicenter study conducted in China reported that involvement of two adjacent vertebrae was observed in the vast majority of cases, whereas single-vertebra involvement was less frequent, with the lumbar region being the most common site of involvement.

The most common presenting symptom is low back pain that gradually increases over weeks or even months, does not completely resolve with rest, and may worsen at night. Systemic symptoms such as fever, night sweats, fatigue, loss of appetite, and weight loss may accompany the clinical picture. Physical examination may reveal tenderness over the affected spinal segment, paravertebral muscle spasm, and restricted range of motion. Since neurological complications may develop in advanced cases, careful assessment for lower-extremity weakness, sensory deficits, and sphincter dysfunction is required (Yüksel et al., 2006).

Diagnosis is established through the combined evaluation of clinical findings, serological tests (standard tube agglutination test and Rose Bengal test), blood or tissue cultures, and magnetic resonance imaging (MRI) findings. MRI is considered the gold-standard imaging modality for demonstrating vertebral body edema, disc involvement, and possible abscess formation. Differential diagnosis should primarily include tuberculous spondylitis (Pott disease) and pyogenic spondylodiscitis, as well as other infectious and inflammatory spinal disorders (Alp & Doğanay, 2008).

4.1. Imaging-Based Classification Systems

Imaging-based classification systems have become increasingly important in the treatment planning of brucellar spondylitis. The large series of 135 cases reported by Solera et al. (1999) is considered one of the pioneering studies describing the clinical course and radiological characteristics of brucellar spondylitis.

In a more recent multicenter Chinese study (2024), MRI findings in 615 patients were classified into three main types: Type I, reflecting the early inflammatory phase; Type II, characterized by active destruction and abscess formation; and Type III, representing the recovery phase in which bone remodeling predominates. This classification provides

clinicians with guidance in predicting which cases may be adequately managed with medical treatment alone and which cases may require surgical intervention.

The Spondylodiscitis Severity Code (SSC), developed to grade the overall severity of spondylodiscitis, can also be used in brucellar cases. This system categorizes the disease into three severity grades and guides treatment decisions, including conservative follow-up, orthotic treatment, and surgical stabilization.

In a comparative study by Turunç et al., brucellar spondylitis was reported to follow a less destructive course compared with tuberculosis and pyogenic spondylodiscitis. In contrast, tuberculous spondylitis may be associated with more severe complications, including gibbus deformity, kyphosis, and neurological deficits. This distinction provides clinically relevant guidance in determining which patient groups can safely undergo early and more intensive rehabilitation.

4.2. Relationship Between Brucellosis And Sacroiliitis

Sacroiliitis is inflammation of the sacroiliac joint located between the sacrum and the ilium and is one of the most common forms of osteoarticular involvement associated with brucellosis. In some case series, it has been reported as the most common musculoskeletal manifestation, particularly among young adults.

The sacroiliac joint is a true synovial joint and contains numerous pain-sensitive structures; joint stability is maintained by strong ligamentous structures. Because the joint plays an important role in transferring body weight from the upper body to the lower extremities, it is continuously subjected to mechanical loading during daily activities (Physical Therapy and Rehabilitation sources; Wikipedia, 2025).

Pain associated with brucellar sacroiliitis is typically axial, meaning that the area in which the pain is perceived corresponds to the site of pathology. Pain may radiate from the lower back to the hip and gluteal region and, rarely, may extend to the posterior aspect of the thigh. Although unilateral involvement is more common, bilateral involvement has also been reported.

During physical examination, the FABER (flexion-abduction-external rotation) test, Gaenslen test, and direct sacroiliac joint compression tests are among the principal clinical maneuvers

used to provoke pain. Although positivity of these tests supports the diagnosis, imaging (MRI and computed tomography) and serological confirmation are required for definitive diagnosis (Physical Therapy and Rehabilitation sources).

If sacroiliitis remains untreated for a prolonged period, hip joint stiffness, a forward-flexed posture, impaired gait patterns, and pelvic asymmetry may develop. Therefore, early diagnosis and early rehabilitation intervention are of great importance for both pain control and the prevention of secondary postural and biomechanical abnormalities.

4.2.1. Clinical Examination Characteristics in the Assessment of the Sacroiliac Joint

Clinical assessment of the sacroiliac joint requires the combined use of multiple provocation tests because the sensitivity of any single test is limited. The FABER (Patrick) test, Gaenslen test, compression and distraction tests, thigh thrust test, and sacral thrust test are among the commonly used maneuvers. The presence of three or more positive tests significantly increases the likelihood of sacroiliac joint-related pain.

However, the presence of systemic symptoms accompanying brucellar sacroiliitis, such as fever, night sweats, and weight loss, provides important clues for distinguishing it from mechanical or degenerative sacroiliac joint pain. Laboratory evaluation showing elevated erythrocyte sedimentation rate and C-reactive protein levels reflects inflammatory activity and provides practical markers for monitoring treatment response.

4.3. Differential Diagnosis

Distinguishing brucellar spondylitis and sacroiliitis from other causes of low back and hip pain is critical both for appropriate treatment planning and for preventing unnecessary or inappropriate therapeutic interventions. The principal conditions that should be considered in the differential diagnosis include:

- **Tuberculous spondylitis (Pott disease):** It generally follows a more destructive course. Vertebral collapse, gibbus deformity, and paravertebral cold abscess formation are more common than in brucellosis.
- **Pyogenic spondylodiscitis:** It usually has a more acute onset and is associated with high fever and marked systemic toxicity. Pyogenic organisms such as *Staphylococcus aureus* are commonly isolated from blood cultures.

- **Ankylosing spondylitis and other seronegative spondyloarthropathies:** These may present with bilateral sacroiliitis in young adults. However, the chronic and recurrent course of inflammatory back pain, HLA-B27 positivity, and negative Brucella serology may help distinguish these conditions.
- **Degenerative spinal disorders and mechanical low back pain:** These conditions are distinguished from brucellosis by the absence of systemic symptoms and normal inflammatory markers.
- **Malignancy, particularly metastatic vertebral involvement:** This should always be considered in patients of advanced age, particularly in the presence of persistent night pain that does not improve with rest and a history of weight loss.

In recent years, artificial intelligence-assisted deep learning models have also begun to be developed to differentiate brucellar spondylitis from tuberculous spondylitis based on MRI findings. These models have the potential to provide clinicians with an additional decision-support tool, particularly in suspicious cases in which imaging findings overlap. Nevertheless, the cornerstone of differential diagnosis remains a careful clinical history, assessment of epidemiological exposure, serological and microbiological confirmation, and comprehensive evaluation of imaging findings.

4.3.1. Neurophysiological Basis Of Pain In Brucellar Spondylitis And Sacroiliitis

Pain observed in brucellar spondylitis and sacroiliitis arises through a multifactorial mechanism. First, tissue damage caused by *Brucella* infection and the accompanying granulomatous inflammatory response result in the release of cytokines, including tumor necrosis factor-alpha, interleukin-1, and interleukin-6. These cytokines sensitize peripheral nociceptors and produce inflammatory pain.

Second, structural damage occurring in the vertebral body and intervertebral disc may lead to mechanical instability and consequent nociceptive pain. Third, in advanced cases, a neuropathic pain component may develop as a result of nerve-root or spinal-cord compression (Yüksel et al., 2006).

4.3.2. Peripheral and Central Sensitization

Prolonged inflammatory stimulation may cause sensitization not only of peripheral nociceptors but also of neurons in the dorsal horn of the spinal cord, a phenomenon known as

central sensitization. This may cause pain that is initially restricted to the affected region to spread over a wider area, normally non-painful stimuli to be perceived as painful (allodynia), and the overall pain threshold to decrease.

In cases of chronic brucellar spondylitis and sacroiliitis, failure to consider this mechanism may help explain why treatments targeting only peripheral inflammation remain insufficient in some patients.

4.3.3. Muscle Spasm, Avoidance Behavior, and the Vicious Cycle

During chronic pain processes, protective muscle spasm may develop in the paravertebral and pelvic muscles. This condition both increases pain and restricts joint range of motion. Prolonged immobilization and pain-avoidance behavior may lead to muscle atrophy, loss of proprioception, and functional impairment, thereby creating a vicious cycle.

In this cycle, the patient avoids movement because of fear of pain, which increases muscle weakness and joint stiffness; increasing stiffness and weakness further intensify pain. At this point, the objective of physical therapy is both to reduce peripheral inflammation and nociception and to break this vicious cycle by restoring the patient's functional capacity.

4.5. Complications And Long-Term Outcomes

When brucellar spondylitis and sacroiliitis are not treated early and effectively, they may lead to various local and systemic complications. Local complications include paravertebral, epidural, or psoas abscess formation, permanent loss of vertebral body height, segmental instability, and, rarely, permanent neurological deficits resulting from spinal-cord or nerve-root compression.

Epidural abscess and associated cord compression are considered among the most serious complications of brucellar spondylitis and may require emergency surgical decompression (Sonel Tur et al., 2004; Yüksel et al., 2006).

In the long term, chronic low back pain, persistent restriction of joint movement, muscle atrophy, and consequent functional loss may develop in untreated or late-diagnosed cases. In some patients, chronic mechanical pain and musculoskeletal dysfunction may persist for a

prolonged period despite clinical and microbiological resolution of the infection. This may result in loss of work capacity and a persistent reduction in quality of life.

Therefore, in addition to early diagnosis, the initiation of a systematic and continuous rehabilitation process after infection control plays a decisive role in preventing complications.

Relapse is another important problem associated with brucellosis and generally develops because of inadequate treatment duration or monotherapy. Recurrent musculoskeletal symptoms are frequently observed in patients with relapse, which may prolong treatment and require modification of the rehabilitation program. Therefore, regular clinical and serological follow-up during and after treatment is important for the early detection of possible relapse.

4.6. Treatment Approach: Pharmacological Basis

The fundamental principle in the treatment of brucellosis is the combined use of antibiotics with intracellular activity for a sufficiently long duration. The standard regimen recommended by the World Health Organization consists of doxycycline (200 mg/day) combined with rifampicin (600 mg/day) for at least 6 weeks, while complicated osteoarticular involvement generally requires treatment for 8–12 weeks or longer (Nas et al., 2001; Alp & Doğanay, 2008).

Some guidelines recommend adding an aminoglycoside, such as gentamicin or streptomycin, as a third agent during the first 2–4 weeks, particularly in severe cases or in patients with neurological complications. This triple-drug combination has been reported to reduce relapse rates.

Surgical treatment may be considered in cases of spinal instability, progressive neurological deficits, or large epidural abscesses. However, clinical and radiological improvement can be achieved with medical treatment alone in a large proportion of cases (Alp & Doğanay, 2008).

Surgical indications may include severe pain unresponsive to conservative treatment, progressive kyphotic deformity, large abscess formation, and neurological deficits. Even in patients undergoing surgery, antimicrobial treatment is generally continued for at least 6–12 weeks during the postoperative period.

Although antimicrobial treatment aims to eradicate the infection, clinical observations indicate that pain and functional limitations may not resolve rapidly in parallel with antibiotic therapy. Therefore, in addition to analgesics and non-steroidal anti-inflammatory drugs during the acute phase, a physical therapy and rehabilitation program should be introduced at an appropriate stage of the disease (Nas et al., 2001).

Treatment response should be monitored regularly through improvement in clinical symptoms as well as changes in erythrocyte sedimentation rate, C-reactive protein levels, and serological agglutination titers.

4.7. Physical Therapy And Rehabilitation Methods

The physical therapy program for brucellar spondylitis and sacroiliitis should be individualized according to the stage of the disease (acute, subacute, or chronic) and the clinical and radiological findings.

During acute inflammation and active infection, deep modalities requiring heat and aggressive exercise should be avoided. In contrast, superficial and low-intensity approaches aimed at pain control may be preferred. Once the infection has been controlled and acute inflammatory findings have regressed, exercise-based rehabilitation should be gradually intensified.

The following subsections address the principles of application, objectives, and precautions associated with each physical therapy modality separately.

4.8. Approach During the Acute Phase: Rest and Pain Control

During the acute phase, relative rest is recommended to prevent excessive loading; however, complete bed rest should be avoided in order to prevent muscle atrophy and joint stiffness. Cryotherapy may be used during this period to reduce acute inflammation and edema.

In cases of severe pain, low-intensity transcutaneous electrical nerve stimulation (TENS) is a non-invasive and safe method that may be preferred to reduce pain perception within the framework of the gate control theory. Appropriate positioning and the use of lumbar/pelvic supportive orthoses may also provide symptomatic relief by reducing mechanical loading of the painful region (Sacroiliac joint disorders sources, fizik-tedavi.org).

During this period, breathing exercises and low-intensity isometric exercises for the lower extremities should be taught to prevent general deconditioning and immobilization-related complications such as deep vein thrombosis.

All modalities used during the acute phase should be planned in coordination with the infectious diseases team, taking into account the patient's fever, systemic inflammatory markers, and overall clinical condition.

4.9. Electrotherapy Modalities During the Subacute and Chronic Phases

After infection control has been achieved, hot-pack applications may be used to reduce muscle spasm and increase tissue elasticity. Interferential current therapy is another commonly preferred electrotherapy modality because it may reach deeper tissues, increase the pain threshold, and support muscle relaxation.

Therapeutic ultrasound may increase local blood flow and support tissue healing by producing deep tissue heating. However, caution should be exercised when using deep-heating modalities in areas where active infection is suspected. These modalities are most effective when used not as standalone treatments but as adjuncts to an exercise-based rehabilitation program.

Other electrophysical agents, such as low-level laser therapy and short-wave diathermy, may contribute to reducing pain and muscle spasm in selected chronic cases. However, it should be noted that large-scale studies directly evaluating the efficacy of these modalities specifically for brucellar spondylitis and sacroiliitis are limited. Therefore, treatment decisions should be based on general clinical experience derived from similar inflammatory spinal disorders and individual patient characteristics.

4.10. Exercise Therapy

Exercise therapy is a fundamental component of rehabilitation for brucellar spondylitis and sacroiliitis. The program generally consists of the following stages:

- **Stretching exercises:** These aim to maintain joint range of motion by reducing shortening and spasm in the paravertebral, hip-flexor, and piriformis muscles.

- **Post-isometric relaxation and gentle mobilization techniques:** These are applied to reduce muscle tension around the sacroiliac joint.
- **Core stabilization exercises:** Strengthening the transversus abdominis, multifidus, and pelvic floor muscles improves spinal and pelvic stability and reduces repetitive microtrauma.
- **Low-impact aerobic exercises:** Low-intensity activities such as walking help maintain general conditioning while preventing excessive joint loading.
- **Progressive strengthening exercises:** During the chronic phase, these support functional independence by increasing muscle strength and endurance.
- **Balance and proprioception training:** These interventions aim to correct balance impairments associated with prolonged pain and inactivity and reduce the risk of falls.

The intensity and progression rate of the exercise program should be gradually increased according to the patient's pain level, inflammatory markers (erythrocyte sedimentation rate and C-reactive protein), and overall clinical condition.

In similar spinal rehabilitation programs, the addition of balance training to core stabilization exercises has been reported to provide additional benefits in pain and functional scores; these findings may also be considered informative for the rehabilitation of brucellar spondylitis.

When designing an exercise prescription, the balance between "overuse and underuse" should be considered. An excessively aggressive program may cause microtrauma and exacerbation of symptoms in bone and disc tissues that have not yet sufficiently healed, whereas an overly cautious approach may result in persistent muscle atrophy and joint stiffness.

Therefore, assessment of the pain response during each session and gradual adjustment of the program accordingly—the principle of pain-controlled progression—should be adopted as a fundamental practice principle.

4.11. Manual Therapy and Osteopathic Approaches

Soft-tissue mobilization, myofascial release, and gentle joint mobilization techniques directed toward sacroiliac joint dysfunction may help reduce pain and normalize joint mobility.

Such manual techniques should be applied carefully and progressively, particularly in patients in the chronic phase who have no evidence of active infection. Manipulative techniques are

not recommended in cases with active inflammation or structural instability, as aggressive manipulation may increase the risk of neurological complications.

In osteopathic approaches, patterns of hypomobility and hypermobility around the sacroiliac joint should be assessed separately and treatment should be individualized accordingly. In hypomobile joints, gentle mobilization techniques aim to improve mobility, whereas stabilization exercises are considered more appropriate for hypermobile or unstable joints.

4.12. Hydrotherapy

Aquatic exercise programs reduce loading on the joints by taking advantage of buoyancy, thereby allowing painful movements to be performed more comfortably. Stretching and low-resistance strengthening exercises performed in warm water may reduce muscle spasm and allow patients to begin movement earlier and with less pain compared with land-based exercise.

This method may be particularly suitable for patients who cannot tolerate land-based exercises because of severe pain. In addition, the hydrostatic pressure provided by the aquatic environment may contribute to reducing peripheral edema.

4.13. Use of Orthoses and Assistive Devices

The use of a lumbar or lumbosacral brace/orthosis may be considered as a supportive approach, particularly in patients with spinal instability or during the postoperative period.

The literature indicates that the use of a lumbosacral brace for a certain period after surgery may contribute to postoperative rehabilitation. Although orthotic use may increase comfort by limiting painful movement patterns, prolonged and unjustified use may lead to muscle weakness. Therefore, the duration of use should be determined by the treatment team (similar postoperative rehabilitation protocols cited from Zhang et al., 2024).

In patients with sacroiliac joint pain, the use of a sacroiliac belt (pelvic support belt) may also provide symptomatic relief in some cases. These supportive devices may increase stability by limiting excessive movement of the joint and may help reduce pain, particularly during standing or walking.

However, it should be emphasized that these devices should not replace the exercise program and should only be used as complementary tools.

4.14. Contraindications and Precautions in Physical Therapy

The most important consideration in the rehabilitation of brucellar spondylitis and sacroiliitis is to avoid aggressive manual techniques and deep-heating modalities in patients with active infection and signs of systemic toxicity.

In patients with spinal instability, progressive neurological deficits, or large abscess formation, surgical evaluation should be performed before initiating an exercise program.

In addition, intensive exercise programs should not be applied during febrile periods, and general safety principles should be followed, including ensuring that post-exercise pain and fatigue do not persist for more than 24 hours.

4.15. Evidence From The Literature: Evaluation Of Clinical Studies

In a study conducted by Nas et al. (2001) at Dicle University involving 11 patients with brucellar spondylitis or epidural abscess, all patients received a combination of rifampicin and doxycycline for at least 6 months, while eight patients underwent surgical treatment because of spinal instability or neurological findings.

An important point emphasized by the study was that brucellosis should always be considered in the differential diagnosis of patients presenting with low back pain in endemic regions. Early diagnosis facilitates timely initiation of both antimicrobial treatment and rehabilitation, thereby positively influencing prognosis.

In a case reported by Sonel Tur et al. (2004), spinal cord compression, a rare but important complication of brucellar spondylitis, was addressed, and the authors emphasized that early diagnosis was critical for timely planning of both medical and rehabilitative interventions.

Similarly, Yüksel et al. (2006) reported a case of brucellar spondylodiscitis with rapidly progressive epidural abscess presenting with sciatica and emphasized that brucellosis should not be overlooked in the differential diagnosis in endemic regions.

In the review by Alp and Doğanay (2008), the treatment strategy for spinal brucellosis was described as being primarily based on prolonged combination antibiotic therapy. However, surgical treatment may be required in cases of impaired spinal stability or neurological deficits. The authors emphasized that rehabilitation programs added to medical treatment accelerated patients' functional recovery.

More recent studies (Cui et al., 2022; PMC11003786, 2024) have demonstrated that combinations of surgical and pharmacological treatment in lumbar brucellar spondylitis result in significant improvements in Visual Analog Scale (VAS), Oswestry Disability Index (ODI), and Japanese Orthopaedic Association (JOA) scores.

In one retrospective study, the surgical treatment group achieved faster improvement in pain scores compared with purely medical treatment; however, no significant difference in clinical efficacy was found among the groups at the final follow-up. This finding suggests that medical treatment and rehabilitation alone may be sufficient in appropriately selected patients.

Similarly, in a case of lumbar brucellar spondylitis reported by Lim et al. (2012), rehabilitation approaches accompanying medical treatment were reported to contribute to pain reduction and functional recovery.

In a one-year retrospective follow-up study conducted by Zhang et al. (2024) in patients with cervical brucellosis, postoperative rehabilitation programs administered following combined surgical and antimicrobial treatment were reported to contribute to the improvement of neck pain and neurological symptoms.

The MRI-based classification system developed in a multicenter Chinese study was reported to provide clinicians with a practical framework for determining which patients could safely undergo early and intensive rehabilitation.

Taken together, these studies indicate that physical therapy and rehabilitation constitute an important complementary component of the treatment protocol for brucellar spondylitis and sacroiliitis, regardless of whether surgical intervention is performed.

4.16. An Example Case Scenario For Clinical Application

In light of findings compiled from case reports in the literature, presenting a typical patient with brucellar sacroiliitis accompanied by mild lumbar involvement may be useful for illustrating how theoretical knowledge can be translated into clinical practice.

The following is a fictional and educational scenario developed based on similar cases reported in the literature.

4.16.1. Presentation and Assessment

A 35-year-old patient engaged in livestock farming in a rural area presents with progressively increasing pain in the right hip and lower back for approximately six weeks, with worsening at night.

The patient's history includes fever, fatigue, and mild weight loss during the previous month. Physical examination reveals marked tenderness over the right sacroiliac joint, positive FABER and Gaenslen tests, while the neurological examination is within normal limits.

Laboratory evaluation reveals an elevated erythrocyte sedimentation rate, elevated C-reactive protein level, and a positive standard tube agglutination test (titer 1:320). MRI demonstrates signal changes consistent with inflammation in the right sacroiliac joint and mild signal increase at the L5–S1 disc space.

4.16.2. Treatment and Rehabilitation Process

The patient is initiated on a 12-week course of antimicrobial treatment with a combination of doxycycline and rifampicin.

During the first two weeks, pain control is targeted through relative rest, cold application to the painful region, and low-intensity TENS within the framework of an acute-phase approach. Lower-extremity isometric exercises and breathing exercises are used to maintain general conditioning.

As fever subsides and acute-phase reactants begin to decline, approximately from the third week onward, the patient enters the subacute phase, and gentle stretching exercises, low-intensity interferential current therapy, and a gradual mobilization program are initiated.

From the sixth week onward, once pain intensity shows a marked decrease on the VAS and inflammatory markers approach normal levels, core stabilization exercises and low-impact aerobic exercises, including a controlled walking program, are added to the treatment.

At the end of the twelfth week, antimicrobial treatment is completed. At this stage, the patient progresses to strengthening exercises and functional activity training in preparation for returning to work.

The total rehabilitation process lasts approximately 14–16 weeks, with the patient being assessed at regular intervals for pain, function, and serological follow-up.

This fictional scenario reflects the general framework of a process that may vary from patient to patient in actual clinical practice and represents a synthesis of treatment approaches reported in case reports in the literature (Nas et al., 2001; Sonel Tur et al., 2004).

It is essential that the rehabilitation program be individualized by the relevant treatment team according to each patient's clinical presentation, disease stage, and associated complications.

4.17. Planning And Monitoring Of The Rehabilitation Program

An effective rehabilitation program should begin with a comprehensive assessment. Pain intensity should be measured using the Visual Analog Scale (VAS) or Numeric Pain Rating Scale, while functional limitations should be documented using standardized instruments such as the Oswestry Disability Index (ODI).

Joint range of motion, muscle strength, posture, and gait pattern should be evaluated through physical examination. Inflammatory markers (erythrocyte sedimentation rate and C-reactive protein) and serological follow-up (Brucella agglutination titer) should be monitored at regular intervals (Nas et al., 2001; Zhang et al., 2024).

4.17.1. Three-Stage Rehabilitation Model

The rehabilitation program is generally planned using a three-stage approach:

1. **Acute phase:** Pain control and relative rest.
2. **Subacute phase:** Gradual mobilization, stretching exercises, and low-intensity electrotherapy.

3. **Chronic phase:** Core stabilization, strengthening, and functional exercise programs.

Progression criteria at each stage should be determined according to reductions in pain intensity, regression of inflammatory markers, and improvements in functional scores.

Transition from the acute to the subacute phase is generally assessed based on resolution of fever, a downward trend in acute-phase reactants, and reduction in resting pain.

During the transition from the subacute to chronic phase, the patient's ability to perform activities of daily living with no or minimal pain and the substantial normalization of joint range of motion are among the principal criteria.

These transition criteria should not be determined by rigid numerical thresholds but through individualized clinical assessment, requiring a flexible approach based on the experience of the treating physician.

4.17.2. Multidisciplinary Team Approach

The treatment team should ideally have a multidisciplinary structure including an infectious diseases specialist, a physical medicine and rehabilitation specialist, and, when necessary, orthopedic and neurosurgical specialists. Such a structure is important for optimizing both the diagnostic process and treatment plan.

This multidisciplinary approach aims both to eradicate the infection and to facilitate the patient's return to a pain-free and functional life.

When necessary, other healthcare professionals, including dietitians, psychologists, and occupational therapists, may also be included in the team. This can contribute to comprehensive care, particularly in patients dealing with chronic pain.

4.18. Patient Education And Lifestyle Recommendations

The success of the rehabilitation process depends not only on the modalities applied but also on the patient's active participation in treatment.

Patients should be informed about proper body mechanics, particularly during bending, lifting, and prolonged sitting, appropriate sleeping positions, and spine-protective techniques during activities of daily living.

The regular and consistent implementation of a home exercise program should also be emphasized, as it plays a critical role in maintaining progress achieved between clinical sessions.

From a nutritional perspective, patients should be informed that a balanced diet supports general immune function and may contribute to the recovery process.

Because smoking negatively affects bone healing and may make infection control more difficult, smoking cessation counseling should be provided to patients who smoke.

In addition, transmission routes of the disease, including consumption of unpasteurized dairy products and unprotected contact with infected animal tissues, should be explained to patients and family members. This is important both for reducing the risk of reinfection and for protecting public health.

Education regarding strategies for coping with chronic pain should also form part of the rehabilitation process. Pain neuroscience education may help patients understand the mechanisms underlying pain, reduce pain-avoidance behavior, and improve treatment adherence.

Establishing realistic expectations is important both for maintaining patient motivation and sustaining confidence in the treatment process.

4.19. Limitations And Recommendations For Future Research

A substantial proportion of the literature underlying this review consists of case reports and retrospective series with small sample sizes. The number of randomized controlled trials evaluating the efficacy of standardized physical therapy protocols specifically for brucellar spondylitis and sacroiliitis remains quite limited.

This means that current clinical recommendations are largely based on expert opinion, general experience in the rehabilitation of spinal infections, and evidence obtained from other sacroiliac joint disorders such as ankylosing spondylitis.

Future studies should evaluate the efficacy of different physical therapy modalities using randomized controlled designs—for example, comparing exercise therapy alone with a combination of exercise and electrotherapy—in order to strengthen the level of evidence.

In addition, the development of a standardized rehabilitation protocol specifically designed for brucellar spondylitis and sacroiliitis would improve the comparability of treatment approaches among different centers.

Long-term follow-up studies may provide clearer evidence regarding the effects of rehabilitation on relapse rates and the development of chronic pain.

Finally, multicenter, region-specific epidemiological and clinical studies conducted in Türkiye, Azerbaijan, and the surrounding Caucasian countries, where brucellosis is endemic, are expected to contribute both to accelerating the diagnostic process and to developing rehabilitation guidelines specific to the region.

5. CONCLUSION

Brucellosis is a systemic zoonotic infection that is prevalent in endemic regions and frequently affects the musculoskeletal system. Brucellar spondylitis and sacroiliitis are important complications that may cause severe and persistent pain, restricted joint mobility, and functional impairment. Although prolonged combination antimicrobial therapy constitutes the cornerstone of treatment, the incorporation of physical therapy and rehabilitation approaches into the treatment protocol is of great importance for effective pain control and accelerated functional recovery.

During the acute phase, relative rest, low-intensity electrotherapy aimed at pain control, and appropriate positioning are recommended. In the subacute and chronic phases, an individualized rehabilitation program incorporating progressive stretching, core stabilization, strengthening exercises, and, when necessary, hydrotherapy and manual therapy may reduce pain severity, improve functional capacity, and enhance quality of life in patients with brucellar spondylitis and sacroiliitis. Accurate differential diagnosis, appropriate imaging-based classification, and regular clinical and laboratory monitoring constitute the fundamental components of safe and effective rehabilitation planning.

Physical therapy programs planned through a multidisciplinary approach and progressively adapted according to the stage of the disease should be considered an integral complementary component of antimicrobial treatment in the management of musculoskeletal complications of brucellosis. Patient education and lifestyle modifications also play a supportive role in maintaining and consolidating the clinical benefits achieved. Future randomized controlled

trials in this field will provide stronger evidence for current clinical recommendations and establish a more robust scientific basis for physical therapy and rehabilitation practices in regions where brucellosis is endemic.

6. DISCUSSION

The existing literature indicates that antimicrobial therapy is the indispensable cornerstone of treatment for brucellar spondylitis and sacroiliitis; however, physical therapy and rehabilitation methods significantly complement this treatment in terms of pain control and functional recovery. In particular, low-intensity electrotherapy and positioning techniques applied during the acute phase, and exercise-based approaches during the subacute and chronic phases, have been reported to reduce pain severity and accelerate patients' return to activities of daily living.

Nevertheless, it is observed that a large proportion of the existing studies consist of case reports or small-sample retrospective series, while only a limited number of studies have evaluated the efficacy of a standardized physical therapy protocol specifically for brucellar spondylitis and sacroiliitis using randomized controlled designs. This suggests that current recommendations are largely adapted from experience gained in the rehabilitation of general spinal infections and other sacroiliac joint pathologies, such as ankylosing spondylitis.

Furthermore, in countries where brucellosis is endemic, particularly Türkiye and Azerbaijan, considering brucellosis in the differential diagnosis of patients presenting to primary healthcare services with low back or hip pain is of great importance for early diagnosis and timely initiation of rehabilitation. Delayed diagnosis may contribute not only to chronic infection but also to permanent functional impairment. The imaging-based classification systems and differential diagnostic criteria discussed in this review may provide clinicians with a practical framework for the process of early and accurate diagnosis.

When evaluating the role of physical therapy approaches in brucellar spondylitis and sacroiliitis, it should be recognized that treatment is not limited to providing symptomatic relief but may also contribute to the prevention of long-term complications, including chronic pain, muscle atrophy, and postural abnormalities. This multidimensional benefit indicates that physical rehabilitation plays not only a supportive but also a preventive role in the treatment of brucellosis and the management of its musculoskeletal complications.

7. LIMITATION

A substantial proportion of the literature underlying this review consists of case reports and small-sample retrospective series. The number of randomized controlled studies evaluating the efficacy of a standardized physical therapy protocol specifically designed for brucellar spondylitis and sacroiliitis remains quite limited. Consequently, current clinical recommendations are largely based on expert opinion, experience in the rehabilitation of general spinal infections, and evidence derived from other sacroiliac joint pathologies, such as ankylosing spondylitis.

Future studies should evaluate the efficacy of different physical therapy modalities using randomized controlled designs. For example, comparisons between exercise therapy alone and a combination of exercise therapy and electrotherapy would be particularly valuable for strengthening the level of evidence. In addition, the development of a standardized rehabilitation protocol specifically tailored to brucellar spondylitis and sacroiliitis would improve the comparability of treatment approaches across different centers. Long-term follow-up studies may provide a clearer understanding of the effects of rehabilitation on recurrence rates and the development of chronic pain.

Finally, multicenter, region-specific epidemiological and clinical studies conducted in Türkiye, Azerbaijan, and neighboring Caucasian countries, where brucellosis is endemic, may contribute both to accelerating the diagnostic process and to developing region-specific rehabilitation guidelines.

8. DECLARATION

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9. ETHICAL DECLARATION

The *Istanbul Medisosal Journal of Education and Research in Health Sciences* is a nationally based scientific journal in the field of health sciences that aims to uphold the fundamental principles of scientific research and publication ethics, including integrity, transparency, objectivity, and respect for the findings and intellectual creations of others. The journal is committed to promoting and implementing these principles throughout the research and publication process. The criteria set forth in the Declaration of Helsinki have also been taken into consideration.

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LEADERSHIP AND TEAMWORK IN HEALTHCARE ORGANISATIONS

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ABSTRACT

Healthcare institutions are complex organizations that require effective management approaches due to their direct impact on human life. In this context, leadership and teamwork are among the most important factors that enhance the quality of healthcare services. Leadership is defined as the process of guiding, motivating, and directing employees toward common organizational goals, and it has a significant influence on employee commitment, service quality, patient safety, and organizational performance. Various leadership styles, including autocratic, democratic, humanistic, bureaucratic, and charismatic leadership, are examined within the healthcare context. In particular, participative and employee-centered leadership approaches are emphasized for their positive effects on motivation and quality improvement. The multidisciplinary nature of healthcare services necessitates collaboration among professionals from different areas of expertise.

Teamwork enables the integration of knowledge, skills, and experience toward shared objectives, thereby improving the quality of patient care, reducing medical errors, and increasing patient satisfaction. Furthermore, teamwork strengthens communication among

healthcare professionals, enhances job satisfaction, and contributes to the efficient delivery of healthcare services. As a result, successful healthcare service delivery requires the integration of effective leadership and strong teamwork. Leaders who encourage participation, support employees, and foster team spirit play a critical role in improving service quality, organizational efficiency, patient safety, and employee satisfaction. Therefore, developing leadership competencies and promoting teamwork are essential for the sustainable success of healthcare institutions.

Keywords: Healthcare institutions, leadership, teamwork, healthcare management, patient safety, service quality.

1. INTRODUCTION

Leadership In Healthcare Institutions

Health Institutions Are Among The Most Complex Organizations In Terms Of Management Because They Provide Services That Directly Affect Individuals' Quality Of Life And Public Health. Scientific And Technological Advances In Healthcare, Continuously Increasing Service Expectations, The Growing Emphasis On Patient Safety, And Intensifying Competition Within The Healthcare Sector Have Made It Necessary For These Institutions To Continuously Improve Not Only Medically But Also From A Managerial Perspective.

Today, The Success Of Healthcare Institutions Depends Not Only On Their Physical Facilities And Technological Infrastructure But Also On The Effective Management Of Their Human Resources. In This Context, Leadership Emerges As One Of The Fundamental Elements Of Management, Supporting The Direction Of Employees Toward Common Goals, The Adoption Of Organizational Objectives, And Adaptation To Change. Effective Leaders Are Regarded As Managers Who Are Capable Of Establishing Strong Communication, Supporting Employee Development, Strengthening Team Spirit, And Facilitating The Achievement Of The Institution's Strategic Objectives.

The Multidisciplinary Nature Of Healthcare Services Requires Physicians, Nurses, Pharmacists, Technicians, And Other Healthcare Professionals To Work In Coordination. Effective Communication And Collaboration Among Team Members Improve The Quality Of Patient Care, Reduce The Risk Of Medical Errors, And Contribute To The Safer Delivery Of Healthcare Processes. In Addition, Teamwork Positively Influences Employee Satisfaction, Organizational Commitment, And Institutional Efficiency.

The Primary Aim Of This Study Is To Evaluate The Effects Of Leadership And Teamwork In Healthcare Institutions On Service Quality, Employee Performance, Patient Safety, And Organizational Success In Light Of The Current Literature. Furthermore, The Contributions Of Different Leadership Approaches To The Effectiveness Of Healthcare Services And The Strategic Importance Of Teamwork In Healthcare Institutions Are Comprehensively Examined.

1.1. The Concept Of Leadership

Leadership Is Regarded As A Dynamic Management Process That Influences, Directs, And Motivates Individuals Toward Common Goals. In The Management Science Literature, Leadership Is Considered Not Merely The Exercise Of Managerial Authority But Also A Strategic Element That Brings Out Employees' Potential, Manages Change, And Facilitates The Achievement Of Organizational Objectives (Eren, 1996; Gümüş, 2017).

Effective Leaders Create An Environment Of Trust Among Employees, Enabling Organizations To Make The Best Use Of Team Members' Knowledge And Experience. In Addition, Through Strong Communication Skills, They Increase Employee Motivation And Contribute To The Adoption Of Common Goals (Tağraf & Çalman, Pp. 136–137).

Leadership In Healthcare Institutions Is Of Critical Importance For Improving Service Quality, Ensuring Patient Safety, And Enhancing Employee Commitment. Healthcare Managers' Adoption Of A Leadership Approach That Is Adaptable To Change, Committed To Ethical Values, Supportive Of Teamwork, And Encouraging Of Employee Development Has Positive Effects On Organizational Performance (Gün & Aslan, 2018; Gök, 2023).

Accordingly, Adopting An Effective Leadership Approach In Healthcare Institutions Makes A Significant Contribution To The Sustainable Improvement Of Both Employee Satisfaction And The Quality Of Patient Care.

1.2. Types Of Leadership

Leadership Approaches Have Evolved Over Time In Response To Changes In Organizational Structures, Employee Expectations, And Environmental Conditions. Each Leadership Approach Affects The Way Managers Communicate With Employees, Make Decisions, And Achieve Organizational Goals In Different Ways. Therefore, It Is Not Possible To State That A Single Leadership Style Is The Most Successful Approach Under All Circumstances. An Appropriate Leadership Approach Should Be Determined By Considering The Characteristics Of The Organization, Employee Profile, And Field Of Service (Gümüş, 2017).

The Leadership Approaches Most Commonly Encountered In Healthcare Institutions Include Autocratic (Authoritarian), Democratic (Participative), Humanistic (Relationship-Oriented), Bureaucratic, And Charismatic Leadership. Each Of These Leadership Styles Produces

Different Outcomes In Terms Of Employee Motivation, Teamwork, And Service Quality (Karakaya, 2020).

1.2.1. Autocratic (Authoritarian) Leadership

In Autocratic Leadership, Decision-Making Authority Is Largely Concentrated In The Leader. The Leader Gives Limited Consideration To Employees' Opinions During The Decision-Making Process And Conducts Organizational Activities According To Rules Determined By The Leader. Although This Approach Can Provide Advantages, Particularly In Situations Requiring Rapid Decision-Making, It May Negatively Affect Employee Participation In Management And Motivation (Güney, 1997; Karakaya, 2020).

1.2.2. Democratic (Participative) Leadership

Democratic Leadership Is A Leadership Approach That Values Employees' Opinions And Suggestions In Decision-Making Processes, Encourages Participation, And Aims To Strengthen Collaboration Among Team Members. Under This Leadership Approach, Rather Than Making Decisions Independently, The Manager Acts According To A Shared Understanding By Benefiting From Employees' Knowledge And Experience. Consequently, Employees Perceive Themselves As Important Members Of The Organization, Develop A Stronger Sense Of Responsibility, And Demonstrate Greater Motivation Toward Achieving Organizational Goals (Polatoğlu, 2022).

In Healthcare Institutions, A Democratic Leadership Approach Contributes Significantly To Establishing Effective Communication Among Different Professional Groups And Enabling Team Members To Actively Participate In Decision-Making Processes. In Particular, Considering The Opinions Of Physicians, Nurses, And Other Healthcare Professionals Helps Ensure That Patient Care Processes Are Conducted More Safely And Effectively. Furthermore, Taking Employees' Views Into Consideration Increases Organizational Commitment And Job Satisfaction While Supporting The Development Of An Atmosphere Of Trust Within The Team (Karakaya, 2020).

The Literature Indicates That Democratic Leadership Contributes Positively To The Development Of Innovative Thinking, The Strengthening Of Problem-Solving Skills, And The Improvement Of Team Performance. In Institutions Where Employee Participation In Management Is Encouraged, Communication Channels Are Reported To Be More Open,

Conflicts Are Managed More Effectively, And Organizational Efficiency Increases (Gümüş, 2017).

In Conclusion, Democratic Leadership Is Considered One Of The Effective Leadership Approaches In Healthcare Institutions Because It Supports Employees' Professional Development, Strengthens Teamwork, And Promotes A Patient-Centered Approach To Healthcare Delivery. Therefore, Healthcare Managers' Adoption Of A Participative Management Approach Can Make A Significant Contribution To Improving Both Employee Satisfaction And The Quality Of Healthcare Services (Gün & Aslan, 2018; Gök, 2023).

1.2.3. Humanistic (Relationship-Oriented) Leadership

Humanistic Leadership Is A Leadership Approach That Emphasizes Employees' Needs And Individual Development. Managers Who Adopt This Leadership Approach Seek To Establish Strong Communication With Employees, Motivate Them, And Create A Supportive Work Environment. Recognition And Rewards, Trust, And Mutual Respect Are Among The Fundamental Characteristics Of This Leadership Style (Şimşek Et Al., 2011).

1.2.4. Bureaucratic Leadership

In Bureaucratic Leadership, Organizational Rules, Procedures, And Hierarchical Structures Are Prioritized. Decisions Are Made In Accordance With Existing Legislation, And Responsibilities Are Assigned Within Defined Boundaries Of Authority. Particularly In Healthcare Institutions Where The Risk Of Error Is High, Bureaucratic Leadership Can Offer Important Advantages In Maintaining Standardized Practices And Ensuring Service Safety (Karakaya, 2020).

1.2.5. Charismatic Leadership

Charismatic Leadership Is Based On Motivating Employees Toward Common Goals Through The Leader's Personal Characteristics, Vision, And Persuasive Communication Skills. Charismatic Leaders Are Regarded As Individuals Who Support Change, Inspire Employees, And Contribute To The Achievement Of Organizational Objectives During Challenging Periods. This Leadership Approach Can Strengthen Employee Commitment And Contribute To Improved Organizational Performance (Ercan, 2021).

1.3. Leadership And Its Importance İn Healthcare Institutions

Healthcare Institutions Are Organizations That Require A High Level Of Managerial Responsibility Because They Provide Services That Directly Affect Human Life. The Safe, Effective, And Sustainable Delivery Of These Services Depends Not Only On Technological Capabilities But Also On Effective Leadership. Leaders Are Key Actors Who Determine The Institution's Strategic Objectives, Direct Employees Toward Common Goals, And Ensure The Delivery Of High-Quality Healthcare Services (Vadnjal, Bernik, & Baričič, 2009).

Population Growth, The Increasing Number Of Older Adults, The Rising Prevalence Of Chronic Diseases, And Changing Expectations Regarding Healthcare Services Have Made It Necessary For Healthcare Managers To Possess More Effective Leadership Skills. Accordingly, Leaders Are Expected Not Only To Perform Managerial Duties But Also To Adopt A Management Approach That Leads Change, Motivates Employees, And Strengthens Teamwork (Gün & Aslan, 2018).

An Effective Leadership Approach Increases Employees' Commitment To The Organization, Strengthens Communication, And Contributes To The Development Of A Culture Of Trust Within The Institution. Various Studies Have Demonstrated That Employees With High Organizational Commitment Have Greater Job Satisfaction, Lower Intentions To Leave Their Jobs, And Assume Greater Responsibility For Achieving Organizational Objectives (Yıldırım, 2011).

The Nhs Leadership Academy Identifies The Key Characteristics Of Successful Leaders İn Healthcare Institutions As Supporting Team Members, Increasing Employee Participation, Creating A Shared Vision, Encouraging Information Sharing, Supporting Innovative Thinking, And Continuously Promoting Employees' Professional Development. These Characteristics Are Regarded As Fundamental Principles Of Contemporary Healthcare Management (Gün & Aslan, 2018).

In Conclusion, Leadership İn Healthcare Institutions İs Not Limited To Carrying Out Managerial Activities. Effective Leaders Are Regarded As Strategic Managers Who Increase Employee Motivation, Strengthen Team Spirit, Prioritize Patient Safety, And Support The Sustainable Success Of The Organization (Korkutan Et Al., 2021).

1.4. The Relationship Between Quality And Leadership In Healthcare Institutions

Quality In Healthcare Is Not Limited To The Effectiveness Of Treatment And Care Services Provided; It Encompasses Many Factors, Including Patient Safety, Employee Satisfaction, Accessibility Of Services, And Organizational Efficiency. Therefore, The Establishment And Sustainability Of A Quality Culture In Healthcare Institutions Are Directly Associated With Effective Leadership Practices (Karaca, 2014).

Leaders Are Responsible For Establishing The Organization's Quality Objectives, Directing Employees Toward These Objectives, And Ensuring That A Culture Of Continuous Improvement Is Established. Managers With An Effective Leadership Approach Support Employees' Professional Development, Strengthen Collaboration Among Team Members, And Contribute To The Adoption Of A Patient-Centered Approach To Service Delivery. This Enables Both Improved Employee Performance And Safer, Higher-Quality Healthcare Delivery (Gök, 2023).

Research Indicates That Increased Levels Of Job Satisfaction And Motivation Among Employees Positively Affect Service Quality. In Particular, Managers Who Adopt A Transformational Leadership Approach Are Reported To Encourage Employee Participation In Decision-Making Processes, Develop A Sense Of Responsibility, And Facilitate The Implementation Of Innovative Practices. Consequently, A Culture Of Continuous Improvement Is Strengthened And Patient Satisfaction Increases (Güngör & Polat, 2022).

Successful Implementation Of Quality Management Requires Strong And Committed Leadership From Senior Management. Sharing Organizational Objectives With Employees, Regularly Monitoring Performance Indicators, Developing Data-Driven Decision-Making Processes, And Supporting Continuous Training Activities Are Among The Fundamental Elements Of Quality Management (Karaca, 2014).

In Conclusion, Making Quality Sustainable In Healthcare Institutions Is Possible Not Only Through The Implementation Of Technical Standards But Also Through The Adoption Of A Leadership Approach That Motivates Employees Toward Common Goals, Supports Teamwork, And Encourages Continuous Improvement. Therefore, Effective Leadership And Quality Management Should Be Regarded As Two Complementary Fundamental Elements Of Management.

1.5. Competition And Leadership In Healthcare Services

Technological Developments In The Healthcare Sector, Increasing Patient Expectations, The Growing Number Of Private Healthcare Organizations, And Improved Access To Healthcare Services Have Significantly Intensified The Competitive Environment In Recent Years. Today, Healthcare Institutions Are No Longer Organizations That Merely Provide Treatment Services; They Have Become Organizations Competing Through A High-Quality, Reliable, And Patient-Centered Approach To Healthcare Delivery (Gök, 2023).

The Fundamental Objective Of Competition In Healthcare Services Is To Meet Individuals' Health Needs In The Most Effective, Safe, And Economical Manner. Accordingly, Healthcare Institutions Seek To Improve Service Quality, Increase Patient Satisfaction, Use Resources More Efficiently, And Implement Innovative Practices. Achieving Success In A Competitive Environment Requires Not Only Reducing Costs But Also Investing In Qualified Human Resources, Following Technological Developments, And Supporting Continuous Quality Improvement Initiatives (Gök, 2023).

The Role Of Leaders In This Process Is Highly Important. Effective Leaders Accurately Analyze Changing Environmental Conditions And Develop Strategies To Enhance The Organization's Competitive Capacity. They Also Support Training Programs Aimed At Developing Employees' Knowledge And Skills, Encourage Innovative Thinking, And Strengthen Teamwork. In This Way, Healthcare Institutions Can Adapt More Rapidly To Changing Patient Expectations (Korkutan Et Al., 2021).

To Maintain A Sustainable Competitive Advantage, Healthcare Managers Should Adopt A Quality-Oriented Management Approach Without Compromising Ethical Principles. The Balance Established Among Patient Safety, Employee Satisfaction, And Organizational Performance Is Among The Fundamental Determinants Of The Long-Term Success Of Healthcare Organizations. Therefore, Leadership Is Regarded As One Of The Strategic Management Tools That Can Provide A Competitive Advantage.

1.6. Teamwork And Leadership In Healthcare Services

The Effective, Safe, And High-Quality Delivery Of Healthcare Services Depends On The Coordinated Efforts Of Different Professional Groups. Therefore, In Contemporary Healthcare Management, Teamwork Is Regarded Not Merely As A Management Approach But As An Integral Component Of Patient Care. Physicians, Nurses, Pharmacists,

Technicians, And Other Healthcare Professionals Contribute To The Success Of Healthcare Services By Working Collaboratively Toward Common Goals (Alsaqqa, 2020).

Successful Teamwork Depends On Effective Communication Among Team Members, The Development Of Mutual Trust, And The Establishment Of A Shared Sense Of Responsibility. Leaders Working In Healthcare Institutions Should Support Collaboration By Creating A Work Environment In Which Team Members Can Benefit From Their Knowledge And Experience And Should Encourage Employees' Professional Development. Such A Management Approach Enhances Team Performance And Contributes To Improving The Quality Of Patient Care (Gün & Aslan, 2018).

Effective Leaders Accurately Assess Team Members' Abilities, Ensure A Fair Distribution Of Responsibilities, And Support Employee Participation In Decision-Making Processes. In Addition, Establishing A Culture Of Open Communication, Resolving Problems Through Collective Reasoning, And Implementing Continuous Feedback Mechanisms Are Among The Fundamental Factors That Increase The Efficiency Of Teamwork (Alsaqqa, 2020).

Strengthening Teamwork In Healthcare Services Not Only Increases Employee Satisfaction But Also Supports Patient Safety, Reduces The Rate Of Medical Errors, And Enables Healthcare Services To Be Delivered More Effectively. Therefore, It Is Of Great Importance For Leaders To Adopt A Management Approach That Develops Team Spirit, Motivates Employees, And Promotes Interdisciplinary Collaboration.

2. AIM

The primary aim of this study is to comprehensively evaluate the effects of leadership and teamwork on healthcare service delivery in healthcare institutions. The study examines, in line with the existing literature, the contributions of leadership approaches to employee motivation, organizational commitment, service quality, patient safety, and organizational performance.

In addition, the importance of teamwork within the multidisciplinary structure of healthcare services is addressed, and the contributions of effective communication, coordination, and collaboration among team members to patient care processes are evaluated. Furthermore, the effects of different leadership models on team performance are compared, and

recommendations are developed regarding effective management approaches that can be implemented in healthcare institutions.

Based on the findings obtained from the study, the research aims to formulate recommendations that can guide healthcare managers and contribute to future scientific research on the subject.

3. METHODOLOGY

This study is a qualitative literature review conducted to examine the importance of leadership and teamwork in healthcare institutions. The study reviewed books, academic articles, master's and doctoral theses, and scientific publications in the national and international literature on healthcare management, leadership, teamwork, quality in healthcare services, patient safety, and organizational commitment.

The document analysis method was used to obtain the data. Within this scope, publications related to leadership and teamwork in healthcare institutions were systematically reviewed, and sources directly related to the subject were included in the evaluation. The information obtained was analyzed using the content analysis method and classified under similar themes.

During the research process, the concept of leadership, types of leadership, the importance of leadership in healthcare institutions, characteristics of teamwork, the structure of healthcare teams, and the effects of teamwork on healthcare services were evaluated. In addition, the relationship between leadership and teamwork was examined, and their effects on the quality of healthcare services, employee performance, patient satisfaction, and patient safety were analyzed.

The findings of the study were obtained through the comparison and interpretation of the studies included in the reviewed literature, and the contributions of effective leadership and teamwork to organizational success in healthcare institutions were identified.

4. FINDINGS

As a result of the literature review, it was observed that leadership and teamwork in healthcare institutions have significant effects on service quality, employee performance, organizational commitment, and patient safety. The reviewed studies indicate that effective

leadership practices increase employee motivation, strengthen organizational commitment, and contribute to the more efficient delivery of healthcare services.

According to the findings of the study, managers who adopt a democratic and participative leadership approach in healthcare institutions support employees' participation in decision-making processes, which positively affects employee satisfaction and job performance. In contrast, an autocratic leadership approach was found to limit employees' participation in management and may have negative effects on motivation.

The reviewed sources emphasize that teamwork is an important factor in improving the quality of patient care. Effective communication and collaboration among team members were found to reduce the rate of medical errors, improve patient safety, and facilitate more effective implementation of care processes. In addition, teamwork was found to increase job satisfaction among healthcare professionals and strengthen internal coordination within healthcare institutions.

A strong relationship was observed between leadership and teamwork in healthcare institutions. Leaders' ability to establish an environment of trust among team members, facilitate the establishment of common goals, and support employees' professional development are among the key factors that enhance team performance. In particular, transformational and servant leadership approaches have been reported to increase team members' organizational commitment and willingness to work.

Based on the overall evaluation of the studies in the literature, it was concluded that effective leadership and strong teamwork in healthcare institutions are of critical importance for increasing patient satisfaction, improving service quality, enhancing employee performance, and ensuring the sustainability of organizational success.

4.1. Teamwork In Healthcare Institutions

Healthcare services have a multidisciplinary structure that requires professionals from different occupational groups to bring together their knowledge, skills, and experience toward a common goal. Therefore, teamwork is considered one of the fundamental elements of providing high-quality, safe, and effective healthcare services.

Teamwork is a working model in which physicians, nurses, pharmacists, technicians, and other healthcare professionals work through mutual cooperation and effective communication to maximize the quality of patient care (Özer & Saygılı, 2020).

Effective teamwork in healthcare institutions requires not only the fulfillment of individual responsibilities but also acting with a sense of shared responsibility. Sharing knowledge and experience, participating in decision-making processes, and supporting one another among team members improve the quality of patient care, reduce medical error rates, and contribute to enhancing patient safety (Çıraklı et al., 2015).

For successful teamwork to be established, open communication, mutual trust, cooperation, common goals, and effective leadership are of great importance among team members. Salas, Sims, and Burke (2005) stated that effective teams should possess strong leadership, mutual performance monitoring, the ability to support one another when necessary, adaptability to changing circumstances, and a team-oriented approach.

The effective implementation of teamwork in the healthcare sector not only supports the professional development of employees but also strengthens organizational coordination. In addition, an environment of trust established among team members increases employee satisfaction and organizational commitment while contributing to the more planned and efficient delivery of healthcare services. Research has demonstrated that effective teamwork increases patient satisfaction, positively influences the treatment process, and makes an important contribution to the sustainability of healthcare quality (Önen & Dinçer, 2014; Burns, Bradley, & Weiner, 2012).

Therefore, improving teamwork in healthcare institutions has strategic importance not only in terms of enhancing coordination among employees but also in strengthening patient-centered care and ensuring sustainable organizational success.

4.2. What Is a Team?

A team is a small working group in which individuals with different knowledge, skills, and experiences work collaboratively to achieve predetermined goals toward a common objective. Team members not only fulfill their individual responsibilities but also contribute to organizational success by supporting one another through a shared sense of responsibility. In this respect, teamwork creates a level of synergy that is greater than the sum of individual

performances (Canlı, 2010).

Although the concepts of team and group are sometimes used interchangeably in the literature, there are important differences between them. In groups, individuals generally perform their tasks independently, whereas in teams, members work through continuous communication and coordination to achieve common goals.

Therefore, teamwork is regarded as a dynamic process requiring mutual trust, cooperation, and a shared sense of responsibility (Canlı, 2010; Özbay & Arslan, 2007).

4.3. Stages of Team Formation

The formation of an effective team requires a certain period of time and an adaptation process. For individuals who do not know one another to work efficiently toward common goals, team development must proceed through certain stages. This process progresses through forming, conflict, establishment of rules, performance development, and completion of the task (Canlı, 2010).

At the initial stage, team members attempt to get to know one another and learn about the team's objectives. During the subsequent stage, disagreements may arise due to differences in opinions; however, team cohesion is gradually established through the development of common working principles. As the development process progresses, team members fulfill their roles and responsibilities more effectively, cooperation becomes stronger, and performance improves. After the established objectives have been achieved, the team completes its task and disbands (Canlı, 2010).

4.4. Types of Teams

Different types of teams may be established in organizations depending on the nature of their activities. Healthcare institutions also utilize teams with different roles and responsibilities to ensure the effective delivery of services. These include self-managed teams, cross-functional teams, project teams, quality circles, virtual teams, and senior management teams (Canlı, 2010).

Self-managed teams are teams that can operate largely independently in planning, implementing, and evaluating tasks. Cross-functional teams are formed by bringing together employees from different areas of expertise to solve a specific problem or carry out a common

project. Project teams are established for a specific period, whereas quality circles consist of employees who voluntarily participate in activities aimed at improving service quality. Virtual teams, which have become increasingly common with technological developments, maintain communication through digital platforms. Senior management teams consist of managers who make the organization's strategic decisions and are responsible for its overall management (Canlı, 2010; Burns, Bradley, & Weiner, 2012).

Proper identification and effective management of team types in healthcare institutions make important contributions to improving service quality, strengthening coordination among employees, and enhancing patient safety.

4.5. Healthcare Team

A healthcare team is an association of individuals who come together within healthcare institutions to provide comprehensive and high-quality healthcare for specific objectives within a common framework, where decisions are made collectively and implemented collaboratively. For long-term illnesses, team-based care that is interconnected and integrated rather than fragmented and disconnected is considered more effective and successful. The primary focus of healthcare teams is patient health, as well as the individual and the family. All healthcare professionals work to meet the needs of the individual (Önen & Dinçer, 2014: 23).

The concept of teamwork in healthcare institutions is based on several fundamental principles. Since healthcare is a high-risk field, there is considerable potential for errors. Every year, medical errors result in injuries and deaths among thousands of patients.

Healthcare services involving care and treatment are provided by well-trained professionals who specialize in their respective fields and possess different skills. Effective and high-quality teamwork is ultimately aimed at protecting and improving the patient's health. Bringing together professionals around a specific goal for patient care is regarded as one of the most effective approaches to providing healthcare (Millward, 2001).

4.6. Teamwork in Healthcare Institutions

Healthcare services have a multidisciplinary structure that requires professionals from different areas of expertise to work in coordination toward a common goal. Therefore, teamwork is regarded as one of the indispensable management elements in providing patient-

centered, safe, and high-quality healthcare services. Teamwork in healthcare institutions is a systematic approach that enables physicians, nurses, pharmacists, technicians, and other healthcare professionals to combine their knowledge, skills, and experience toward common goals and provide effective services (Özer & Saygılı, 2020).

The primary purpose of teamwork is to contribute to the safer, faster, and more efficient management of patient care processes by ensuring effective communication and cooperation among healthcare professionals. Numerous studies have demonstrated that healthcare institutions implementing effective teamwork experience increased information sharing, faster decision-making processes, reduced medical error rates, and improved patient safety (Çıraklı , 2015). Furthermore, mutual trust and a shared sense of responsibility developed among team members positively affect professional satisfaction and organizational commitment.

Open communication, mutual respect, adoption of common goals, clear definition of roles and responsibilities, and effective leadership are of great importance in establishing successful teams in healthcare services. Salas, Sims, and Burke (2005) stated that high-performing teams are those that are integrated around a common purpose, support one another, adapt to changing circumstances, and continuously evaluate their performance.

Teamwork not only improves the quality of patient care but also strengthens organizational coordination, enhances the effectiveness of service processes, and contributes to the efficient use of resources. According to Burns, Bradley, and Weiner (2012), healthcare institutions with strong interdisciplinary collaboration experience higher employee satisfaction, greater continuity of service delivery, and more positive patient outcomes.

4.7. Importance and Benefits of Healthcare Teams

The use of teams in healthcare institutions has increased considerably, and healthcare institutions increasingly prefer team-based work. According to healthcare professionals, teamwork has become an integral component of effective healthcare service delivery. Working as a team aims to ensure that patients receive higher-quality healthcare services (Çıraklı, 2015: 142).

One of the most important benefits of teamwork is that individuals from different areas of expertise come together and share their knowledge and skills. Healthcare professionals and employees work together as a team to contribute to patients' treatment and recovery processes. Consequently, patient care can be provided more effectively.

The benefits of teamwork in healthcare institutions can be summarized as follows:

Increases efficiency in healthcare institutions.

Improves patient safety and satisfaction.

Strengthens communication among healthcare professionals.

Facilitates access to healthcare services.

Reduces errors through teamwork (Özcan, 1–2).

Reduces hospital length of stay and costs.

Increases patient satisfaction.

5. CONCLUSION

The complex structure of healthcare institutions and the provision of services that directly affect human life make it necessary to implement effective leadership and strong teamwork simultaneously within these organizations. The literature indicates that leadership has a significant influence on employee motivation, organizational commitment, service quality, and patient safety (Gün & Aslan, 2018; Gök, 2023).

The studies examined within the scope of this research demonstrate that, in particular, democratic and participative leadership approaches increase employees' participation in decision-making processes, strengthen employee satisfaction, and positively influence team performance (Polatoğlu, 2022; Karakaya, 2020). In contrast, an autocratic leadership approach may have negative effects on employee motivation and organizational commitment (Güney, 1997).

The findings in the literature indicate that teamwork in healthcare services is one of the fundamental factors in improving patient safety, reducing medical errors, and enhancing the quality of care (Çıraklı et al., 2015; Burns, Bradley, & Weiner, 2012). In addition, trust-based communication and collaboration among team members are reported to strengthen internal coordination and increase the effectiveness of service delivery (Özer & Saygılı, 2020).

As a result of the research, effective leadership and strong teamwork were evaluated as two fundamental and complementary management elements. When leaders adopt a management

approach that supports employees, encourages their professional development, and strengthens team spirit toward common goals, both employee satisfaction and organizational performance are enhanced (Gümüş, 2017; Gök, 2023).

Accordingly, it is recommended that leadership development programs for healthcare managers be expanded, in-service training programs supporting teamwork be increased, and employees be provided with greater opportunities to participate actively in decision-making processes. Furthermore, future research examining the relationship between leadership styles and team performance in different healthcare institutions using quantitative research methods would contribute to obtaining stronger scientific evidence on the subject (Taşer et al., 2022; Gün & Aslan, 2018).

In conclusion, the provision of high-quality, safe, and sustainable healthcare services in healthcare institutions depends on the simultaneous development of an effective leadership approach that supports employee participation and a strong team culture. The harmonious implementation of these two elements can significantly contribute to the organizational success of healthcare institutions by increasing both patient satisfaction and employee productivity.

6. LIMITATION

This study has several limitations. Since the study is based on a literature review, the findings are limited by the scope, methodology, and scientific quality of previously published studies. A substantial proportion of the studies examining leadership and teamwork in healthcare institutions have been conducted using different sample groups and research designs, which may limit the generalizability of the findings to all healthcare institutions.

In addition, the fact that the studies were conducted in different countries, healthcare systems, and organizational settings may lead to variations in the outcomes of leadership approaches and teamwork.

As no primary data were collected in this study, the direct perspectives of healthcare professionals, managers, and patients were not included. Nevertheless, the evaluation of the existing literature demonstrates the importance of leadership and teamwork in healthcare institutions in terms of service quality, employee performance, and patient safety.

Future studies involving large samples from different healthcare institutions and professional groups and employing both quantitative and qualitative research methods may contribute to providing stronger evidence to support these findings.

7. DECLARATIONS

Evaluation: The manuscript is evaluated by both internal and external reviewers.

Conflict of Interest: The authors declare that they have no conflict of interest regarding this article.

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8. ETHICAL STATEMENT

The *Istanbul Medisosal Journal of Education and Research in Health Sciences* is a nationally based scientific journal in the field of health sciences that aims to uphold the fundamental principles of scientific research and publication ethics, including integrity, transparency, objectivity, and respect for the findings and intellectual creations of others. The journal is committed to promoting and implementing these principles throughout the research and publication process. The criteria set forth in the Declaration of Helsinki have also been taken into consideration.

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THE IMPACT OF HEALTH MISINFORMATION ON ORGANISATIONAL TRUST ON SOCIAL MEDIA: A STRUCTURED LITERATURE REVIEW OF COVID-19 VACCINE POSTS ON THE X (TWITTER) PLATFORM

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ABSTRACT

Objective: This study examines the effect of health misinformation circulating on social media on trust in health institutions, in the context of COVID-19 vaccine posts on the X (Twitter) platform. **Method:** Rather than collecting original data, a structured literature review was adopted; the search protocol, the inclusion and exclusion criteria, and the characteristics of the thirty-one sources used in the synthesis are reported in tabular form. The findings were then reorganised within a five-category coding framework consistent with the directed content analysis approach. **Results:** Misinformation concentrates in three dominant types: exaggerated claims about side effects, false claims about vaccine content, and conspiracy narratives questioning the legitimacy of the vaccine development process.

Perceived source credibility is transmitted to institutional trust not directly but through heuristic processes and in-network response. The effect of corrective attempts varies

markedly according to the audience's prior attitude. Themes prominent in studies conducted in Türkiye largely overlap with the international pattern.

Conclusion: Misinformation and institutional trust are not two independent variables but two faces of a mutually reinforcing cycle. The target of intervention is therefore not only correcting information but protecting and repairing trust.

Keywords: health misinformation, institutional trust, infodemic, source credibility, vaccine hesitancy, structured literature review

1. INTRODUCTION

The trajectory of health communication over the last fifteen years points to a fundamental transformation in the ways in which information is produced and circulated. Whilst the flow of information in traditional health communication was largely one-way and institution-controlled, with the proliferation of social media platforms this flow has taken on a multi-directional, unregulated and accelerated structure. Control has shifted. Chou, Oh and Klein (2018) aptly emphasise that the social media ecosystem has created an environment in which not only accurate information but also unsubstantiated opinions, half-truths and deliberately distorted content circulate with equal visibility. The problem is not merely the existence of false content; the real issue is that this content is made to compete with accurate information under the same algorithmic and social conditions – and often proves more successful than it. The competition is not a level playing field, and the ground is tilted in favour of misinformation.

The COVID-19 pandemic has served as a turning point that has brought the scale of this problem into sharp relief. World Health Organisation officials have brought the concept of an ‘infodemic’ to the fore, noting that the pandemic was accompanied not only by a biological outbreak but also by an informational one (Zarocostas, 2020).

A large-scale data analysis by Cinelli et al. (2020), covering five major platforms, revealed that the spread of information relating to COVID-19 exhibited dynamics similar to those of epidemiological models, with reliable and unreliable sources generating engagement at almost the same rate in terms of content production. The classic assumption that ‘the authority of an information source naturally comes to the fore’ has, at least in the context of social media, largely lost its validity.

Authority no longer emerges of its own accord.

Within this broader picture, vaccine communication is one of the areas where misinformation is produced most intensively and leads to the most tangible health consequences. An experimental study conducted by Loomba and colleagues (2021) in the United Kingdom and the United States demonstrated that even short-term exposure to misinformation leads to statistically significant declines in the intention or propensity to be vaccinated. Meanwhile, a study by Roozenbeek and colleagues (2020), covering five countries, documented that

susceptibility to misinformation is negatively associated not only with vaccine hesitancy but also with compliance with public health guidelines; conversely, trust in scientists and science acts as a factor that reduces this susceptibility.

When these two studies are considered together, it becomes apparent that the relationship between misinformation and organisational trust is not one-way, but rather forms a mutually reinforcing vicious circle: whilst low organisational trust increases susceptibility to misinformation, exposure to misinformation also reinforces existing mistrust.

Interpreting this picture solely as an individual or cognitive error leads to overlooking the social dimension of the issue. An approach that is gaining increasing acceptance in the health communication literature suggests treating exposure to misinformation and institutional trust not as two independent variables, but as two different manifestations of the same social trust crisis. If trust in health institutions is already weak within a society, misinformation easily takes root in this environment and serves as a repository of evidence that legitimises existing scepticism; in societies where trust is relatively strong, however, the same content has a much more limited impact. For this reason, the issue must be addressed not only from the perspective of ‘combating misinformation’ but also from the perspective of ‘how to safeguard or restore institutional trust’.

The aim of this study is to examine the aforementioned cycle through a concrete case study, specifically in the context of posts regarding COVID-19 vaccines on Platform X. Rather than collecting original data, the study follows a methodology that systematically reviews the existing literature and restructures the findings within a content analysis coding framework; the rationale for this choice is explained in detail in the Methods section.

It should be noted here that the evidence base provided by large-scale/multi-national studies already existing in the field offers a more reliable foundation for synthesis than an original coding exercise conducted with a limited sample. The study also aims to go beyond a purely descriptive summary by addressing findings that are in tension with one another in the literature, as well as the methodological limitations of certain studies. In the following sections, the conceptual framework is first presented, followed by a review of the relevant literature, a detailed description of the methodology, and finally a discussion of the findings within the context of organisational trust.

1.2. Conceptual Framework

1.2.1 Misinformation, Disinformation and the Infodemic

The pair of concepts ‘misinformation’ and ‘disinformation’, which are frequently used interchangeably in the literature, differ in terms of the element of intent. According to the definition proposed by Vraga and Bode (2020), misinformation refers to content that contradicts the best scientific evidence but is not necessarily produced with malicious intent, whilst disinformation refers to content that is produced with the intent to mislead and is generally produced in an organised manner. This distinction is not merely an academic nuance; it is a methodological necessity in the analysis of anti-vaccine discourse, as the same platform hosts both posts by well-meaning but misinformed individuals and the products of organised disinformation campaigns. Indeed, research conducted by Broniatowski and colleagues (2018) on Twitter bots and Russian troll accounts revealed that accounts intervening in vaccine debates at a much higher rate than organic users often served a polarising function; these accounts not only promoted anti-vaccine views but also played a role in amplifying the debate.

The concept of ‘infodemiology’, developed by Eysenbach (2002) prior to the pandemic, is a pioneering framework that proposes monitoring the dissemination of health information online using epidemiological methods. This framework was revisited by the World Health Organisation during the pandemic, and an infodemic was defined as the simultaneous and excessive spread of both accurate and inaccurate information, making it difficult for individuals to distinguish between reliable and unreliable sources (Zarocostas, 2020). In the Turkish context, the review by Özen and Topbaş (2023) has adapted this conceptual framework to the local literature, emphasising that the management of an infodemic is directly linked to health literacy, particularly digital health literacy. According to the authors, the ability to assess which information to trust and on what grounds is a competence or skill just as important as access to information.

The systematic review by Wang, McKee, Torbica and Stuckler (2019) demonstrates that health-related misinformation is produced on social media across a wide range of topics—such as vaccines, smoking, substance use and nutrition—following similar patterns. According to the review, misinformation content is frequently reinforced by emotional appeal,

simplified causality and personal narrative elements, which make it more engaging than scientific content. Indeed, the measure of success is not accuracy, but engagement.

Similarly, the systematic review by Suárez-Lledó and Álvarez-Gálvez (2021) noted that, in a significant proportion of the studies examined, health misinformation was identified at rates ranging from 20 per cent to 80 per cent across different platforms, and that this wide variation was largely dependent on the choice of topic and the type of platform. This variation is related to the measurement design itself.

1.2.2. Institutional Trust: Conceptual and Theoretical Foundations

Institutional trust is a well-established concept in the organisational behaviour literature and has largely been transferred to the field of health communication from this source. According to the classic integrated trust model by Mayer, Davis and Schoorman (1995), trust in a party is a combination of three components; namely: competence (ability), that is, the perception that the other party is competent and skilled in their field; benevolence, that is, the belief that the other party looks after the well-being of the person placing their trust in them, beyond their own interests; and integrity, that is, the impression that there is consistency between the other party's words and actions. When this three-part framework is applied to healthcare organisations, competence corresponds to the organisation's capacity to produce accurate and up-to-date information; benevolence corresponds to the perception that the organisation will prioritise the public interest; and integrity corresponds to the consistency between the organisation's past statements and its current stance. These three components are not the same thing.

This distinction has a practical consequence: anti-vaccine misinformation generally targets the institution's integrity, whereas institutions' habitual response in a crisis is mostly geared towards reinforcing the competence component—that is, providing more data and more detailed explanations.

This mismatch partly explains why well-intentioned communication campaigns often miss the mark; for what the public is questioning is often not the organisation's knowledge, but its transparency. A large-scale survey conducted by Freeman and colleagues (2022) in the UK also supports this finding: conspiracy beliefs regarding the coronavirus are intertwined with a more general pattern of distrust towards the government and scientific institutions. According

to the researchers, conspiracy beliefs are not an isolated attitude but a specific manifestation of deep-rooted scepticism towards social institutions; consequently, correcting a single piece of misinformation does not resolve the underlying mistrust. The target, therefore, is not the individual claim but the ground itself.

A comparative country analysis by Roozenbeek et al. (2020) found that trust in scientists and science, alongside numeracy, is one of the two strongest factors in reducing susceptibility to misinformation.

In this context, institutional trust functions not merely as an outcome, but as a protective precondition against misinformation. When assessing the communication strategies of healthcare organisations, therefore, consideration must be given not only to ‘the extent to which they convey accurate information’, but also to ‘the extent to which they adopt a discourse that builds trust’.

Trust in healthcare organisations has a particular fragility within the context of social media. Whilst in traditional media, institutional spokespersons reach the public after passing through a specific editorial filter, on social media the official accounts of the same institutions compete on the same level of visibility as individual user accounts, anonymous pages and even bots. This levelling of the playing field weakens the institutional voice’s advantage of authority and requires trust to be renegotiated with every individual post. Authority cannot be gained once and retained forever. Another dimension of this is the temporal nature of trust: institutional trust is shaped not by a single positive or negative experience, but by impressions accumulated over a long period; however, social media creates an environment where this cumulative process can be rapidly eroded by a single striking post. The fact that a healthcare organisation has historically followed a consistent and transparent communication policy may not always compensate for the loss of trust caused by a single contradictory statement made during a crisis. The fact that trust can be built slowly but destroyed quickly is a fundamental reality that corporate communicators cannot afford to ignore. Trust builds slowly, but crumbles quickly.

1.2.3. Source Credibility and Heuristic Evaluation Models

The question of how individuals evaluate online information was systematically addressed in the study by Metzger and Flanagin (2013). Faced with an abundance of information,

individuals resort to cognitive-heuristic methods (heuristics) rather than systematically evaluating each piece of content individually. Among these, the endorsement heuristic (where a piece of content receiving a large number of likes and shares reinforces the impression that it is reliable), the consistency heuristic (whether the content aligns with the individual's pre-existing beliefs) and the expectation violation heuristic (where a source displaying an unexpected stance reinforces the perception of reliability) stand out. These heuristic mechanisms align directly with social media's interaction-focused architecture, thereby increasing the likelihood that misinformation with high engagement will appear credible. Visibility is taking the place of accuracy.

This framework helps to explain why anti-vaccine content is found to be more persuasive than statements from official health authorities among certain user groups. Kata's (2010) pioneering study analysing anti-vaccination websites demonstrated that such content is structured around personal testimonies, a discourse on parental responsibility and an emphasis on the right to access alternative information, rather than scientific language.

According to Kata, this discourse is based on a postmodern understanding of knowledge; it does not accept scientific expertise as the sole valid source of knowledge, but presents personal experience and intuitive knowledge as an equally legitimate basis. This observation also contains an indirect critique of the 'knowledge deficit model' long embraced by health organisations – that is, the assumption that the cause of misbelief is a lack of knowledge and that the solution lies in providing more accurate information: the problem is often not a lack of knowledge, but rather a different epistemological framework regarding which sources of knowledge are deemed legitimate.

A study by Schmidt et al. (2018), which examined the polarisation of the vaccination debate on Facebook, also confirms a similar pattern. According to this, users gradually cluster around ideologically homogeneous groups—so-called 'echo chambers'—within which the reliability of a source is determined by the degree to which it aligns with the group's dominant view. Institutional trust, therefore, is a group-based phenomenon shaped by one's positioning within a social network rather than an individual attitude.

1.2.4. Risk Perception and Health Behaviour

The impact of misinformation on health behaviour occurs largely through risk perception. Misinformation regarding vaccines typically manipulates two aspects of risk perception simultaneously: underestimating the risk of the disease and exaggerating the risk of the vaccine. The experimental findings of Loomba et al. (2021) demonstrated that when participants were exposed to scientifically presented but misleading content, they developed exaggerated concerns regarding the side effects of vaccines, and that these concerns statistically significantly reduced their intention to be vaccinated. It is noteworthy that scientifically presented misinformation is more effective than overtly conspiracy-based content; this suggests that the source's formal markers of legitimacy (such as graphics, statistics and the appearance of academic references) play a decisive role in intuitive trust assessments.

The 'accuracy nudge' approach developed by Pennycook and colleagues (2020) makes an important contribution in this regard. Most users do not pay sufficient attention to assessing the accuracy of content before sharing it; this inattention stems not from a deliberate desire to misinform, but from attention being directed towards other factors such as entertainment, social approval and a sense of belonging. Institutional trust interventions must therefore address not only content accuracy but also the user's attention architecture.

1.2.5. Relevant Literature: Social Media Research in the Context of COVID-19 Vaccine Misinformation

Social media research on COVID-19 vaccines has generated a rapidly expanding body of literature since the first year of the pandemic. A significant portion of this literature has focused on quantitatively measuring the speed and scope of the spread of misinformation. The study by Vosoughi, Roy and Aral (2018)—conducted prior to the pandemic but which has become one of the field's key reference points—demonstrated that false news spreads on Twitter significantly faster, more deeply and to a wider audience than true news. According to the researchers, the primary reason for this difference is not bot accounts, but the fact that human users find misleading content to be 'newer' and more emotionally stimulating. This finding is also corroborated in the context of vaccine misinformation: the more surprising, anger-inducing or fear-inducing the content is, the faster it spreads.

There is a point of tension here that warrants attention. Whilst Vosoughi and colleagues argue that human behaviour is the primary driver of the rapid spread of fake news, Broniatowski and colleagues (2018) demonstrate that organised bot and troll accounts have intervened heavily in vaccine debates.

Although these two findings may appear contradictory at first glance, they actually point to mechanisms operating at different levels. Whilst the findings of Vosoughi et al. focus on the general dissemination dynamics of content, those of Broniatowski et al. measure the intensity of intervention in a specific, politically charged debate. In other words, bots do not invent misinformation themselves, but rather selectively amplify content that is already spreading rapidly amongst human users, thereby polarising the debate. This distinction has concrete implications for corporate communicators: bot detection and account verification measures alone are not sufficient, as the root of the problem lies in human users' emotional and social motivations for sharing.

A multi-platform comparison by Cinelli et al. (2020) demonstrated that the circulation of information regarding COVID-19 varies across platforms, yet user engagement can remain high on every platform regardless of the source's reliability.

The unique architecture of the X platform—comprising its short-form text format, rapid reposting mechanism and algorithmic news feed—provides a structure that is particularly conducive to the spread of misinformation. Whilst the short format makes it difficult to convey nuanced scientific explanations, it facilitates the dissemination of simplified and assertive statements of misinformation.

Burki's (2019) evaluation, written from a clinical perspective, highlights that healthcare professionals generally adopt a late and reactive stance when combating misinformation on social media, whereas anti-vaccine content creators pursue an earlier, more systematic and emotionally more effective communication strategy. Even when organisations produce accurate information, the speed at which this information circulates and its emotional appeal lag behind those of misinformation; this asymmetry is a key factor explaining why institutional trust can erode over time.

Southwell and colleagues (2019) note that misinformation is often treated as a misunderstood challenge in the field of public health. The fight against misinformation is mostly framed as a

problem of individual cognitive deficiency, yet the real issue lies in the structural characteristics of social trust networks and the information ecosystem. This approach aligns directly with the perspective of the present study, which centres on institutional trust: for the fight against misinformation to be sustainable, not only verification but also trust-building is required.

When considering the literature as a whole, it is evident that the findings obtained from different methodological approaches (network analysis, experimental surveys, bot detection, systematic reviews) demonstrate a striking consistency. Misinformation is emotionally charged, targets institutional authority, and its impact is largely determined by pre-existing levels of trust. This consistency is another reason why the present study has opted for a structured literature review methodology; it is difficult for a single new sample to make a significant contribution to such a robust evidence base, whereas a systematic synthesis of existing findings can provide a clearer picture of the field as a whole.

2. AIM

The primary aim of this study is to examine the potential effects of health-related misinformation circulating on social media on perceptions of trust in healthcare institutions, specifically in the context of COVID-19 vaccines and on the X (Twitter) platform. In this regard, the study is based on the approach that misinformation is not merely a communication issue affecting individuals' health-related knowledge and attitudes; it is also a multidimensional phenomenon that can have consequences for the credibility of healthcare institutions, the perception of scientific authority and the legitimacy of institutional communication. In particular, the study aims to assess the discursive patterns within which claims regarding the safety, composition and development processes of vaccines emerged during the COVID-19 pandemic, and how these claims are linked to perceptions of institutional trust.

Another objective of the study is to present a comprehensive framework for evaluating misinformation regarding COVID-19 vaccines in terms of source reliability, emotional framing, interaction and dissemination dynamics, and the discourse of institutional trust. In this context, the aim is to conduct a comparative analysis of the types of misinformation identified in existing research and their relationship with users' assessments of health institutions.

Furthermore, the aim is to understand the role played by social media users' interactions, network-based evaluation processes and pre-existing levels of trust in the spread of misinformation. Rather than generating original social media data, the study adopts a structured review of existing scientific studies and a re-evaluation of the findings within the framework of directed content analysis. The aim is thus to identify the commonalities and differences between research findings obtained through various methods, to compare studies conducted in Turkey with patterns in the international literature, and to provide a more comprehensive explanation of the relationship between health misinformation and institutional trust. By discussing the limitations of approaches that focus solely on correcting inaccurate content in the fight against misinformation, the study aims to highlight the importance of communication strategies aimed at maintaining and strengthening trust in health institutions.

3. METHODOLOGY

3.1. Scope and Limitations of the Study

This study has limited its scope in three dimensions. The first is the platform limitation: the analysis is restricted to the X (Twitter) platform, as this platform is the most frequently examined medium in research on health misinformation, owing to its short-form nature and structure that is directly open to public debate. Secondly, there is a subject-matter limitation: the study is restricted to posts relating to COVID-19 vaccines, focusing in depth on a single health issue rather than general health misinformation. Thirdly, there is a temporal limitation: the study is confined to the period from January to June 2021, when mass vaccination programmes began and the debate was at its peak. This timeframe was chosen because it coincides with the data collection periods of large-scale studies in the literature and represents the period when vaccine hesitancy was most prominent (Loomba et al., 2021; Roozenbeek et al., 2020). Within these constraints, rather than collecting and coding original social media data, the study adopted a method that systematically reviewed existing empirical research corresponding to the specified scope and reorganised its findings within a content analysis coding framework. The rationale behind this method is that a sample of 50–100 posts collected by a single researcher carries the risk of reproducing large-scale patterns already documented in the literature with a lower degree of reliability. A structured literature review makes it possible to synthesise these patterns based on a more reliable evidence base.

3.2. The Structured Literature Review Process

The search process was conducted using combinations of key terms such as ‘COVID-19 vaccine misinformation Twitter’, ‘vaccine hesitancy social media trust’, ‘health misinformation institutional trust’ and ‘infodemic COVID-19 social media’. The inclusion criteria were defined as follows: publication in a peer-reviewed journal; addressing health misinformation, institutional trust, source reliability or vaccine hesitancy in the social media context, either empirically or conceptually; and publication between 1995 and 2023. Exclusion criteria included studies focusing solely on technical natural language processing methods and failing to address the health communication dimension, as well as non-peer-reviewed preprints and journalistic news content. The process draws inspiration from the logic of a systematic review; however, the aim is not to calculate a new effect size but to reinterpret existing findings through the lens of institutional trust. The components of the screening protocol are summarised in Table 1 for the sake of the review’s reproducibility. In a structured review, making the protocol transparent is not merely a formal requirement; it is the only way for the reader to assess which exclusion criteria were used to establish the selected evidence base.

Table 1. Screening protocol

Component	Content
Databases Searched	[To be completed: databases used for the literature search]
Search Strings	“COVID-19 vaccine misinformation Twitter”; “vaccine hesitancy social media trust”; “health misinformation institutional trust”; “infodemic COVID-19 social media”; for the Turkish literature, “COVID-19 aşı tereddüdü sosyal medya” and “sağlık yanlış bilgisi”
Publication Period	1995–2025
Inclusion Criteria	Studies published in peer-reviewed journals that empirically or conceptually address health misinformation in social media environments, institutional trust, source credibility, or vaccine hesitancy
Exclusion Criteria	Studies focusing solely on technical natural language processing methods without addressing the health communication dimension; non-peer-reviewed preprints; journalistic news content
Number of Sources Included in the Synthesis	31

It is also necessary to clearly state the limitations of this process. A structured literature review does not possess the formal rigour of a systematic review—that is, elements such as double-blind screening, multiple reviewers/consensus and a formal flow chart; consequently, the researcher’s subjective judgement plays a greater role in the selection of sources than in a fully systematic review. As the search was conducted largely in English-language databases, potentially relevant studies published in other languages may have been excluded. This reflects the fact that the field is still shaped by the Anglo-American research tradition. The picture presented is not culturally universal.

At the end of this process, twenty-two sources used in the conceptual framework, relevant literature and discussion sections were identified. These sources include large-scale network analyses (Cinelli et al., 2020; Vosoughi et al., 2018), multi-country survey studies (Roozenbeek et al., 2020; Freeman et al., 2022), platform-specific bot and troll analyses (Broniatowski et al., 2018; Schmidt et al., 2018), experimental intervention studies (Loomba et al., 2021; Pennycook et al., 2020), systematic reviews (Wang et al., 2019; Suarez-Lledó and Alvarez-Gálvez, 2021), conceptual/theoretical articles (Vraga and Bode, 2020; Southwell et al., 2019; Metzger and Flanagin, 2013; Mayer et al., 1995) and a methodological critique (Garry et al., 2022).

3.3. Characteristics of the Studies Used in the Synthesis

The sources used in the synthesis do not all stem from a single methodological tradition. This diversity is both a strength and a limitation of the review; for bringing together findings from different research designs requires the reader to be able to discern the type of evidence on which each finding is based. Table 2 summarises the empirical and review-based studies on which the synthesis is based, in terms of methodology, data and context.

Mayer et al. (1995), Metzger and Flanagin (2013), Vraga and Bode (2020), Eysenbach (2002), the studies by Hsieh and Shannon (2005), Southwell et al. (2019) and Chou et al. (2018) were not included in the table as they are of a conceptual/theoretical nature; they are discussed separately in the conceptual framework section.

Table 2. Characteristics of the empirical and review studies used in the synthesis

Study	Method	Data and Context	Key Findings
Kata (2010)	Discourse analysis	Anti-vaccine web content (International)	The postmodern framework of knowledge and the questioning of institutional authority
Broniatowski et al. (2018)	Account/bot analysis	Twitter accounts (USA)	Bot and troll accounts amplify the debate in a polarizing direction
Schmidt et al. (2018)	Network analysis	Facebook vaccine debate (International)	Echo-chamber structures and polarization
Vosoughi et al. (2018)	Large-scale network analysis	Twitter news cascades (USA)	False news spreads faster and more widely than true news
Burki (2019)	Review article	Clinical literature (International)	Assessment of the clinical consequences of misinformation
Wang et al. (2019)	Systematic review	Multi-topic health misinformation (International)	Emotional appeal, simplified causality, and personal narrative patterns
Akyüz (2020)	Content analysis	Circulating fake news (Türkiye)	Thematic patterns of fake news production during the pandemic
Cinelli et al. (2020)	Multi-platform data analysis	Five major platforms (International)	Information diffusion exhibits epidemiological dynamics
Pennycook et al. (2020)	Experimental intervention	Online participants (USA)	Accuracy prompts reduce the intention to share content
Roozenbeek et al. (2020)	Multi-country survey	Five-country sample (Comparative)	Trust in scientists reduces susceptibility to misinformation
Loomba et al. (2021)	Randomized experiment	Samples from the United Kingdom and the United States (Comparative)	Short-term exposure significantly reduces vaccination intentions
Porsuk & Cerit (2021)	Content analysis	Ekşi Sözlük discussion threads (Türkiye)	Thematic evolution of the vaccine debate on a user-generated platform
Suarez-Lledó & Alvarez-Gálvez (2021)	Systematic review	Cross-platform prevalence (International)	The prevalence of misinformation ranges from 20% to 80%
Freeman et al. (2022)	Large-scale survey	UK sample (United Kingdom)	Conspiracy beliefs are intertwined with general institutional distrust
Garry et al. (2022)	Methodological critique and survey	Conspiracy belief measures (United Kingdom)	Measurement design can systematically influence findings
Sütcü et al. (2022)	Text mining and content analysis	1,258 anti-vaccine tweets (Türkiye)	“Plandemic,” concerns about side effects, and biological weapon themes are prominent
Yılmaz & Bilen (2022)	Qualitative meaning-making analysis	Vaccine hesitancy narratives (Türkiye)	Hesitancy is shaped through meaning-making processes within online networks
Davidson et al. (2023)	Conceptual and policy analysis	Platform API regimes (International)	Platform-controlled data access threatens open science
Özen & Topbaş (2023)	Review	Turkish literature (Türkiye)	Infodemic management is directly associated with digital health literacy
Blakey (2024)	Case narrative and interview	Researchers’ experiences (International)	The closure of academic data access and the decline of transparency

Study	Method	Data and Context	Key Findings
Freelon et al. (2025)	Historical and normative analysis	Access regimes of six platforms (International)	The post-API era of data access and platform-induced vulnerability
van der Linden et al. (2025)	Consensus statement	Psychology literature (International)	Evidence-based principles for combating health misinformation

3.4. Content Analysis Coding Framework

The findings obtained from the reviewed literature were recoded around pre-existing theoretical categories, in line with the ‘directed content analysis’ approach defined by Hsieh and Shannon (2005). In this approach, coding categories are derived not from the data but from existing theory and research findings, and are subsequently supported by concrete examples. The table below summarises the five core categories developed within the scope of this study, which may also be utilised in future original content analysis studies.

Table 3. The directed content analysis coding framework used in the study

Category	Subdimensions	Relevant Literature
Source Type	Official health institution, journalistic source, unverified individual account, account suspected of being a bot/troll	Broniatowski et al. (2018)
Type of Misinformation	False causality, distorted statistics, conspiracy narrative, fabricated expert reference	Kata (2010); Wang et al. (2019)
Emotional Tone	Fear, anger, ridicule/derision, reassuring/calm tone	Vosoughi et al. (2018)
Institutional Trust Discourse	Supporting the institution, questioning the institution, directly rejecting the institution	Freeman et al. (2022)
Engagement and Dissemination	Number of reposts, number of replies, rate of dissemination	Cinelli et al. (2020)

In this study, the framework has been used to reinterpret the findings drawn from the existing literature in terms of these categories; it is also capable of serving as a basis for an original coding study to be carried out in the future. The categories are not strictly delineated; ‘institutional trust discourse’ and ‘emotional tone’ often overlap. This overlap, however, is not a flaw in the framework, but rather a consequence of the multidimensional nature of the phenomenon.

4. FINDINGS

4.1. Types of Misinformation and Patterns of Prevalence

The reviewed literature indicates that misinformation regarding COVID-19 vaccines is concentrated in three predominant types: exaggerated or fabricated claims about side effects, misinformation regarding vaccine composition (for example, claims that the vaccine alters genetic material) and conspiracy narratives questioning the legitimacy of the vaccine development process. Wang et al.'s (2019) review notes that these three types are distributed in varying proportions across different platforms, but that a common feature of each is the establishment of a simplified cause-and-effect relationship. Consistent with Kata's (2010) analysis, this content is typically built upon the implicit assumption that official institutions are deliberately withholding information, which serves as a direct attack on institutional trust. The target is not the information itself, but the institution's motives.

A systematic review by Suarez-Lledó and Alvarez-Gálvez (2021) demonstrates that the prevalence of misinformation varies according to platform architecture: on short-form text platforms (such as X), misinformation is generally produced in a claim-based format without providing evidence, whereas on video-based platforms, it is produced in a longer, narrative format. This differentiation suggests that organisational communication strategies must be tailored to the specific platform; short, direct correction messages that are effective on X may prove insufficient in combating narrative-based misinformation on video-based platforms.

4.2. The Impact of Perceived Source Reliability on Organisational Trust

One of the most striking findings of this study is that the relationship between source reliability and organisational trust is not direct, but is mediated through intuitive processes. When assessed in the light of Metzger and Flanagin's (2013) framework, although posts by official health organisations carry formal/visible signs of credibility (corporate logo, data source/professional language), these signs do not automatically instil trust in the majority of users. Instead, users conduct a secondary assessment of credibility by examining how the content is received within their own social circles—that is, by looking at comments, reposts and replies.

When considered alongside Schmidt et al.'s (2018) 'echo chamber' finding, this suggests that institutional trust on social media is a network-based phenomenon rather than an individual

one. When a healthcare organisation's post reaches a network cluster lacking trust, it is met with scepticism despite possessing the same formal indicators of credibility; indeed, it can sometimes become a focal point for comments suggesting that 'the organisation is concealing its true intentions'. It is clear that organisational communication must focus not only on the quality of content but also on which network clusters it reaches and through which intermediary users (influencers/local healthcare workers). The route is just as important as the message.

Özen and Topbaş's (2023) review highlights the role of digital health literacy in this regard. As individuals' information evaluation skills improve, there is a growing tendency to focus on the internal consistency and verifiability of content rather than on the formal legitimacy markers of the source. Institutional trust can be strengthened in the long term not only through communication tactics but also through investments in health literacy at a societal level.

An evaluation of these three findings (Metzger and Flanagin, 2013; Schmidt et al., 2018; Özen and Topbaş, 2023) taken together indicates that institutional trust must be built simultaneously across three distinct levels: the development of health/media literacy at the individual level; the support of trusted intermediaries/contact points and local interaction points at the network level; and, at the institutional level, the adoption of a communication style that prioritises the verifiability of content over formal authority. It is not surprising that interventions focusing on only one of these three levels result in the limited and short-lived effects frequently observed in the literature.

4.3. Emotional Framing and Diffusion Dynamics

When the findings of Vosoughi, Roy and Aral (2018) are considered alongside the multi-platform analysis by Cinelli et al. (2020), it becomes apparent that emotional intensity is the key factor determining the rate at which anti-vaccine content spreads. Framing based on fear and anger generates significantly higher levels of engagement than the reassuring/informative tone typically favoured by official institutions. This is precisely where the dilemma for corporate communicators lies: whilst increasing emotional intensity may boost engagement in the short term, it can conflict with perceptions of institutional seriousness and credibility. The dilemma is real and not easily resolved.

Pennycook and colleagues' (2020) 'truth-seeking impulse' approach appears to offer a partial solution to this dilemma. Rather than attempting to persuade users directly with an emotional

counter-message, brief and neutral reminders that encourage users to consider accuracy before sharing can reduce the likelihood of misinformation based on emotional framing being shared. Building corporate trust, therefore, can be supported not only through content production but also through platform- or design-level interventions such as pre-sharing warnings and verification labels. The point of intervention is not the content, but the architecture.

4.4. Anti-Authority Discourse and Conspiracy Narratives

The findings of Freeman et al. (2022) show that the majority of anti-vaccine content forms part of a broader anti-authority worldview, rather than being merely an isolated instance of misinformation. According to this view, official institutions (ministries of health, pharmaceutical companies and international health organisations) operate within a network of hidden interests and conflicts of interest. This framework is not the sort that can be resolved by correcting a single piece of misinformation; the correction attempt itself can be reinterpreted within the same conspiracy framework as ‘an institution’s attempt to defend itself’.

Findings from the bot analysis conducted by Broniatowski et al. (2018) indicate that this pattern is deliberately fuelled by organised actors. The intervention of Russian troll accounts in the vaccine debate points to a strategy aimed at eroding the general legitimacy of institutional authority by polarising the debate itself, rather than taking a direct anti-vaccine stance. In this respect, the loss of trust in institutions is sometimes not a direct target, but rather a by-product of a broader strategy of social polarisation. The target is not the vaccine, but authority itself.

4.5. The Limited Impact of Corrective Interventions

Findings in the literature indicate that the impact of corrective interventions by healthcare organisations varies significantly depending on the target audience’s pre-existing attitudes. The experimental findings of Pennycook et al. (2020) show that fact-based interventions have a significant effect on users who have not yet formed a firm opinion, but that this effect is virtually negligible among users with strongly anti-vaccine attitudes. A practical implication regarding how to prioritise corporate communication resources emerges from this: fact-checking campaigns conducted with limited resources should prioritise the undecided middle ground rather than targeting the already convinced anti-vaccine audience.

The findings of Roozenbeek and colleagues (2020) also support this approach; individuals with high levels of scientific literacy and general trust in institutions tend to question misinformation of their own accord, even when confronted with it. A long-term institutional trust strategy should therefore not be limited to corrective measures during a crisis, but should also include a sustained investment in communication that fosters scientific literacy and general trust in institutions at a societal level prior to a crisis.

4.6. Application of the Coding Framework to the Literature

When the findings presented so far are mapped back to the five-category coding framework defined in Chapter 4, a pattern emerges. The framework has been applied not to original contributions in this study, but to the findings of the reviewed literature; each category highlights which studies provide evidence at what level and in which categories the evidence remains weak (see Table 4).

Table 4. Mapping of coding categories to the reviewed literature

Category	Corresponding Concept in the Literature	Type and Strength of Evidence	Research Gap
Source Type	Official institutional accounts competing for visibility on the same level as bot and troll accounts (Broniatowski et al., 2018; Cinelli et al., 2020)	Platform data; strong	The direct effect of source type on perceived trustworthiness has not been measured
Type of Misinformation	Claims about adverse effects, misinformation concerning vaccine content, and conspiracy narratives (Kata, 2010; Wang et al., 2019; Sütçü et al., 2022)	Review and content analysis; strong	The relative effect sizes across different types are unknown
Emotional Tone	Fear- and anger-based framing accelerating the spread of information (Vosoughi et al., 2018; Wang et al., 2019)	Network analysis; strong	The transfer of emotional tone to institutional trust is inferred indirectly
Institutional Trust Discourse	The interrelationship between conspiracy beliefs and general institutional distrust (Roozenbeek et al., 2020; Freeman et al., 2022)	Survey; moderate to strong	The direction of causality remains unclear due to the cross-sectional design
Engagement Level	High engagement contributing to perceptions of credibility (Metzger & Flanagin, 2013; Schmidt et al., 2018)	Platform data and theory; moderate	The effect of engagement thresholds on trust has not been measured

The mapping highlights two points simultaneously. Firstly, the strength of the evidence is not evenly distributed across the categories: whilst the ‘type of misinformation’ and ‘emotional tone’ categories are supported by large-scale network analyses and systematic reviews, the ‘institutional trust discourse’ category relies predominantly on survey data, and the ‘level of engagement’ category on platform data. Secondly, and more importantly, the intersections between categories are where the evidence is weakest; for example, the specific impact on institutional trust when a particular type of misinformation is combined with a particular emotional tone has not been directly measured. Thus, the framework’s primary function becomes apparent here: rather than organising existing findings, it highlights which cells remain empty.

5. DISCUSSION

5.1. Methodological Tensions in the Literature and the Limits of the Evidence

The findings presented so far may give the impression that the literature paints a relatively consistent picture. On the other hand, scientific integrity requires us to acknowledge that this consistency is not absolute. The findings of Freeman et al. (2022) regarding the prevalence of conspiracy beliefs, for example, have been questioned from a methodological perspective. Garry, Ford and Johns (2022) pointed out that Freeman and colleagues’ questionnaire design offered only one ‘disagree’ option against four ‘agree’ options, and that there was no ‘don’t know’ option; they argued that this unbalanced scale structure could overstate the prevalence of conspiracy beliefs. It was found that when a balanced scale was used, the rate of support for conspiracy beliefs fell significantly below the level reported by Freeman and colleagues. This criticism serves as a reminder that the findings of a single study should not be taken as absolute truth, and that the measurement tool itself carries a layer of interpretation.

This methodological debate points to a broader issue: the majority of research on misinformation and institutional trust relies on self-reported survey data. The relationship between a person stating that they ‘agree’ with a conspiracy statement and the extent to which this belief actually influences their health behaviour is often assumed rather than directly observed.

Although the experimental design by Loomba et al. (2021) constitutes an exception in this regard, studies validated by behavioural data—that is, actual vaccination records or actual sharing behaviour—remain in the minority across the field. This situation also constitutes a

limitation of the synthesis presented in this study: whilst the synthesised findings provide strong evidence at the level of attitudes and intentions, the evidence base regarding actual behavioural outcomes is relatively weaker.

A similar caveat applies to the critique of the ‘knowledge deficit’ model, which is a practical extension of Kata’s (2010) discussion of the postmodern framework of knowledge. This model assumes that the fundamental reason for believing misinformation is a lack of knowledge, and therefore that the solution lies in providing more and more accurate information. Kata’s findings and the discussion on source reliability addressed in this study demonstrate that the model falls short when it comes to anti-vaccine discourse. However, this does not imply that information serves no purpose. On the contrary, the findings suggest that accurate information is a necessary but not, on its own, sufficient condition: unless it is accessed via a reliable source and a trustworthy network, the likelihood of accurate information leading to behavioural change remains low.

5.2. The Turkish Context: Comparing Local Findings with International Patterns

It is necessary to compare the picture emerging from the international literature with data from Turkey in order to ascertain how much of the pattern is universal and how much is context-specific. The study by Sütçü et al. (2022), which analysed 1,258 tweets shared with anti-vaccine hashtags in Turkey using text mining and content analysis, provides a suitable basis for this comparison. The researchers categorised the posts under eighteen themes; the emphasis on the ‘plandemic’, concerns about post-vaccination side effects, and the claim that the vaccine was produced as a biological weapon as part of a global project were identified as the prominent themes (Sütçü et al., 2022).

These three themes correspond almost exactly to the three dominant types of misinformation derived from the international literature in Chapter 5: concerns about side effects correspond to the first type; the claim that the vaccine is a biological weapon corresponds to misinformation regarding vaccine composition; and the emphasis on ‘plandemic’ corresponds to the conspiracy narrative questioning the legitimacy of the vaccine development process. Indeed, the study by Porsuk and Cerit (2021), which examined entries on Ekşi Sözlük, and the research by Yılmaz and Bilen (2022), which analysed the processes of making sense of vaccine hesitancy in Turkey, also point to a similar picture. Akyüz’s (2020) analysis of fake

news circulating in Turkey during the pandemic, meanwhile, demonstrates that the same pattern was present in the early months of the outbreak, even before the vaccine debate began.

The case of Turkey is not an exception to the international pattern, but rather a confirmation of it. However, one should not treat this overlap as absolute. On closer inspection, what overlaps is the thematic content of misinformation; how institutional trust interacts with this content, however, may vary from country to country. Roozenbeek and colleagues' (2020) five-country comparison demonstrated that the same content produces different effects in societies with varying levels of trust. The level of trust in healthcare institutions in Turkey and the relationship between this level and political affiliation have not yet been measured as systematically in the existing Turkish literature as they have in international studies. Consequently, the conclusions that can be drawn from this comparison are limited: the content of misinformation is common, but the magnitude of its impact remains an open question.

5.3. The Post-API Era: The Impact of Platform Transformation on Research Feasibility

A significant portion of the empirical evidence underpinning this review was generated during the period when the X platform was open to academic data access. That period has now come to an end. The process that Freelon (2018) termed the 'post-API era' began with platforms restricting access to research data; in the case of X specifically, it reached a sharp turning point in 2023 with the termination of the free academic access programme, following the change of ownership in 2022 (Blakey, 2024). An analysis by Freelon and colleagues (2025), comparing the access regimes of six platforms, reveals that this restriction is not unique to X, but is experienced most severely on X.

This shift has three implications for this study. The first is methodological: the rationale for opting to synthesise the existing literature rather than collecting original data in Chapter 4 is, given the cost of access, not only one of reliability but also one of practical feasibility. Secondly, it relates to the evidence: as the majority of the studies examined are based on data collected between 2018 and 2022, the extent to which the findings remain valid under today's platform architecture cannot be directly tested. Thirdly, and more generally, as Davidson et al. (2023) point out, platform-controlled data access regimes directly threaten the principle of open science, undermining independent researchers' ability to verify platform-sourced claims.

It is possible to establish a direct link here with the debate on institutional trust. The ability to independently assess the communication effectiveness of healthcare organisations on social media depends on the data on that platform being open to research. When data is restricted, the access and engagement figures reported by the organisations themselves can no longer be verified from the outside. Overall, the decline in platform transparency is not merely a methodological issue, but also a matter of institutional accountability. However, this observation does not diminish the value of the existing literature; it merely serves as a reminder that such literature pertains to a specific historical period.

5.4. Interpreting the Findings within the Conceptual Framework

When the findings are considered in light of the conceptual framework established in the second chapter, three conclusions emerge. Firstly, the component mismatch in Mayer et al.'s (1995) tripartite model is empirically supported: the dominant theme of anti-vaccine content is not the institution's lack of knowledge, but the claim that the institution is concealing something. The 'pandemic' and biological weapon themes identified by Sütçü et al. (2022), as well as the finding on conspiracy beliefs by Freeman et al. (2022), all point in the same direction. Whilst institutions strive to prove their competence, the debate continues to revolve around the issue of honesty.

Secondly, Metzger and Flanagin's (2013) intuitive evaluation framework aligns with the finding that source credibility is established not by formal indicators but by in-network reactions. This implies that institutional trust is a network-level phenomenon rather than an individual attitude. Thirdly, the limited impact of correction efforts is consistent with the evidence gathered in the consensus statement by van der Linden et al. (2025): correction alone is insufficient against misinformation; interventions must be designed in conjunction with components of preparatory measures and source trust. Taken together, all three theoretical strands reach the same conclusion. Misinformation is not a knowledge gap but a trust gap; the correct target of intervention is therefore trust, not knowledge.

6. LIMITATION

The most fundamental limitation of this study is that no primary content analysis was conducted on an original social media dataset; instead, the existing literature was systematically synthesised. Whilst this approach offers advantages in terms of reliability, it raises the question of the extent to which the findings for the period under review accurately

reflect the significant structural and policy changes experienced by the X platform since 2021 (algorithm updates, changes to moderation policies, and alterations to the platform's name and ownership structure). The second limitation is that the study relies heavily on the international literature in English; discourse patterns specific to Turkish-speaking user groups have been represented by only a limited number of local sources (Özen and Topbaş, 2023). Thirdly, as the study focuses on a single health topic (COVID-19 vaccines), it remains unclear to what extent the findings can be generalised to other health topics, such as the HPV vaccine, the flu vaccine or misinformation regarding general medication side effects. Fourthly, as discussed in Section 5.6, a significant portion of the evidence in this field consists of self-reported survey data; this leads both to biases inherent in the design of the measurement tool and to the inability to directly observe the relationship between attitudes and behaviour.

Finally, as the concept of organisational trust itself is a multidimensional construct, the coding framework used in this study is only able to capture the discursive manifestations of trust and cannot directly measure the underlying psychological and social determinants.

7. CONCLUSIONS AND RECOMMENDATIONS

This study examined the relationship between health misinformation on social media and institutional trust, specifically focusing on COVID-19 vaccine-related posts on the X platform, through a structured literature review. The findings suggest that this relationship is characterised by a mutually reinforcing cycle rather than a unidirectional causality: low institutional trust makes individuals more susceptible to misinformation, whilst exposure to misinformation reinforces existing distrust. Breaking this cycle appears possible not only through the increased production of accurate information but also through structural interventions that strengthen the perception of source reliability. Recalling Mayer, Davis and Schoorman's (1995) tripartite framework, it should not be forgotten that whilst organisations often invest in the competence component, it is the perception of integrity that is most frequently eroded.

Within this framework, three concrete recommendations can be developed. Firstly, healthcare organisations' social media communication should be designed not merely to convey information, but with the aim of building trust through networks; this requires collaboration with local healthcare workers, patient communities and trusted intermediary users. Secondly, corrective campaigns should be prioritised whilst taking resource constraints into account,

targeting undecided user groups rather than strongly convinced opposing audiences. Thirdly, beyond short-term crisis communication, ongoing investment in scientific and digital health literacy at a societal level forms the most solid foundation for long-term institutional trust.

In the Turkish context, these recommendations may have concrete implications. Given the digital health literacy gap highlighted by Özen and Topbaş (2023), the conduct of social media communication by healthcare institutions not only through centralised institutional accounts but also via intermediaries—such as GPs, community health centres and local healthcare workers—who already possess a certain level of trust capital, could serve as a concrete application of the principle of network-based trust-building. The fact that such intermediaries are already engaged in one-to-one relationships with their patients can turn the ‘sense of consistency’ defined by Metzger and Flanagin (2013) to the institution’s advantage, as the information comes from a source the patient already trusts. However, this strategy also has its limits in terms of scalability: a communication model reliant on local intermediaries may lead to a proliferation of conflicting voices if it is not synchronised with the consistent and up-to-date messages that central institutions need to produce rapidly during large-scale crises.

This tension raises a clear question that future application-oriented research must address: how the balance between central consistency and local reliability can be established, particularly for Turkish-speaking user groups; this emerges as a directly related follow-up research question that falls outside the scope of this study. None of these recommendations, of course, should be interpreted as a definitive formula. Given the methodological limitations discussed in Section 5.6, the evidence base currently provided by the literature indicates not which intervention works to what extent, but rather which mechanisms are most likely to be at work.

For future research, applying the content analysis coding framework developed in this study to a real sample—for example, a cluster of 50–100 posts gathered around a specific hashtag—would provide an opportunity both to test the framework’s validity and to document discourse patterns specific to Turkish-speaking user groups. Longitudinal studies validated by behavioural outcome data (such as actual vaccination rates) and recent comparative research focusing on how the structural transformations the X platform has undergone since 2021 have affected the dynamics of misinformation represent the most prominent gaps in the literature.

8. DECLARATIONS

Assessment: It has been assessed by internal and external consultants.

Ethics Committee Approval: This study is a review based on an examination of the existing literature and does not involve human or animal participants; therefore, it does not require ethics committee approval.

Conflict of Interest: The author declares that there is no conflict of interest.

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9. ETHICAL DECLARATION

The Istanbul Medisosal Education and Research Medical Journal's publication ethics: This is a national scientific journal in the field of health sciences that aims to ensure scientific research and publications are conducted in accordance with fundamental principles such as integrity, transparency, objectivity and respect for the findings and work of others, and which works to achieve this. The criteria of the Declaration of Helsinki have been taken into account.

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THE ROLE OF PHYSIOTHERAPY IN IRRITABLE BOWEL SYNDROME

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ABSTRACT

Irritable bowel syndrome (IBS) is characterised by abdominal pain, bloating and variable bowel habits (constipation, diarrhoea or a combination of both); it is diagnosed in the absence of any organic pathology and is one of the most common functional gastrointestinal disorders worldwide. According to the Rome IV criteria, the global prevalence of IBS ranges from 10–20 per cent, whilst in Turkey it has been reported to range from 8–15 per cent in various studies. A complex interplay of factors plays a role in the pathophysiology of the condition, including brain-gut axis dysfunction, visceral hypersensitivity, changes in gastrointestinal motility, low-grade inflammation, microbiota imbalance and psychosocial stress factors. The limited efficacy and potential for side effects of pharmacological treatments have led patients and clinicians to turn to non-pharmacological and holistic approaches; in this context, physiotherapy and rehabilitation methods have begun to attract increasing interest. This review summarises the pathophysiological foundations of IBS ; the efficacy of methods such as diaphragmatic breathing exercises, abdominal massage, exercise therapy, yoga and mind-body interventions, pelvic floor physiotherapy, biofeedback, electrotherapy, physical agents and

micro-physiotherapy on IBS symptoms is discussed in the light of the current literature. Current evidence suggests that regular aerobic exercise and diaphragmatic breathing techniques can reduce the severity of gastrointestinal symptoms, that abdominal massage can increase bowel motility, particularly in cases where constipation is predominant, and that yoga and mind-body interventions thereby providing symptomatic relief indirectly. However, due to methodological heterogeneity and limitations in sample size across studies, the level of evidence remains moderate to low. Consequently, it is considered that the inclusion of physiotherapy methods, alongside pharmacological and dietary treatments, within a personalised and multidisciplinary approach to IBS management may have a positive impact on patients' symptom burden and quality of life.

Keywords: Irritable bowel syndrome, physiotherapy, rehabilitation, diaphragmatic breathing, abdominal massage, pelvic floor

1. INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder characterised by abdominal pain or discomfort, accompanied by changes in bowel habits (frequency and/or consistency of stools), and diagnosed in the absence of any underlying structural or biochemical abnormality. Although the condition is not life-threatening, its recurrent and unpredictable symptoms have a significant negative impact on patients' daily activities, work performance and overall quality of life. IBS is one of the most common reasons for consultations at gastroenterology outpatient clinics worldwide and also places a significant economic burden on healthcare systems.

1.1. Definition, Rome IV Criteria and Epidemiology

The Rome IV criteria are currently used for the diagnosis of IBS. According to these criteria, a diagnosis of IBS can be made provided that abdominal pain associated with bowel movements has been present on at least four days per month over the past three months, accompanied by at least one of the following: a change in bowel movement frequency or a change in stool consistency or appearance, and that symptoms began at least six months prior to diagnosis.

The Rome IV criteria provide a more specific diagnostic framework by removing the term 'discomfort'—which appeared in the previous Rome III criteria—from the diagnostic criteria, as this term had led to differences in translation and cross-cultural interpretation. In the classification using the Bristol Stool Form Scale, IBS is divided into four subtypes based on the predominant stool characteristic: constipation-predominant IBS (IBS-C), diarrhoea-predominant IBS (IBS-D), mixed-type IBS (IBS-M) and unclassified IBS. Global prevalence estimates vary between 10 per cent and 20 per cent, depending on the diagnostic criteria used and the geographical region, and the condition is approximately twice as common in women as in men. The condition usually begins in young adulthood, may persist into middle age, and tends to show a decline in prevalence in later life.

1.2. Epidemiology of Irritable Bowel Syndrome in Turkey

Community-based studies conducted in Turkey report that the prevalence of IBS varies between 8 per cent and 15 per cent, depending on the diagnostic criteria used. In a cross-sectional study conducted among adults attending primary care centres, an assessment using

the Rome III criteria revealed that a significant proportion of participants had previously been diagnosed with IBS, and that the vast majority of this group were women (Doğan Kaya, 2019).

These findings demonstrate that IBS is a common health problem frequently encountered in clinical practice in Turkey, requiring a careful diagnostic and treatment approach across different levels of healthcare, from primary to tertiary care.

1.3. Pathophysiology: The Brain-Gut Axis and the Multifactorial Model

Although the pathophysiology of IBS has not yet been fully elucidated, it is now accepted that the condition should be assessed within the framework of a multifactorial model. In this model, the following mechanisms play a key role: (1) bidirectional communication dysfunction in the gut-brain axis, (2) visceral hypersensitivity, (3) changes in gastrointestinal motility, (4) imbalance in the gut microbiota (dysbiosis), (5) low-grade mucosal inflammation and impaired intestinal barrier function, (6) genetic predisposition, and (7) psychosocial stress factors. Each of these mechanisms may contribute to varying degrees from patient to patient, which explains the clinical heterogeneity of IBS.

The gut-brain axis refers to the bidirectional communication network between the central nervous system, the autonomic nervous system, the enteric nervous system and the gut microbiota. A disruption in this axis can lead both to stress and mood at the central level affecting bowel function and to afferent signals from the gut influencing the perception of anxiety and pain in the central nervous system. This two-way relationship explains why physiotherapy-based stress management, breathing exercises and mind-body interventions are considered a sensible complementary approach in the treatment of IBS.

2. AIM

The aim of this review is to examine the pathophysiological basis and clinical characteristics of IBS and to evaluate the role of physiotherapy and rehabilitation methods in the management of IBS symptoms in the light of the current literature. The scope of the study includes: the clinical subtypes of IBS and associated comorbidities; the pathophysiological mechanisms related to physiotherapy; diaphragmatic breathing exercises; abdominal massage; exercise therapy, yoga and mind-body interventions, pelvic floor physiotherapy and

biofeedback, electrotherapy and physical agents, micro-physiotherapy approaches, evidence derived from recent clinical trials and patient education are systematically addressed. This review is intended to serve as a practical reference resource for clinicians working in the field of physiotherapy and rehabilitation, gastroenterology specialists and undergraduate students studying in this field.

3. METHODOLOGY

This study is a narrative (traditional) literature review conducted to evaluate the role of physiotherapy and rehabilitation interventions in irritable bowel syndrome (IBS). As part of the study, the current literature on the pathophysiology, clinical characteristics and subtypes of IBS, as well as physiotherapy approaches, was reviewed. Clinical studies and reviews concerning diaphragmatic breathing exercises, abdominal massage, exercise therapy, yoga and mind-body practices, pelvic floor physiotherapy, biofeedback, electrotherapy, physical agents and micro-physiotherapy were evaluated. The findings from the literature were analysed comparatively in terms of the effects of physiotherapy methods on IBS symptoms, bowel function, stress and quality of life; the levels of evidence for the methods and the methodological limitations in the existing literature were discussed.

4. FINDINGS

4.1.Clinical Characteristics And Subtypes Of Ibs

The clinical presentation of IBS centres on abdominal pain, a feeling of bloating, flatulence and variable bowel habits. Abdominal pain is usually cramp-like and may be partially or completely relieved by a bowel movement. A sensation of bloating is reported as the most distressing symptom by a significant proportion of patients and tends to increase throughout the day. The severity and frequency of symptoms may fluctuate over time; flare-ups may occur during periods of stress, following the consumption of certain foods, or at specific times during the menstrual cycle.

4.1.1. Subtypes

- Constipation-predominant IBS (IBS-C): In a significant proportion of bowel movements, the stool is hard or pellet-like; this is characterised by infrequent bowel movements, excessive straining and a feeling of incomplete evacuation.

- Diarrhoea-predominant IBS (IBS-D): In a significant proportion of bowel movements, the stools are loose, watery or mushy, characterised by a sudden and urgent need to pass stools.
- Mixed-type IBS (IBS-M): This presents as periods of both constipation and diarrhoea occurring simultaneously or in succession.
- Unclassified IBS: This encompasses cases that do not fit a distinct subtype and exhibit mixed or variable stool characteristics.

Distinguishing between subtypes is important both in selecting pharmacological treatment and in shaping the physiotherapy approach. For example, whilst abdominal massage and pelvic floor exercises are prioritised in cases where constipation predominates, stress management and relaxation techniques are more prominent in cases where diarrhoea predominates.

4.1.2. Associated Comorbidities

IBS is frequently observed alongside other chronic pain syndromes and psychiatric conditions. Fibromyalgia, chronic fatigue syndrome, interstitial cystitis and chronic pelvic pain syndrome are among the conditions frequently reported to co-occur with IBS. It has been reported that IBS comorbidity is common in patients with fibromyalgia, and that these two conditions share common pathophysiological mechanisms (central sensitisation, autonomic dysfunction). This association indicates that physiotherapists should also enquire about IBS symptoms when assessing patients with fibromyalgia. Anxiety and depression are reported as common co-occurring psychiatric conditions in a significant proportion of IBS patients.

These comorbidities can both increase the perceived severity of the condition and negatively affect the response to treatment. Furthermore, in female patients, pelvic floor dysfunction (dyssynergic defecation, pelvic floor muscle spasm) may overlap with IBS symptoms, highlighting the need for differential assessment and specialised pelvic floor

4.2. Mechanisms Related To Physiotherapy In The Pathophysiology Of Ibs

To understand how physiotherapy methods may influence IBS symptoms, it is necessary to review three key mechanisms in the pathophysiology of the condition that can be linked to physical interventions: autonomic nervous system balance, the mechanical role of the

abdominal and pelvic floor muscles, and the effect of respiratory patterns on bowel function via the diaphragm.

4.2.1. The Autonomic Nervous System and the Stress-Gut Axis

The balance between the sympathetic and parasympathetic nervous systems plays a decisive role in gastrointestinal motility and secretion. Whilst parasympathetic activation (vagal tone) has a regulatory effect on bowel motility and supports digestion, sustained sympathetic activation (the stress response) can lead to irregularities in bowel function and an increase in visceral sensitivity. It has been reported that autonomic nervous system indicators, such as heart rate variability (HRV), are frequently impaired in patients with IBS. It has been suggested that certain physiotherapy techniques, such as manual lymphatic drainage and abdominal massage, may indirectly contribute to bowel function by increasing parasympathetic activity and improving HRV parameters (Drouin et al., 2020).

4.3. The Mechanical Role of the Abdominal and Pelvic Floor Muscles

The abdominal wall muscles (rectus abdominis, transversus abdominis, and the internal and external oblique muscles) and the pelvic floor muscles play a mechanically

significant role in regulating intra-abdominal pressure and propelling intestinal contents. Weakness, excessive tension or poor coordination (dyssynergy) in these muscle groups may contribute to defecation difficulties, particularly in cases of IBS where constipation is predominant. Electromyographic studies have shown that the activation patterns of the anterolateral abdominal wall muscles during rectal filling and emptying may differ in individuals with functional constipation compared to healthy individuals.

4.4. Respiratory Pattern, Diaphragm Function and Visceral Motility

The diaphragm functions not only as the primary respiratory muscle but also as a structure that supports the mechanical motility of the intra-abdominal organs. The diaphragm's rhythmic up-and-down movement can create a gentle massaging effect on the liver, stomach and intestines, thereby supporting visceral blood flow and peristalsis. A shallow and rapid chest-type breathing pattern is frequently associated with increased sympathetic activation and chronic stress; this condition can lead to a reduction in diaphragmatic mobility and, consequently, an adverse effect on visceral functions. For this reason, diaphragmatic

Breathing Training Is Emerging As A Physiotherapy Approach That Targets Both Autonomic Nervous System Balance And Mechanical Visceral Motility.

4.5. General Framework Of Current Pharmacological And Dietary Treatment Approaches

Pharmacological approaches to the treatment of IBS are tailored to the patient's predominant symptom. In cases where constipation is predominant, fibre supplements, osmotic laxatives and secretagogues are used; in cases where diarrhoea is predominant, anti-diarrhoeal agents and bile acid sequestrants are used; and when abdominal pain and bloating are the main symptoms, antispasmodics and low-dose tricyclic antidepressants are preferred. The low-FODMAP diet has emerged in recent years as a dietary approach that is gaining increasing acceptance in the management of IBS. However, a significant proportion of pharmacological treatments are based on low to moderate levels of evidence and often prove insufficient in achieving complete symptom control. These limitations are directing both patients and clinicians towards non-pharmacological and holistic treatment options. Cognitive behavioural therapy and gut-focused hypnotherapy are listed as second-line treatment options in European and North American gastroenterology guidelines. In this context, physiotherapy-based approaches are also being considered as a complementary treatment component that both directly targets gastrointestinal function and reduces stress and Autonomic Imbalance.

4.6. The Role Of Physiotherapy In The Treatment Of Ibs: A General Overview

Physiotherapy should be positioned as an approach that aims to complement, rather than replace, pharmacological treatment in the management of IBS. The main interventions that physiotherapists can offer to IBS patients include: diaphragmatic breathing and relaxation training, abdominal massage, personalised exercise programmes, yoga and mind-body techniques, pelvic floor assessment and biofeedback, selected physical agents (electrotherapy, balneotherapy) and manual techniques such as micro-physiotherapy. In a review published in the Russian literature, it is stated that IBS is a leading pathology among functional gastrointestinal disorders and that, in cases where pharmacological treatment proves insufficient, various physiotherapeutic methods such as interferential currents, cryotherapy, sinusoidal modulated currents, pulsed magnetic fields and balneo-peloidotherapy may help to normalise bowel motor function through their analgesic and sedative effects (Filimonov et al., 2013).

When planning a physiotherapy programme, the patient's predominant subtype (IBS-C, IBS-D, IBS-M), accompanying comorbidities (fibromyalgia, anxiety, pelvic floor dysfunction) and individual preferences should be taken into account. For example, whilst abdominal massage and pelvic floor exercises may be prioritised in a patient with predominant constipation, diaphragmatic breathing and relaxation techniques may take precedence in a patient with pronounced stress-induced flare-ups.

4.7. Diafragmatic Breathing Exercises

Diaphragmatic breathing is a breathing pattern characterised by the active and deep engagement of the diaphragm, in contrast to shallow chest breathing. This technique both promotes a general relaxation response by increasing activation of the parasympathetic nervous system

and supports visceral motility by enhancing the diaphragm's mechanical massage effect on the intra-abdominal organs. In a randomised controlled trial conducted in paediatric patients with chronic functional constipation, it was demonstrated that the combination of diaphragmatic breathing exercises with abdominal muscle training and abdominal massage significantly increased the frequency of bowel movements compared with laxative treatment alone (Silva et al., 2013).

4.7.1. Principles of Application

Diaphragmatic breathing training is usually initiated with the patient lying on their back, with one hand placed on the chest and the other on the abdomen. The patient is asked to breathe in such a way that, whilst the chest wall moves minimally, the abdominal

wall rises during inhalation and falls during exhalation. It is recommended that the training be carried out for 10–15 minutes a day, in 2–3 sessions, during the initial phase, and that it be gradually adapted to be performed whilst sitting and standing as well. The aim is that, through regular practice, patients will be able to consciously switch to diaphragmatic breathing during stressful moments and thereby manage acute symptom flare-ups.

4.7.2. The Effect of Breathing Exercises on General Relaxation and Autonomic Balance

It is known that slow, deep diaphragmatic breathing increases heart rate variability and reduces sympathetic over-activation. This physiological change may help to reduce stress-induced symptom flare-ups, which are frequently observed in patients with IBS. Furthermore, it has been reported that regular practice of breathing exercises improves sleep quality and reduces general anxiety levels; both of these factors are among the key variables that indirectly influence the severity of IBS symptoms.

4.8. Abdominal Massage

Abdominal massage is a manual physiotherapy method used in the management of constipation and associated abdominal pain, involving rhythmic and superficial pressure techniques applied in a clockwise direction, following the anatomical course of the colon. In a randomised controlled trial conducted by Lämås and colleagues (2009), 60 patients with constipation were divided into two groups: one receiving abdominal massage in addition to laxative treatment, and the other receiving laxative treatment alone; at the end of the eight-week follow-up, the group receiving abdominal massage showed significant improvement in the total score of the Gastrointestinal Symptom Rating Scale (GSRS), as well as in the subscores for constipation and abdominal pain and a significant increase in bowel movement frequency was also observed. A review by Sinclair (2011) noted that abdominal massage increases colonic motility through mechanical stimulation, whilst also promoting a general relaxing effect by supporting parasympathetic activation. In a comparative study by Drouin et al. (2020), the effects of manual lymphatic drainage, abdominal massage and electrical stimulation on functional constipation were compared; it was reported that all three methods led to positive changes in autonomic nervous system indicators and defecation parameters, with abdominal massage in particular yielding a significant improvement in the low-to-high frequency ratio.

4.8.1. Technique

Abdominal massage is performed whilst the patient is lying on their back, with their knees slightly bent and their abdominal muscles relaxed. The therapist applies gentle yet firm pressure using clockwise circular movements, starting from the ascending colon (right lower quadrant), moving across the transverse colon and down the descending colon towards the left

lower quadrant. The session usually lasts 15–20 minutes; it is recommended that the treatment be carried out several times a week, or that the patient be taught to perform daily self-massage as part of a home programme. It has been reported that self-massage may constitute a cost-effective alternative to professional treatment in the long term.

4.8.2. Contraindications

Active gastrointestinal bleeding, a flare-up of acute inflammatory bowel disease, recent abdominal surgery, certain stages of pregnancy and suspected acute abdominal conditions are among the situations in which abdominal massage is contraindicated. Therefore, before commencing abdominal massage, the patient's gastroenterological assessment must be complete and any organic pathologies must have been ruled out.

4.9. Exercise Therapy And Physical Activity

The effect of regular physical activity on IBS symptoms stands out as one of the physiotherapy approaches with the strongest evidence in the literature. In a randomised controlled trial conducted by Johannesson et al. (2011), which included patients with partially active IBS, participants were divided into a group that increased their physical activity to a moderate-to-vigorous level over 12 weeks and a control group that maintained their current lifestyle; a significant reduction in IBS symptom severity scores was observed in the physical activity group compared with the control group.

This study is regarded as one of the key pieces of evidence showing that regular physical activity reduces the risk of IBS symptoms worsening. A systematic review encompassing 14 randomised controlled trials reported that physical activity interventions such as yoga, tai chi and aerobic exercise significantly improved gastrointestinal symptoms. However, the same review emphasised that adherence to exercise programmes may be low; for example, a significant proportion of individuals with inflammatory bowel disease are physically inactive, and the rate of participation in health-promoting levels of physical activity remains quite low. This finding highlights the importance of motivational strategies and personalised programmes aimed at improving the sustainability of exercise programmes in IBS patients.

4.9.1. Principles of Exercise Prescription

- Low- to moderate-intensity aerobic exercise: Activities such as walking, cycling at a gentle pace or swimming are recommended for at least 3–5 days a week, for 20–30 minutes at a time.
- Gradual progression: Exercise intensity and duration should be increased gradually in line with the patient's symptomatic response; sudden and intense increases in exercise may lead to a flare-up of symptoms in some patients.
- Core stabilisation and abdominal muscle exercises: These may help to regulate intra-abdominal pressure and support pelvic floor function.
- Mind-body integration: Maintaining breath awareness during exercise is recommended to provide both physical and autonomic benefits. When planning an exercise programme, it should be borne in mind that excessively high-intensity or prolonged exercise may trigger gastrointestinal symptoms in some patients (exercise-induced gastrointestinal distress). Consequently, it has been reported that IBS is not sufficiently recognised or effectively managed, particularly among endurance athletes; this highlights the need to raise awareness of IBS within the sporting population.

4.10. Yoga and Mind-Body Interventions

Yoga is a mind-body practice that combines physical postures (asana), breathing techniques (pranayama) and meditation, and is one of the most frequently studied complementary approaches in the management of IBS. In a randomised controlled trial conducted by Schumann et al. (2018), a 12-week yoga programme was compared with a low-FODMAP diet; it was reported that both interventions resulted in a significant improvement in the severity of gastrointestinal symptoms, whilst the yoga group also showed positive changes in quality of life and body awareness indicators.

In a 12-week randomised controlled trial conducted by Kavuri and colleagues (2015), patients who underwent a comprehensive 'Restorative Yoga Module' showed significant improvements in Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS) and Irritable

Bowel Syndrome Quality of Life (IBS-QOL) scores compared to the waiting-list control group, as well as a marked reduction in anxiety and depression indicators. In a randomised study by D'Silva and colleagues (2023) evaluating a meditation and yoga programme delivered in a virtual setting, a significant reduction in IBS-SSS scores was reported in the treatment group compared with the control group, and it was emphasised that the programme was feasible and safe when delivered remotely.

However, in a recent systematic review and meta-analysis published in 2025, which included 11 randomised controlled trials (535 patients), it was noted that yoga did not provide a statistically significant advantage over control groups in terms of the severity of gastrointestinal symptoms, anxiety, depression or quality of life; furthermore, due to the marked methodological heterogeneity and high risk of bias among the included studies, larger-scale and methodologically robust studies are required before yoga can be recommended for the treatment of IBS. These conflicting findings indicate that the role of yoga in the treatment of IBS remains controversial and should be assessed in conjunction with individual patient preferences.

4.10.1. Other Mind-Body Approaches

Psychologically based interventions, such as gut-directed hypnotherapy and cognitive behavioural therapy, whilst not falling directly within the scope of physiotherapy, are generally implemented alongside physiotherapy approaches as part of a multidisciplinary IBS treatment team. It has been reported that gut-focused hypnotherapy can positively influence postprandial gastrocolic reflex activity, colonic motility and visceral hypersensitivity by regulating the brain-gut axis. Physiotherapists working in coordination with such psychological approaches whilst delivering relaxation training and breathing techniques may enhance treatment efficacy.

4.11. Pelvic Floor Physiotherapy and Biofeedback

In some cases of IBS where constipation is the predominant symptom, an underlying or concomitant condition of dyssynergic defecation (paradoxical contraction of the pelvic floor muscles during bowel movements) may be identified. In such cases, general IBS treatment alone may not be sufficient; a specialised pelvic floor assessment and biofeedback therapy may be required. Pelvic floor physiotherapy aims to teach the patient how to relax the pelvic

floor muscles correctly during defecation, using biofeedback techniques supported by anorectal manometry or superficial electromyography.

4.11.1. Assessment Process

Prior to pelvic floor physiotherapy, the patient's defecation pattern, straining difficulties, sensation of incomplete emptying and, where necessary, the need for digital support should be assessed in detail. During the physical examination, pelvic floor muscle tone at rest and during voluntary contraction should be assessed, as well as whether paradoxical contraction occurs during the defecation manoeuvre. Where deemed necessary, the diagnosis of dyssynergic defecation should be confirmed using advanced investigations such as anorectal manometry or defecography.

4.11.2. Biofeedback Therapy

In biofeedback therapy, pelvic floor muscle activity is presented to the patient via surface electromyography or pressure sensors in the form of visual or auditory feedback; the patient uses this feedback to achieve correct muscle coordination during defecation

(increased intra-abdominal pressure accompanied by pelvic floor relaxation). This treatment may provide more lasting symptomatic relief compared to standard laxative therapy, particularly in patients with IBS with predominant constipation

where dyssynergic defecation has been confirmed. Treatment is usually planned as weekly or fortnightly sessions, totalling 4–8 sessions

4.11.3. Reinforcement with a Home Exercise Programme

In addition to biofeedback sessions, educating patients on pelvic floor relaxation exercises they can perform at home and on the correct defecation posture (for example, optimising the anorectal angle by elevating the feet) contributes to making the treatment benefits permanent.

4.12. Electrotherapy and Physical Agents

Electrotherapy modalities have long been used as an approach in the treatment of IBS, particularly in Eastern European and Russian physiotherapy literature. In a review by Filimonov et al. (2013), it was reported that interferential currents, sinusoidally modulated

currents, pulsed magnetic field applications, cryotherapy and balneo-peloidotherapy (mineral water and mud baths), were reported to provide analgesic and sedative effects in different clinical forms of IBS, whilst also potentially contributing to the normalisation of bowel motility.

In a study by Shklyayev and colleagues, it was reported that sinusoidal-modulated current electrophoresis, administered in conjunction with chloride-bromide saline baths, may be an effective approach in the treatment of various forms of IBS. Furthermore, a study conducted on patients with lumbar spinal dorsopathy and associated IBS demonstrated that combined rehabilitation programmes (including exercise, electrotherapy and manual techniques) had positive effects on both spinal symptoms and associated gastrointestinal symptoms (Sevostyanova et al., 2018).

This finding highlights the importance of assessing concomitant IBS symptoms during musculoskeletal rehabilitation and, where necessary, incorporating them into the treatment plan.

4.12.1. Transcutaneous Electrical Nerve Stimulation (TENS)

When applied at low intensity to the abdominal region, TENS can reduce pain perception within the framework of the gate control theory and, in some studies, has been shown to have effects that support the balance of the autonomic nervous system. In cases of IBS where chronic abdominal pain is predominant, it is considered that TENS may be evaluated as a non-invasive and low-cost complementary approach; however, it should be noted that the level of evidence in this area remains limited and that further controlled studies are required.

4.13. Micro-Physiotherapy and Manual Therapy Approaches

Micro-physiotherapy is a manual therapy approach that aims to stimulate the body's self-healing mechanisms using micro-massage techniques applied with very light pressure. A study conducted by Grosjean and colleagues (2017) reported that this technique improved abdominal pain, bloating and bowel irregularities in patients with IBS. These findings suggest that micro-physiotherapy may be a viable option for patients seeking a non-pharmacological treatment alternative. However, the underlying mechanisms of action of micro-physiotherapy have not yet been fully explained scientifically, and the number and methodological quality of studies evaluating this method are limited. Therefore, the role of micro-physiotherapy in the

treatment of IBS should be assessed cautiously within the framework of evidence-based medicine as an experiential complementary approach, and it is expected to be supported by larger-scale randomised controlled trials.

4.13.1. Stress Management Programmes

In a classic controlled study conducted by Shaw and colleagues (1991), it was demonstrated that a stress management programme delivered by physiotherapists and relevant healthcare professionals was effective in reducing symptom severity in patients with IBS. These programmes typically include relaxation exercises, mindfulness-based techniques and training in recognising stress triggers. When physiotherapists deliver such programmes as part of a holistic approach, alongside diaphragmatic breathing and an exercise prescription, this can enhance the effectiveness of treatment.

4.14. Evidence from the Literature: Evaluation of Clinical Trials

When the current literature is evaluated as a whole, it is evident that the evidence regarding the effectiveness of physiotherapy approaches in IBS varies depending on the methodology. Exercise therapy stands out as the approach with the strongest and most consistent evidence; a randomised controlled trial by Johannesson et al. (2011) demonstrated that an increase in regular physical activity significantly reduced the severity of IBS symptoms. Abdominal massage also has moderate-quality evidence, particularly in cases where constipation is predominant, as supported by the study by Lämås et al. (2009). The literature on yoga and mind-body interventions presents conflicting results; whilst some individual randomised controlled trials (Kavuri et al., 2015; D'Silva et al., 2023) report positive results, a recent meta-analysis (2025) has shown that the overall effect is not statistically significant and that studies carrying a high risk of bias weaken the evidence base in this area.

This suggests that yoga can be offered as a complementary option depending on the individual patient's preference, but that there is not yet sufficient evidence to recommend it as standard treatment. Pelvic floor physiotherapy and biofeedback are recognised as targeted approaches that provide clinically meaningful improvement, particularly in cases of constipation-predominant IBS where dyssynergic defecation has been confirmed. Evidence regarding electrotherapy and physical agents, however, is largely based on studies from Eastern Europe,

whilst large-scale randomised controlled trials evaluating these methods in the Western literature appear to be limited (Filimonov et al., 2013; Sevostyanova et al.,

2018). Micro-physiotherapy and stress management programmes, whilst showing promising preliminary findings, are still considered to be at an early stage in terms of the level of evidence (Grosjean et al., 2017; Shaw et al., 1991). Overall, the current evidence suggests that, in IBS, physiotherapy yields the best results not as a stand-alone treatment, but

as part of a personalised, multi-component treatment package administered in conjunction with pharmacological and dietary approaches. This finding once again emphasises the importance of the biopsychosocial model and a multidisciplinary approach in the management of IBS.

4.15. An Illustrative Case Scenario for Clinical Practice

In light of the findings compiled from studies in the literature, illustrating the physiotherapy process for a typical patient with constipation-predominant IBS and mild anxiety symptoms may be useful in demonstrating how theoretical knowledge can be translated into clinical practice. Below is a fictional scenario, created for educational purposes, based on similar cases in the literature.

4.15.1. Referral and Assessment

A 28-year-old female office worker presents at the gastroenterology outpatient clinic with complaints of abdominal pain and bloating that have persisted for approximately one year and become more pronounced during stressful periods, along with infrequent bowel movements occurring only two to three days a week. The assessment revealed no organic pathology, and a diagnosis of constipation-predominant IBS was made according to the Rome IV criteria. The patient describes a sensation of incomplete evacuation during straining and is referred to the physiotherapy and rehabilitation outpatient clinic for a pelvic floor assessment.

4.15.2. Evaluation of the Physiotherapy Process

On evaluation, mild pelvic floor muscle tension and a paradoxical contraction pattern during defecation manoeuvres are identified. The treatment programme consists of four main components: (1) six sessions in total of biofeedback-assisted pelvic floor relaxation training, delivered twice weekly; (2) 10 minutes of diaphragmatic breathing exercises daily; (3) a

moderate-intensity walking programme for 20–30 minutes, three days per week; and (4) weekly instruction in abdominal self-massage following the course of the colon, with continuation as a daily home programme. At the end of the six-week follow-up period, the patient's defecation frequency has increased to five days per week, while difficulty with straining and the sensation of incomplete evacuation have markedly decreased. In addition, a reduction in the frequency of symptom exacerbations during periods of stress is observed.

The patient reports that they have begun to consciously practise the diaphragmatic breathing technique before stressful work meetings and that this predictably reduces episodes of abdominal pain. This hypothetical scenario represents a realistic clinical synthesis of physiotherapy components consistent with findings reported in the literature (Lämås et al., 2009; Silva et al., 2013; pelvic floor biofeedback studies).

4.16. Planning of the Treatment Programme and Multidisciplinary Approach

An effective physiotherapy programme for IBS should begin with a comprehensive assessment. Standardised assessment tools such as the IBS Symptom Severity Scale (IBS-SSS) and the IBS Quality of Life Questionnaire (IBS-QOL) should be used, while stool consistency should be documented using the Bristol Stool Form Scale. Levels of anxiety and depression should be screened using instruments such as the Hospital Anxiety and Depression Scale (HADS), and psychiatric or psychological consultation should be sought when necessary. In patients with suspected pelvic floor dysfunction, a detailed pelvic floor examination and, where indicated, anorectal function tests should be planned.

4.16.1. Graded Programme Model

The treatment programme can generally be planned using a graded approach: (1) in the first stage, patient education, diaphragmatic breathing and basic relaxation techniques are introduced; (2) in the second stage, abdominal massage, an individualised exercise prescription and, where necessary, pelvic floor assessment are incorporated; and (3) in the third stage, yoga or other mind–body interventions may be added according to the symptomatic response, while complementary physical modalities such as electrotherapy or balneotherapy may be considered in selected cases. At every stage of the programme, maintaining a symptom diary and reassessing IBS-SSS scores at regular intervals are recommended.

4.16.2. Multidisciplinary Team Approach

Considering the biopsychosocial nature of IBS, it is recommended that the treatment team adopt a multidisciplinary structure comprising a gastroenterologist, a specialist in physical medicine and rehabilitation or physiotherapist, a dietitian, and, when necessary, a psychologist or psychiatrist. This approach enables both the patient's gastrointestinal symptoms and accompanying psychosocial and musculoskeletal findings to be addressed comprehensively. Particularly in patients with comorbid conditions such as fibromyalgia or chronic pelvic pain, this multidisciplinary structure may play an important role in improving treatment outcomes.

5. DISCUSSION

The current literature indicates that, given the complex and multifactorial pathophysiology of IBS, single-dimensional treatment approaches are frequently insufficient. Physiotherapy approaches offer a flexible and individualised treatment option that can contribute to this multifaceted condition through both direct mechanical and visceral effects (abdominal massage and pelvic floor physiotherapy) and indirect effects mediated through the autonomic nervous system and the stress axis (diaphragmatic breathing, exercise and yoga). Although interventions such as exercise therapy and abdominal massage have comparatively stronger evidence, the level of evidence for approaches such as yoga and micro-physiotherapy appears to be more variable and, in some cases, contradictory. This highlights the importance of physiotherapists transparently communicating the current level of evidence to patients when making treatment recommendations and establishing realistic expectations.

At the same time, the absence of an overall significant effect for a particular intervention does not necessarily mean that the intervention cannot benefit specific subgroups, such as patients with high levels of stress or low body awareness. Therefore, the principle of an individualised approach remains applicable in this context. Pelvic floor physiotherapy and biofeedback emerge as targeted approaches with relatively strong evidence in patients with confirmed dyssynergic defecation; however, it is not appropriate to generalise this approach to all patients with IBS-C. Appropriate patient selection is a key determinant of treatment success. Similarly, the evidence concerning electrotherapy and balneotherapy is largely derived from specific geographical regions, particularly Eastern Europe, indicating that caution should be

exercised when considering the generalisability of these interventions to different healthcare systems and populations.

6. LIMITATIONS

There are important methodological limitations in the literature underpinning this review. A substantial proportion of the studies have small sample sizes, there are considerable differences in control-group designs, and the number of studies employing blinded assessment is limited. As observed in the yoga literature, findings concerning some physiotherapy approaches are inconsistent across studies, making it difficult to formulate generalisable clinical recommendations.

7. CONCLUSION AND RECOMMENDATIONS

Irritable bowel syndrome is a common functional gastrointestinal disorder characterised by abdominal pain, bloating and altered bowel habits, with a substantial impact on quality of life and a multifactorial pathophysiology. The limited effectiveness of pharmacological and dietary treatments increases the importance of non-pharmacological and holistic approaches; in this context, physiotherapy and rehabilitation methods are attracting increasing clinical interest. Diaphragmatic breathing exercises, abdominal massage, individualised exercise prescriptions, yoga and mind-body interventions, pelvic floor physiotherapy and biofeedback, selected electrotherapy and physical-agent applications, and micro-physiotherapy techniques are among the physiotherapy approaches that may be used in the management of IBS.

Among these approaches, exercise therapy and abdominal massage have comparatively stronger evidence, whereas the level of evidence for approaches such as yoga and micro-physiotherapy appears to be more limited and variable. The role of physiotherapy in IBS management is not to replace pharmacological treatment but rather to complement it and to establish an individualised treatment package according to the patient's symptom profile, IBS subtype and associated comorbidities. Treatment models planned within a multidisciplinary framework, bringing together gastroenterology, physical medicine and rehabilitation, dietetics and, when necessary, mental health professionals, are considered to represent the most effective approach to reducing symptom burden and improving quality of life in patients with IBS. Future randomised controlled trials based on standardised protocols and involving adequate sample sizes will strengthen the evidence base underlying current clinical

recommendations and enable the role of physiotherapy in IBS management to be defined more clearly.

7.1. Patient Education and Lifestyle Recommendations

Patient education is an integral component of an IBS physiotherapy programme. Patients should be informed, in clear and understandable language, that IBS does not cause organic damage but is a chronic functional disorder, and that symptoms may fluctuate in association with stress, dietary factors and lifestyle-related factors. Such education can reduce patients' anxiety regarding their symptoms and improve adherence to treatment.

General lifestyle recommendations, such as maintaining regular sleep patterns, regular meal times and adequate fluid intake, should accompany the physiotherapy programme. Patients should also be provided with practical strategies to identify stress triggers in their daily lives and to use diaphragmatic breathing or brief relaxation techniques when they encounter such situations. In addition, to ensure long-term adherence to the exercise programme, selecting types of physical activity that the patient enjoys and can readily integrate into their daily routine is an important factor contributing to treatment success.

Encouraging the habit of keeping a symptom diary can help patients identify their individual triggers and can also assist the treatment team in individualising the programme. The diary should include daily stress levels, sleep quality, physical activity, dietary habits and gastrointestinal symptoms.

7.2. Recommendations for Future Research

Future studies should evaluate standardised physiotherapy protocols specific to IBS subtypes using randomised controlled designs with adequate sample sizes, multicentre settings and blinded outcome assessment. Furthermore, studies comparing different physiotherapy approaches—for example, exercise alone versus a combination of exercise and diaphragmatic breathing—could determine which components make the most substantial contribution to treatment outcomes. Long-term follow-up studies could provide a clearer understanding of the persistence of physiotherapy-related benefits and its effects on relapse rates.

Finally, studies conducted in Türkiye and countries with similar sociocultural contexts, taking into account local dietary habits, work-related stress factors and healthcare access conditions,

may contribute to the adaptation of IBS physiotherapy practices to local contexts and to the development of more effective clinical guidelines.

8. DECLARATIONS

Assessment: It has been assessed by internal and external consultants.

Ethics Committee Approval: This study is a review based on an examination of the existing literature and does not involve human or animal participants; therefore, it does not require ethics committee approval.

Conflict of Interest: The author declares that there is no conflict of interest.

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Author Contribution: The author was solely responsible for the design of the study, the literature review, the analysis and the writing of the manuscript.

9. ETHICAL DECLARATION

The Istanbul Medisosal Education and Research Medical Journal's publication ethics: This is a national scientific journal in the field of health sciences that aims to ensure scientific research and publications are conducted in accordance with fundamental principles such as integrity, transparency, objectivity and respect for the findings and work of others, and which works to achieve this. The criteria of the Declaration of Helsinki have been taken into account.

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THE AETIOLOGY, CLINICAL ASSESSMENT AND MANAGEMENT OF DYSPEPSIA: AN ANALYSIS BASED ON CASE STUDIES AND A LITERATURE REVIEW

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ABSTRACT

Dyspepsia is a common clinical condition characterised by symptoms such as epigastric pain or burning, postprandial fullness and early satiety, originating from the upper gastrointestinal tract. Functional dyspepsia, gastro-oesophageal reflux disease (GORD), peptic ulcer disease (PUD) and *Helicobacter pylori* infection are among the primary causes considered in the assessment of dyspepsia. The aim of this study is to examine the aetiology, clinical assessment, alarm symptoms, association with *H. pylori* infection, diagnostic approach and treatment options for dyspepsia in line with the current literature, and to evaluate the two case examples found in the source text in the light of the literature.

The study was designed as a narrative literature review. Current guidelines, systematic reviews, meta-analyses and clinical trials were evaluated. The cases in the source text were

treated not as participants in a new study, but as illustrative cases that concretise the information from the literature from a clinical perspective.

The literature indicates that age, alarm symptoms, *H. pylori* infection, NSAID use and reflux symptoms should be assessed together in dyspepsia. Consequently, an individualised, risk-based and evidence-based approach is crucial in the management of dyspepsia.

Keywords: Dyspepsia, functional dyspepsia, *Helicobacter pylori*, gastro-oesophageal reflux disease, peptic ulcer, endoscopy, epigastric pain.

1. INTRODUCTION

Dyspepsia is a clinical term used to describe symptoms originating from the upper gastrointestinal tract. Epigastric pain or burning, a feeling of fullness after eating, and early satiety are among the key symptoms of dyspepsia. However, dyspepsia does not in itself indicate a specific disease diagnosis; it may present as the common clinical manifestation of various organic and functional gastrointestinal disorders (Ford et al., 2020; National Institute for Health and Care Excellence [NICE], 2014).

In the source text, dyspepsia is defined as recurrent pain and discomfort in the middle of the upper abdomen; it is noted that symptoms such as bloating, early satiety and a burning sensation behind the sternum may also accompany this presentation. Furthermore, gastro-oesophageal reflux disease, peptic ulcer disease and functional dyspepsia are listed among the primary causes; chronic pancreatitis, biliary disease, gastroparesis and gastric or pancreatic malignancies are cited as less common causes.

The prevalence of dyspepsia in the general population varies depending on the diagnostic criteria used. A systematic review and meta-analysis conducted by Barberio et al. (2020) demonstrated that the prevalence of uninvestigated dyspepsia varies according to different Rome criteria. This finding highlights that the definition of dyspepsia can significantly influence the results of epidemiological studies. Functional dyspepsia is diagnosed in cases where there is no underlying structural disease sufficient to explain the symptoms. According to the Rome IV criteria, functional dyspepsia requires the presence of at least one of the following symptoms—disturbing postprandial fullness, early satiety, epigastric pain or epigastric burning—and the absence of any underlying structural disease that could explain the symptoms (Rome Foundation, 2016). The Rome Foundation's current diagnostic criteria classify functional dyspepsia as a disorder of gastroduodenal gut-brain interaction.

The pathophysiology of functional dyspepsia cannot be explained by a single mechanism. It is thought that gastric emptying and accommodation disorders, visceral hypersensitivity, the gastrointestinal microbiota, mucosal factors and changes in the gut-brain axis all play a role (Ford et al., 2020; Talley & Ford, 2015). One of the major organic causes of dyspepsia is peptic ulcer disease (PUD). *H. pylori* infection and the use of NSAIDs are among the key risk factors for the development of PUD. The source text emphasises the relationship between PUD and *H. pylori* infection and NSAID use.

Gastro-oesophageal reflux disease (GORD) is also an important clinical condition that may present alongside dyspeptic symptoms. Particular attention must be paid to the symptomatic overlap between dyspepsia and GERD, especially in patients presenting with typical reflux symptoms such as retrosternal burning and regurgitation. The NICE guidelines recommend a structured approach to the assessment and treatment of dyspepsia and GERD symptoms (NICE, 2014)

2. AIM

The primary aim of this case report is to examine the aetiology of dyspepsia, its clinical features, the characteristics of functional dyspepsia, its association with *H. pylori* infection, alarm features, the approach to endoscopic evaluation, and current treatment options in accordance with the scientific literature. The secondary aim of the study is to evaluate the two example cases presented in the source text (actual cases examined by the physician) in conjunction with the current scientific literature and to demonstrate why dyspeptic symptoms may require different diagnostic approaches depending on individual patient characteristics.

3. METHODOLOGY

This study was conducted based on the examination and analysis of the original cases, supported by relevant scientific literature. The initial source material for the study consisted of the source text presented by Dr Amil Mənsimov, which included information on the aetiology and assessment of dyspepsia, *H. pylori* testing, alarm features, gastro-oesophageal reflux disease (GORD), peptic ulcer disease (PUD), functional dyspepsia, and the illustrative cases examined. The information provided in the source text served as the basis for the development and presentation of the clinical cases. To broaden the literature review, published systematic reviews, meta-analyses, clinical guidelines, and international consensus reports addressing dyspepsia and functional dyspepsia were utilised.

The following topics were specifically examined in the study:

- Definition and epidemiology of dyspepsia,
- Functional dyspepsia,
- The relationship between PUD and NSAID use,
- *H. pylori* infection,
- Symptoms associated with GORD,
- Alarm features,

- Endoscopic evaluation,
- Pharmacological treatment,
- Lifestyle modifications.

4. FINDINGS

4.1. Aetiology of Dyspepsia

The literature review demonstrated that dyspepsia is a heterogeneous clinical condition. Functional dyspepsia, gastro-oesophageal reflux disease (GORD), and peptic ulcer disease (PUD) are among the principal causes, whereas biliary disorders, gastroparesis, pancreatic diseases, and gastrointestinal malignancies occur less frequently (Ford, 2020). The source text also identified GORD, PUD, and functional dyspepsia among the most common causes of dyspepsia. In addition, medications such as NSAIDs, iron preparations, certain antibiotics, and potassium preparations were reported to cause dyspeptic symptoms. Therefore, obtaining a detailed medication history is important when evaluating patients with dyspeptic symptoms. In particular, NSAID use should be specifically assessed because of its association with peptic ulceration and gastrointestinal mucosal injury.

4.2. Functional Dyspepsia

Functional dyspepsia is a common disorder of gut–brain interaction encountered in clinical practice. According to the Rome IV criteria, the principal symptoms of functional dyspepsia are postprandial fullness, early satiation, epigastric pain, and epigastric burning. These symptoms must not be adequately explained by a structural disease (Rome Foundation, 2016).

Functional dyspepsia is classified into two principal clinical subgroups:

Postprandial Distress Syndrome (PDS)

Epigastric Pain Syndrome (EPS)

Postprandial fullness and early satiation are particularly prominent in PDS, whereas epigastric pain or burning is more characteristic of EPS (Rome Foundation, 2016). Ford et al. (2020) reported that the pathophysiology of functional dyspepsia is multifactorial and may involve various mechanisms, including gastric motor function, visceral hypersensitivity, the gut microbiota, and psychosocial factors. Similarly, Talley and Ford (2015) stated that functional

dyspepsia cannot be explained solely by gastric acid and that interactions between the gastrointestinal tract and the central nervous system play an important role in its development.

4.3. Epidemiology of Dyspepsia

The prevalence of dyspepsia varies according to the diagnostic criteria and research methods used. The systematic review and meta-analysis by Barberio et al. (2020) demonstrated that prevalence estimates may differ substantially depending on which Rome criteria are applied.

Therefore, the diagnostic criteria used should be clearly specified when assessing the prevalence of dyspepsia. Differences in the definitions used across different versions of the Rome criteria may particularly affect epidemiological findings (Barberio, 2020). This is also important for the comparability of clinical studies.

4.4. *Helicobacter pylori* and Dyspepsia

H. pylori is an important aetiological factor in the evaluation of dyspepsia. As it is strongly associated with PUD, the detection and eradication of the infection are clinically important.

The source text recommended non-invasive **H. pylori** testing in appropriate patients after excluding alarm symptoms, classical GORD or biliary symptoms, and NSAID use.

In the current approach, the urea breath test and stool antigen test are important non-invasive methods for detecting **H. pylori**. Testing should be performed at an appropriate time, taking into account that PPI and antibiotic use may affect test results.

The Maastricht VI/Florence consensus report by Malfertheiner et al. (2022) emphasised that antibiotic resistance is an important determinant in the treatment of **H. pylori** infection. Therefore, previous antibiotic exposure and regional resistance patterns should be considered when selecting treatment. The 2024 ACG guideline likewise supports consideration of current resistance patterns in the treatment of **H. pylori** infection (Chey et al., 2024). The guideline was published in PubMed in 2024 and appears in volume 119, issue 9, pages 1730–1753.

Therefore, the older antibiotic combinations described in the source text should not be regarded as standard treatment in current clinical practice without further consideration. Treatment should be determined in accordance with current clinical guidelines.

4.5. Alarm Features

Identifying alarm features is important in the evaluation of dyspepsia. Dysphagia, gastrointestinal bleeding, anaemia, unexplained weight loss, recurrent vomiting, and new-onset symptoms in older patients are clinical features that may increase the likelihood of serious organic disease. The source text indicated that alarm symptoms may assist in distinguishing serious conditions such as complications of PUD or malignancy and recommended endoscopic evaluation in patients presenting with alarm symptoms.

However, it should be recognised that alarm features do not, in isolation, definitively indicate malignancy. A systematic review and meta-analysis by Vakil et al. (2006) reported that the diagnostic value of alarm features for predicting upper gastrointestinal malignancy was limited. Therefore, although alarm features constitute an important component of clinical decision-making, they should be assessed together with the patient's age, family history, duration of symptoms, and other risk factors.

4.6. Endoscopic Evaluation

Endoscopy is an important diagnostic modality in the evaluation of dyspepsia, particularly in patients in whom organic disease is suspected. The source text indicated that newly developed epigastric pain in older patients should be evaluated for potentially serious organic pathology. According to the ACG/CAG clinical guideline on dyspepsia, endoscopic evaluation is recommended in patients aged 60 years and over (Moayyedi, 2017).

Nevertheless, age thresholds may differ between clinical guidelines. Therefore, clinicians should consider not only the patient's age but also their overall risk profile and symptom characteristics. The NICE guideline likewise recommends that the need for endoscopy in adults with dyspepsia and GORD should be assessed according to the patient's clinical features (NICE, 2014). The current online guideline covers dyspepsia, GORD, *H. pylori* eradication, and endoscopic evaluation.

4.7. Relationship Between GORD and Dyspepsia

There is substantial symptomatic overlap between dyspepsia and GORD. In particular, retrosternal burning and regurgitation are characteristic symptoms of GORD. The source text indicated that GORD symptoms may be exacerbated by smoking, alcohol consumption, large meals, and recumbency.

The current approach to GORD recommends an individualised assessment based on the patient's symptoms. Yadlapati et al. (2022) stated that the nature of symptoms, response to treatment, and, when necessary, objective assessment of reflux should be considered together when evaluating GORD.

The NICE guideline also indicates that GORD and dyspeptic symptoms may coexist and that the therapeutic approach should be determined according to the clinical characteristics of the patient (NICE, 2014).

4.8. PUD and NSAID Use

PUD is an important organic cause of dyspepsia. *H. pylori* infection and NSAID use are important risk factors for the development of PUD. The source text likewise indicated that PUD is associated with *H. pylori* infection and NSAID use and that complications such as gastrointestinal bleeding and perforation may occur. Therefore, the use of aspirin and other NSAIDs should be specifically assessed in patients presenting with dyspepsia.

4.9. Pharmacological Treatment

Pharmacological treatment of functional dyspepsia may include proton pump inhibitors (PPIs), H₂-receptor antagonists, prokinetic agents, and, in selected patients, neuromodulators (Black et al., 2022).

The efficacy of PPIs in functional dyspepsia has been investigated in several studies. The Cochrane systematic review by Pinto-Sanchez et al. (2017) demonstrated that PPI therapy may provide a modest benefit over placebo in improving symptoms of functional dyspepsia. Similarly, the meta-analysis by Wang et al. (2007) demonstrated that PPI therapy may provide symptomatic benefit in functional dyspepsia compared with placebo.

The Cochrane review by Moayyedi et al. (2006) also evaluated the efficacy of different pharmacological treatments for non-ulcer dyspepsia. In addition to pharmacological treatment, patient education and reassuring physician–patient communication are important in functional dyspepsia. The British Society of Gastroenterology guideline recommends tailoring treatment according to the symptom pattern and individual patient characteristics (Black et al., 2022).

4.10. Neuromodulator Treatments

Given the multifactorial nature of functional dyspepsia, neuromodulator therapy may be considered in selected patients. In a randomised controlled trial conducted by Talley et al. (2015), the effects of amitriptyline and escitalopram on functional dyspepsia were investigated. The study reported that amitriptyline could contribute to symptom improvement in certain patient groups, whereas escitalopram did not demonstrate a similar degree of benefit. These findings indicate that the treatment of functional dyspepsia is not limited to acid-suppressive therapy alone.

4.11. Example Case 1: 60-Year-Old Male Patient

The first case presented in the source text involved a ****60-year-old male patient****. The patient had experienced epigastric pain for two months. It was reported that he did not use NSAIDs and did not report heartburn, while his physical examination and laboratory test results were normal.

The differential diagnosis in this case should include PUD, functional dyspepsia, gastroparesis, and malignancies originating from the upper gastrointestinal tract and pancreas. The source text also indicated that newly developed symptoms in older patients should be evaluated for potentially serious organic pathology.

From the perspective of the current ACG/CAG guideline, upper gastrointestinal endoscopy is an appropriate approach in a 60-year-old patient to evaluate for underlying organic pathology (Moayyedi, 2017).

This case demonstrates that normal laboratory findings do not completely exclude serious upper gastrointestinal pathology and that clinical decision-making should not be based solely on laboratory results.

4.12. Example Case 2: 43-Year-Old Female Patient

The second example case involved a 43-year-old female patient. The patient had a long-standing history of heartburn, smoked two packs of cigarettes per day, and consumed two glasses of wine daily. Her retrosternal burning was reported to worsen particularly at night.

Compared with the first case, this clinical presentation demonstrated a more prominent symptom pattern suggestive of GORD.

The patient's smoking and alcohol consumption should also be assessed as lifestyle-related factors. In the management of GORD, identifying factors that exacerbate the patient's symptoms and implementing appropriate lifestyle modifications are important (Yadlapati, 2022).

The source text also recommends reducing or discontinuing smoking and alcohol consumption and modifying behaviours that may exacerbate reflux. In this case, given that the symptoms demonstrate typical features of GORD, the clinical assessment may be primarily reflux-oriented. If there is no adequate response to treatment or if atypical features are present, further diagnostic evaluation may be considered.

4.13. Comparison of Two Case Studies

The comparison of the two case studies illustrates the heterogeneous nature of dyspepsia.

Characteristic	Case 1	Case 2
Age	60	43
Sex	Male	Female
Primary symptom	Epigastric pain	Heartburn/retrosteral burning
Symptom duration	2 months	Long-standing
NSAID use	None	Not specified
Smoking	Not specified	2 packs per day
Alcohol consumption	Not specified	2 glasses of wine per day
Primary assessment	Exclusion of organic pathology	GORD-focused assessment
Key diagnostic tool	Endoscopic evaluation	Clinical assessment and response to treatment

In the first case, the priority is to rule out organic pathologies due to the patient's age and the onset of epigastric pain. In the second case, however, typical reflux symptoms and lifestyle risk factors come to the fore. This difference demonstrates that a single algorithm for the management of dyspepsia and upper gastrointestinal symptoms cannot be applied in the same way to all patients.

5. DISCUSSION

This literature review demonstrates that dyspepsia is a heterogeneous clinical condition that may arise from a range of organic and functional mechanisms. Functional dyspepsia constitutes an important proportion of patients presenting with dyspeptic symptoms. Ford et al. (2020) reported that functional dyspepsia is a multifactorial disorder associated with gastrointestinal motor and sensory functions and gut–brain interactions. Talley and Ford (2015) likewise emphasised the multifaceted nature of the pathophysiology of functional dyspepsia.

The Rome IV criteria provide a standardised clinical framework for defining functional dyspepsia. According to these criteria, postprandial fullness, early satiation, epigastric pain, and epigastric burning constitute the principal symptoms (Rome Foundation, 2016).

Standardised diagnostic criteria are also important in the epidemiological assessment of dyspepsia. The meta-analysis by Barberio et al. (2020) demonstrated that the use of different diagnostic criteria may result in different prevalence estimates. *H. pylori* represents an important treatable factor in the management of dyspepsia. Given its association with PUD, detection and eradication of the infection are clinically important. The Maastricht VI/Florence consensus report emphasises the importance of antibiotic resistance in determining treatment success (Malfertheiner, 2022).

The 2024 ACG guideline likewise supports consideration of current antibiotic resistance patterns when treating *H. pylori* infection (Chey et al., 2024). Therefore, the older treatment approaches presented in the source text should not be directly transferred to current clinical practice. The 2024 ACG guideline is verifiable through PubMed. Assessment of alarm features is important in patients with dyspepsia. However, previous evidence has demonstrated that alarm symptoms alone cannot reliably predict malignancy (Vakil, 2006).

Therefore, they should be evaluated in conjunction with the patient's age and other risk factors. In this context, the 60-year-old male patient presented in the source text is particularly noteworthy. The presence of epigastric pain for two months together with an age of 60 years warrants evaluation for possible organic pathology. The source text likewise recommends endoscopic evaluation in this case because of the patient's age and newly developed symptoms. In contrast, the 43-year-old female patient presented with long-standing heartburn

and retrosternal burning that was more pronounced at night. The patient also reported heavy smoking and alcohol consumption. These characteristics place greater emphasis on assessment for GORD.

Given the symptomatic overlap between GORD and dyspepsia, the nature and characteristics of the patient's symptoms should be assessed in detail. Yadlapati et al. (2022) emphasised the importance of an individualised approach to the evaluation of GORD.

Regarding pharmacological treatment, PPIs may be effective in selected patients with functional dyspepsia (Pinto-Sanchez, 2017; Wang, 2007). Nevertheless, rather than continuing treatment unnecessarily for prolonged periods, the patient's clinical response should be regularly assessed. In addition to pharmacological treatment options, neuromodulators may also be beneficial in selected patients with functional dyspepsia. The study by Talley et al. (2015) demonstrated that amitriptyline may provide benefit in selected patients. Overall, the literature supports an integrated approach to the evaluation of dyspepsia, in which **patient age, symptom characteristics, alarm features, *H. pylori* status, medication use, and coexisting features of GORD** are considered together rather than evaluating symptoms in isolation.

6. LIMITATIONS

This study has certain limitations. As the study is based on a literature review and two case reports included in the source text, it does not involve a large patient sample or a control group. Consequently, it is not possible to directly generalise the findings to the general population. Furthermore, the limited availability of clinical, laboratory and endoscopic data relating to the case reports restricts the scope of diagnostic and treatment-related assessments. As this study is a narrative literature review, the findings should not be interpreted as a meta-analytic or systematic synthesis.

7. CONCLUSIONS AND RECOMMENDATIONS

Dyspepsia is a common and heterogeneous clinical condition that may arise from a variety of organic or functional causes. Functional dyspepsia, GORD, PUD, and *H. pylori* infection are among the conditions that should receive particular attention during clinical assessment.

The use of the Rome IV criteria in the diagnosis of functional dyspepsia is important for the

standardisation of clinical practice and clinical research (Rome Foundation, 2016).

A detailed clinical history should be obtained from patients with dyspepsia. The nature and duration of symptoms, their relationship with meals, NSAID use, smoking and alcohol consumption, alarm features, and symptoms suggestive of GORD should be systematically assessed.

Where appropriate, *H. pylori* infection should be investigated, and patients with a positive test should be treated in accordance with current clinical guidelines. In particular, because of antibiotic resistance, older eradication protocols should not be used without first reviewing current treatment recommendations (Malfertheiner et al., 2022; Chey et al., 2024).

Endoscopic evaluation should be considered in patients presenting with alarm features or new-onset symptoms at an older age. However, it should be recognised that alarm features alone do not definitively indicate malignancy (Vakil et al., 2006).

In functional dyspepsia, PPI therapy may be an effective treatment option in appropriate patients (Pinto-Sanchez et al., 2017). In patients who do not respond adequately to treatment, the diagnosis should be reassessed and alternative therapeutic options should be considered.

In patients presenting with GORD symptoms, lifestyle factors and individual symptom triggers should be assessed. The therapeutic approach should be individualised according to the patient's clinical characteristics (Yadlapati et al., 2022).

The two example cases presented in the source text demonstrate that different clinical approaches may be required even among patients presenting with upper gastrointestinal symptoms. In the 60-year-old male patient, exclusion of organic disease is a priority because of newly developed epigastric pain, whereas in the 43-year-old female patient, typical reflux symptoms and lifestyle-related factors place greater emphasis on a GORD-focused assessment. In conclusion, rather than adopting a uniform approach to dyspepsia management, an individualised clinical strategy should be implemented, taking into consideration the patient's age, symptom characteristics, risk factors, alarm features, and *H. pylori* status.

8. DECLARATIONS

Assessment: It has been assessed by internal and external consultants.

Ethics Committee Approval: This study is a review based on an examination of the existing literature and does not involve human or animal participants; therefore, it does not require ethics committee approval.

Conflict of Interest: The author declares that there is no conflict of interest.

Financial Support: No financial support was received from any institution or organisation for this study.

Author Contribution: The author was solely responsible for the design of the study, the literature review, the analysis and the writing of the manuscript.

9. ETHICAL DECLARATION

The Istanbul Medisosal Education and Research Medical Journal's publication ethics: This is a national scientific journal in the field of health sciences that aims to ensure scientific research and publications are conducted in accordance with fundamental principles such as integrity, transparency, objectivity and respect for the findings and work of others, and which works to achieve this. The criteria of the Declaration of Helsinki have been taken into account.

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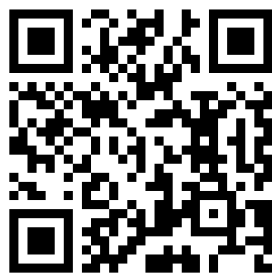
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