Chorea in Kingdom of Saudi Arabia, Causes, Treatment, and Results: A Systematic Review

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Abstract:

Background:*Chorea, characterized by involuntary movements, is a neurological disorder with diverse etiology. Understanding its prevalence, causes, treatment modalities, and outcomes, particularly in Saudi Arabia, is crucial for effective management.* ***Objective****:This Systematic Review aimed to synthesize existing literature on chorea in Saudi Arabia, focusing on its causes, treatment approaches, and outcomes. Methods: A systematic search was conducted in PubMed/MEDLINE and Google Scholar databases to identify relevant studies. The review included diverse study designs such as cohort studies, case series, and cross-sectional studies. Studies investigating chorea prevalence, etiology, treatment strategies, and outcomes in Saudi Arabia were included. Data extraction and synthesis were performed, with a focus on identifying common causes, treatment modalities, and clinical outcomes. Results: The review identified a total of 21 studies meeting the inclusion criteria. The prevalence of chorea in Saudi Arabia was found to be relatively low, with Sydenham's chorea being the most common type reported. While genetic factors were implicated in Huntington's chorea and chorea-acanthocytosis, the etiology of Sydenham's chorea and hemichorea appeared multifactorial, potentially associated with other diseases. Symptomatically, chorea was characterized by involuntary movements, facial grimacing, and emotional instability, consistent with previous literature. Treatment approaches varied, with penicillin commonly used for Sydenham's chorea and pharmacological agents like sodium valproate employed for symptom management. However, evidence-based guidelines were lacking, leading to treatment heterogeneity across studies. Conclusion: Chorea in Saudi Arabia presents with varying etiologies and treatment responses. While genetic factors play a significant role in certain subtypes, others are associated with chronic diseases. Treatment strategies focus on symptom management, but the lack of evidence-based guidelines underscores the need for further research to optimize treatment outcomes and enhance patient care.*

Keywords: *Chorea; Saudi Arabia; Causes; Treatment; Prevalence; Systematic Review.*

Introduction: Chorea, a neurological disorder characterized by involuntary, irregular, and abrupt movements, poses a considerable medical challenge worldwide. This spectrum of disorders encompasses involuntary, non-patterned movements affecting various body regions, disrupting normal activities such as walking and posing significant risks to patients' lives. [1-2]

Comprehensive epidemiological data on chorea in Kingdom of Saudi Arabia are limited, but existing studies suggest it constitutes a significant burden within the country's healthcare system.

The recorded prevalence of chorea in the Middle East region is notably lower compared to international rates, estimated at 3 to 4 cases per 100,000 people [3].

However, the exact prevalence in Kingdom of Saudi Arabia remains uncertain, primarily due to the lack of comprehensive studies accurately determining registered cases.

The causes of chorea vary, from autoimmune diseases to neurodegenerative diseases. One of the most common causes of chorea is hereditary Huntington's disease, which is a neurodegenerative disease that causes cognitive decline and behavioral change [4-5]. Other less common causes are mimic some types of cerebellar ataxia, hereditary prion disease, pallidum odontogenic atrophy, mitochondrial disease, spina bifida, Wilson's disease, iron accumulation in the brain, Friedreich's ataxia, hereditary benign chorea, and Rhett syndrome. [2,4]

The most prominent causes of acquired chorea are cerebrovascular diseases, some complications of the human immunodeficiency virus (HIV), complications of streptococcal infection, complications of rheumatic fever. Some medicines, such as penicillin, levodopa, anticonvulsants, and antipsychotics, may cause chorea [2, 5, 6-9]. Acquired causes also include infections such as cerebrospinal fluid leak, antiphospholipid syndrome, systemic lupus erythematosus, transmissible spongiform encephalopathy, thyrotoxicosis, polycythemia vera, and celiac disease. [5,10]

Patho-physiologically, chorea is closely linked to dysfunction within the basal ganglia-thalamocortical circuits. Disruptions in neurotransmitter systems, particularly dopamine and gamma-aminobutyric acid (GABA), contribute to dysregulated motor control pathways, resulting in choreiform movements. Additionally, autoimmune-mediated processes, metabolic derangements, and structural brain lesions may also precipitate chorea. [9]

Currently, no standard treatment plan exists for chorea, as management depends on the specific underlying pathology, including chorea type, causes, and associated diseases. Treatment aims to control symptoms and improve quality of life through various medications and procedures. In Saudi Arabia, management encompasses pharmacological, rehabilitative, and supportive interventions aimed at alleviating symptoms and enhancing functional outcomes. [2-3,6-7] Pharmacotherapy, including dopamine receptor antagonists, benzodiazepines, and antiepileptic drugs, forms the cornerstone of treatment, though treatment protocols and outcomes may vary due to cultural considerations and medication availability. [5, 6-8]

Previous research in the Kingdom of Saudi Arabia and other middle eastern countries primarily consists of case studies and small cohort studies focusing on individual patients' causes and

treatment. [6, 9-11] While extensive research has been conducted on chorea globally, a systematic review focusing on its anifestations in Kingdom of Saudi Arabia is lacking.

This systematic review aims to fill this gap by providing a comprehensive analysis of chorea within the Saudi Arabian population, providing comprehensive summary, treatment options, and outcomes. By synthesizing available evidence and identifying areas for further research, this study seeks to inform clinical practice, enhance patient care, and guide healthcare policy initiatives aimed at optimizing chorea management in Saudi Arabia.

Method: ***Search strategy and literature search:***

A systematic search of electronic databases, including PubMed/MEDLINE and Google Scholar, was conducted from until December 2023. A set of keywords related to the research title, such as "chorea," "Huntington," "Sydenham's chorea," and "benign chorea," were employed. Additionally, the terms "Saudi Arabia" or "KSA" were appended to designate research conducted within the Kingdom of Saudi Arabia exclusively. All identified studies were written in English and published until the year 2023.

Study selection criteria:

The study selection criteria included studies conducted within Saudi Arabia, focusing on chorea as the primary research subject. Various study designs, including cohort studies, systematic reviews, meta-analyses, and case studies, were considered. However, emphasis was placed on case studies due to their prevalence in the literature. Studies not conducted within Saudi Arabia, those conducted on animals, or those not matching controlled clinical trials and guidelines were excluded.

Study selection process and data extraction:

Two independent reviewers screened the titles and abstracts of retrieved articles, followed by a full-text assessment of potentially relevant studies to determine eligibility for inclusion. Data extraction was conducted independently by two reviewers using a standardized data extraction form. Key data extracted from each included study included study characteristics (e.g., author, publication year, study design), participant demographics (e.g., sample size, age), intervention details, and outcome measures.

Data synthesis and analysis:

Data synthesis involved a narrative summary of the findings based on the homogeneity of included studies. The systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting the findings. Methodological quality assessment of included studies was performed using appropriate tools.

Ethical considerations:

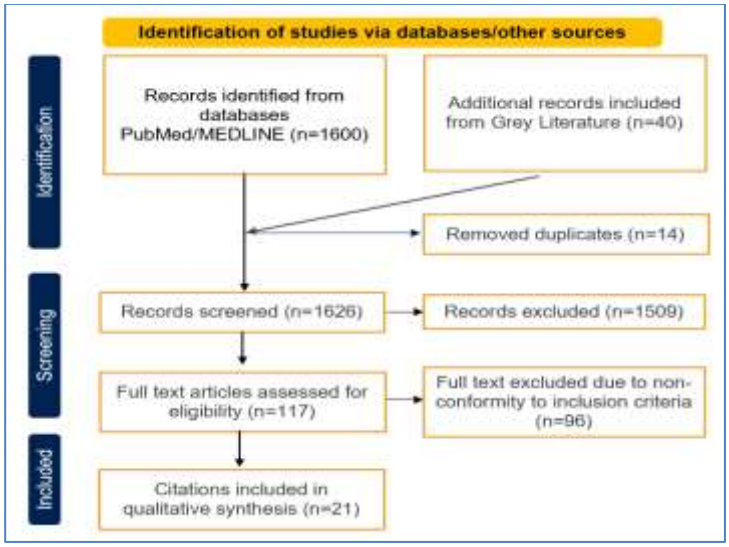
Ethical approval was not required for this systematic review, as it involved the analysis of published literature and did not entail direct contact with human participants. All data were obtained from publicly available sources and were anonymized during analysis to ensure confidentiality and compliance with ethical standards.

Results:

Systematic searches of electronic databases identified a total of 1600 records, with an additional 40 retrieved from grey literature. After removing 14 duplicates, 1509 records were excluded during title and abstract screening, leaving 117 full-text publications for further evaluation regarding inclusion. Following the full-text screening, 21 publications met the inclusion criteria and were included in the analysis (Figure 1).

Figure 1: A PRISMA flowchart selection process summary of the eligible studies

A PRISMA flowchart was created to summarize the selection process of the eligible studies. Potential content was extracted from selected studies.



Study characteristics:

The characteristics of the studies are summarized in Table 1. Spanning from 1987 to 2020, various designs were used, including cohort, case series, and cross-sectional studies. Samples ranged from individual cases to thousands of patients, with diverse age groups, from neonates to adults, and a focus on pediatric populations. For example, Alfrayh et al. [6] studied 260 participants aged 3 months to 15 years, while Daoud et al. [7] analyzed 15 children aged 5-13 years. Studies explored conditions like acute rheumatic fever, Chorea-acanthocytosis, and diabetes-related hemichorea, offering diverse insights into Chorea disease.

Etiology and Causes:

The majority of these studies focused on diagnosing patients, conducting laboratory tests [8,14], and brain MRI scans [14, 15, 24] to identify abnormalities or mutations leading to chorea [18, 22, 23]. Treatment plans varied, with follow-ups spanning from three months [24] to three years [10]. Some studies emphasized the prevalence of Sydenham-type chorea [21, 26], contrasting with the rarity of Huntington's chorea [12]. Chorea was often associated with chronic diseases like rheumatic fever, diabetes, and neurological disorders [6, 8, 16, 20, 24].

Prevalence:

Research in Kingdom of Saudi Arabia highlighted chorea's prevalence, symptoms, and treatments [9, 10, 15, 21], despite its low occurrence [9, 20], particularly among neurological diseases. Studies indicated that chorea cases among children with rheumatic fever were minimal, at 8% [20], and only 2% among patients with neurological disorders [9], suggesting a limited spread of the disease in the Kingdom. Sydenham and hemichorea were prevalent, especially among children aged 5 to 15 [10, 15, 21, 24]. Although Huntington's chorea was rare, some cases were

reported [23, 25], with a prevalence rate of 3 to 4 patients per 100,000 people among certain Arab families [3]. Studies also suggested a higher incidence in males [11, 21], particularly in children.

Genetics:

While genetics and family history played a significant role in Huntington's chorea, some studies indicated that Sydenham's chorea could occur without such a history [21, 26]. For instance, a study on a child with Sydenham chorea revealed no prior family history of chorea or related disorders [21]. In contrast, Huntington's chorea was observed to be limited to specific families in Saudi Arabia, with a 50% chance of inheriting the abnormal gene from affected parents [17].

In other forms of chorea, such as hemichorea in diabetic patients, genetics played a lesser role [24]. Chorea-acanthocytosis showed a recessive genotype in affected families [15], indicating genetic variability among chorea types. Thus, the genetic aspect of chorea varied depending on the specific type of the disease.

Clinical Characteristics & Symptoms:

Chorea's clinical presentation varies widely, influenced by subtype, concurrent conditions, age, and other factors. Symptoms often resemble those of Sydenham's chorea, including involuntary movements, facial grimacing, clumsiness, emotional instability, slurred speech, and eye flutter [10, 21, 26, 25]. In one study of 8 children, chorea episodes lasted from one week to three years [10]. A 5-year-old child had recurrent tonsillitis preceding chorea by two weeks [21]. Similarly, a 12-year-old girl showed symptoms three weeks before presentation, with non-inflamed tonsils [26]. Another subtype, hemichorea, presents as irregular, jerky movements on one side, as seen in a 58-year-old woman with uncontrolled diabetes [24].

Chorea-acanthocytosis, characterized by oral dyskinesia and seizures, varies in symptoms across affected families, including abnormal behavior and tics [15]. Huntington's disease (HD) exhibits distinctive features like middle-aged onset, autosomal dominant inheritance, and progressive dementia. Cognitive deficits, uncontrollable motor movements, and difficulty swallowing are typical [25]. The disease progresses through three levels of increasing severity [25].

Disease Development:

Numerous studies have aimed to understand the pathogenesis of chorea. In Huntington's chorea, researchers identified the mutated huntingtin gene (mHTT), which leads to neuronal degeneration due to abnormal protein accumulation. This gene mutation affects the striatal nuclei, weakening control signals to the pallidum, resulting in involuntary movements. Mutations in FRRS1L have been linked to a Huntington-like phenotype in patients with advanced chorea and dementia [17, 23]. In Chorea-acanthocytosis, mutations in the CHAC gene on chromosome 9q21 were associated with anemia, identified through homozygous mapping and whole-exome sequencing [15, 18]. Other studies explored the genetic basis of chorea in Saudi families, identifying homozygous missense mutations in GM2A and mutations in the CHAC gene [22]. Additionally, biotinidase deficiency and primary antiphospholipid syndrome were investigated as potential causes of chorea [13, 14].

Disease Management: Diagnoses & tests:

Diagnosing chorea involves a comprehensive assessment by psychiatrists or neurologists. Huntington's chorea diagnosis typically involves genetic testing, supported by neuroradiological findings. Magnetic resonance imaging (MRI) or computed tomography (CT) scans may reveal brain atrophy indicative of Huntington's chorea. Predictive genetic testing is available for at-risk family members over 18 years, emphasizing the importance of counseling and informed decision-making [17].

For Sydenham's chorea, clinical examinations are crucial. Patients often present with involuntary movements, but normal physical examinations, including neurological assessments, may not reveal abnormalities. Laboratory tests, such as erythrocyte sedimentation rate and throat cultures, are typically unremarkable. Neuroimaging and electroencephalogram (EEG) results are often normal [21, 26].

In hemichorea cases, MRI findings may show increased signal intensities in specific brain regions, accompanied by diabetic complications like retinopathy [24]. Similarly, generalized chorea cases may exhibit abnormal movements involving multiple limbs, alongside laboratory abnormalities such as thrombocytopenia and elevated antibody levels. Brain MRI may reveal scattered signal abnormalities, indicating possible stroke history [14, 19].

Patients with chorea-acanthocytosis may display abnormal blood cell morphology and lipoprotein profiles. MRI findings often indicate striatal metabolic deficiencies [15]. Treatment may involve addressing underlying conditions, such as diabetes, along with symptomatic management using medications like lorazepam and haloperidol [24].

Disease Management: Treatment

Treatment strategies vary based on chorea type, associated conditions, and patient factors. Huntington's disease management focuses on symptom alleviation, as there's currently no curative therapy. Medications like fluphenazine, tetrabenazine, and pramipexole can help manage motor symptoms, while antidepressants and antipsychotics may address mood disturbances. Investigational treatments include Coenzyme Q10 and polyunsaturated fatty acids [17].

Sydenham's chorea treatment often involves penicillin, haloperidol, or sodium valproate. Haloperidol effectively controls movement manifestations, while sodium valproate modulates neurotransmission to alleviate abnormal movements [7, 8, 10, 21].

In chorea associated with other conditions like diabetes or antiphospholipid syndrome, treatments target underlying diseases alongside symptomatic management. Insulin therapy regulates blood sugar levels in diabetic patients, while medications like aspirin and prednisone are used for antiphospholipid syndrome. Acyclovir is employed in cases of chorea resulting from herpes simplex encephalitis [11, 14, 24].

Table 1: List of characteristics and main study findings for included studies

Study name	Year	Study sample	Age	Study type	Diagnosis	Treatment	Main study findings summary
Alfrayh et al, [6]	1987	Two hundred and sixty	3 months to 15 years	Cohort study	Children with CNS disease including chorea	-	Pathogens studied: 28% prenatal, 13% perinatal, 34% postpartum, 4% mixed. Diagnostic problems: 48% convulsive disorders, 26% febrile convulsions, 20% epilepsy, 2% metabolic. 20% detected cerebral palsy cases, more in males. 11% had head injuries. 4% suffered hydrocephalus. 14% had hereditary degenerative disorders, microcephaly, tumors, rheumatic chorea, spinal cord injury, and miscellaneous issues.
Daoud et al, [7]	1990	15 children	5-13 years	Case series	Sydenham's chorea	Sodium valproate at a dose of 15 to 20 mg/kg/day.	13 children had choreiform movements disappear within a week of valproate treatment. 2 showed incomplete response, 2 relapsed but one responded to valproate reintroduction. Median treatment duration: 6.7 weeks, no significant side effects observed.
Daoud et al. [8]	1991	One girl	7 years	Case study	Chorea	Valproic acid at a dose of 300 mg twice daily	Movements diminished over 7 days, disappeared in 14. No side effects observed, no recurrence after valproate cessation during 1-year follow-up. Valproate effective for rheumatic chorea.
Awada et al. [9]	1992	2,101 patients	Neonate-90 years	Cross-sectional	Patients with neurological disorders including chorea	-	Basal ganglia disorders: 2% of neurological disorders, including Parkinson's, essential tremor, Sydenham chorea, dystonic disorders, and tics. No Huntington's chorea cases recorded.
Al-Eissa et al. [10]	1993	8 children	8-13 years	Case series	Hemichorea	Haloperidol	Male to female ratio 1.7:1. Most had hemichorea, often affecting right side. Common manifestations: involuntary movements, facial grimacing, clumsiness, emotional instability. Chorea duration ranged from 1 week to 3 years, median 11 weeks. Half had mild carditis. Chorea recurred in those without continuous penicillin prophylaxis. Haloperidol effective for motor symptoms.
Gascon et al. [11]	1993	3 children	3 months to 3 years	Case series	Chorea	Two patients received 10-day courses of 30 mg/kg/day of acyclovir One patients received 3-week course of acyclovir at conventional dosages	Patient 2 showed no improvement with repeated acyclovir courses. Patient 1 improved but relapsed. Patient 3 improved with 3-week acyclovir course. Patient 4, suspected HSE, didn't respond to acyclovir and was negative for herpes indicators. Recommendation: 3-week acyclovir course at 30–35 mg/kg/day in 3 divided doses for HSE patients.
Al-Rajeh et al. [12]	1994	137	Adults	Cross-sectional	Cases with movement disorders including chorea	-	Ten cases of Sydenham's chorea noted. Huntington's chorea strikingly rare.
Dabbagh et al. [13]	1994	10	Adults	Retrospective study	Patients' biotin-dependent, chronic progressive encephalopathies	Large dose of Biotin	Four patients had biotinidase deficiency, one had holocarylase synthetase deficiency. Four presented Leigh encephalopathy. All required large biotin doses.
Al-Zahrani et al. [14]	1995	One male patient	Adult	Case study	Chorea	The patient was started on aspirin and prednisone with rapid symptomatic improvement	**Mild thrombocytopenia, high PTT, false positive syphilis serology, weakly positive ANA, and high IgG anticardiolipin antibodies found. MRI showed scattered small areas of high signal intensity bilaterally in centrum semiovale. Chorea possibly initial symptom of primary antiphospholipid syndrome.**
Al Jishi et al. [15]	1995	1 child (boy)	13 years	Case study	Hemichorea	-	A case of SLE with hemichorea, positive anticardiolipin antibodies, and brain MRI lesions. Immune phenomenon possibly linked to striatal neuronal activation.
Abbag, F et al. [16]	1998	Forty patients with acute rheumatic fever	Adults	Retrospective study	patients with acute rheumatic fever including chorea	-	Chorea, erythema marginatum, and subcutaneous nodules were rare.
Bohlega et al. [17]	2002	Three families with Chorea-acanthocytosis	18–35 years	Case series	Chorea-acanthocytosis	-	Chorea-acanthocytosis: autosomal recessive disorder with orofacial dyskinesia, seizures, aberrant behavior, caudate and putamen atrophy, and acanthocytes in blood. Seizures, aberrant behavior, and tics were common symptoms. MRI showed caudate and putamen atrophy. Genetic studies suggested a locus on chromosome 9q21.
Dobson-Stone et al. [18]	2002	43 patients	Adults	Case series	Chorea-acanthocytosis	-	Identified 57 mutations, 54 novel, in CHAC gene. Mutations included nonsense, insertion/deletion, splice-site, and missense. Most mutations predicted to cause absence of gene product, consistent with disease's recessive inheritance. CHAC protein (chorein) shows tolerance to amino-acid substitutions.
Alsharef et al. [19]	2007	One child (girl)	12 years	Case study	generalized chorea and chronic migraine headaches	-	Generalized chorea with hypotonia, ischemic strokes in frontal and occipital regions, flow void appearance in basal ganglia region, and Moyamoya disease diagnosed.
Al Qurashi et al. [20]	2009	The 83 children with AFR	children were aged, 4–12 years	Prospective study	Children with AFR including Chorea	-	Cardiac involvement in 53% cases, isolated in 6%. Rheumatic chorea seen in 5 children, occurring alone in 6%, with arthritis in 36%, and with carditis in 11%. Chorea bilateral in 94%, unilateral in 6%. Emotional lability observed in 95%. Duration ranged from 3 weeks to 5 months.

Lardhi et al. [21]	2014	One child	5 years	Case study	Sydenham chorea	Continuous penicillin prophylaxis	Sydenham chorea common before puberty, with female preponderance. Rheumatic chorea incidence varies in young children. Diagnosis based on neurological signs and pharyngitis history. Continuous penicillin prophylaxis recommended.
Salih et al. [22]	2015	5	Adults	Case series	Adults from one family with a neurodegenerative course dominated by progressive chorea and dementia	-	Homozygous mutation in GM2A identified, causing profound hypotonia, impaired movement, seizures, hyperacusis, and macular cherry red spot.
Salih et al. [23]	2015	4 siblings	-	Case series	four siblings with juvenile onset chorea	-	Homozygous mutation in FRRS1L detected, causing decreased protein abundance and mis-localization.
Al-Quliti et al. [24]	2016	Woman who has diabetes with left side hemic horea	Adult	Case study	Hemic horea	haloperidol and clonazepam.	MRI showed unilateral right striatal hyperintense signal changes. Syndrome described with non-ketotic hyperglycemia, hemichorea, and T1 MRI striatal hyperintensities. Therapeutic response to haloperidol and clonazepam sustained.
Alshammary et al. [25]	2019	All neurological patients who referred to King Fahad Hospital from July 1, 1984, to June 30, 1988.	Adults & children	Retrospective study	Huntington's disease (HD)	Effective speech-language intervention	Huntington's disease may cause speech, language, and swallowing difficulties. Speech may be simpler, with complex cognitive tasks affected. Speech-language intervention essential for improving quality of life.
El-Shorbagy et al. [26]	2020	One child (girl)	12 years	Case study	Childhood nonhereditary chorea.	Carbamazepine therapy	Disease onset sudden after streptococcal pharyngitis. Muscle weakness leads to intermittent "milkmaid's grip." Chorea affects gait, speech, and object control. Negative ASOT noted; its absence doesn't rule out SC. Diagnosis clinical, excluding other causes. Normal lab tests, imaging, EEG. Doppler echocardiography may reveal ARF-related valvular regurgitation. Carbamazepine effective for nonhereditary childhood chorea, without side effects.

Discussion :

Chorea is a complex movement disorder with diverse etiologies and clinical manifestations. This systematic review aimed to explore the causes, treatment strategies, and outcomes of chorea in Saudi Arabia, comparing findings with previous studies to elucidate similarities and differences.

Our review identified a variety of underlying conditions associated with chorea in Saudi Arabian patients, including rheumatic fever, diabetes mellitus, and neurological disorders [6, 8, 16, 20, 24]. These findings are consistent with previous studies conducted in other populations, highlighting the multifactorial nature of chorea etiology. Comparatively, studies from other regions have reported similar associations between chorea and systemic or neurological conditions [27]. Previously conducted studies demonstrated a link between rheumatic fever and Sydenham's chorea, reinforcing the global relevance of this association. [28-29]

The clinical presentation of chorea in Saudi Arabian patients closely resembled that observed in global populations. Sydenham's chorea emerged as the predominant subtype, characterized by involuntary movements, facial grimacing, and emotional instability. Additionally, hemichorea and Huntington's disease were frequently reported, reflecting the heterogeneous nature of chorea presentation [6-14].

Comparatively, studies from diverse geographic regions have reported similar clinical characteristics of chorea, underscoring the universal nature of its symptomatology [30-32]. However, variations in subtype prevalence and symptom severity may exist, influenced by genetic, environmental, and demographic factors unique to each population.

Diagnostic approaches for chorea in Kingdom of Saudi Arabia encompassed clinical examination, laboratory tests, and neuroimaging studies, consistent with international guidelines [33-34]. MRI and CT scans were commonly employed to assess brain morphology and detect structural abnormalities associated with chorea. Genetic testing also played a crucial role in identifying hereditary forms of the disease [20-26].

Similarly, studies from other countries have emphasized the importance of comprehensive diagnostic evaluations in chorea management [33]. Neuroimaging techniques such as MRI and CT scans have been widely utilized to elucidate underlying pathologies and guide treatment decisions across diverse patient populations.[34]

Treatment strategies for chorea in Kingdom of Saudi Arabia encompassed pharmacological interventions, supportive therapies, and multidisciplinary care approaches. Antipsychotics, antiepileptic drugs, and physical therapy were commonly employed to alleviate symptoms and improve functional outcomes in patients with chorea [7-8,10,21].

Comparatively, treatment approaches for chorea have shown consistency across different regions, with a focus on symptom management and improving quality of life. However, variations may exist in medication preferences and therapeutic modalities based on local healthcare infrastructure and resource availability [35-37]. Orsini et al. conducted a retrospective study revealing a lack of evidence-based guidelines for Sydenham's chorea [35]. Their national multicenter cohort study highlighted considerable treatment heterogeneity [36-37]. The findings underscore the necessity for longitudinal studies to evaluate risk factors and identify optimal treatment modalities for Sydenham's chorea.

Treatment outcomes for chorea in Kingdom of Saudi Arabia varied depending on disease etiology, patient age, and comorbidities [7-8,10,21]. While some patients experienced symptomatic relief with pharmacological interventions, others required more intensive supportive care or disease-specific therapies. Long-term follow-up studies are essential to evaluate the efficacy and safety of current treatment strategies and monitor disease progression over time.

Similarly, studies from other regions have reported diverse treatment outcomes in chorea patients, highlighting the complex nature of the disease and the need for individualized management approaches [38-39]. Longitudinal studies assessing the long-term effectiveness of different treatment modalities are crucial for optimizing patient care and improving clinical outcomes.

Strength and limitations:

Strengths of this systematic review include its comprehensive analysis of existing literature on chorea in Saudi Arabia, providing valuable insights into the epidemiology, etiology, and management of the condition within the region. The inclusion of

various study designs and patient populations enhances the breadth and depth of the review's findings. Additionally, the systematic approach ensures a rigorous and unbiased synthesis of evidence, enhancing the reliability of the conclusions drawn. Furthermore, the discussion of treatment modalities and their effectiveness contributes to clinical practice and informs future research directions in the field.

However, several limitations should be considered. Firstly, variations in study methodologies, sample sizes, and diagnostic criteria may limit the comparability of findings across studies. The review's focus on Kingdom of Saudi Arabia may also restrict the generalizability of results to other populations. Furthermore, the lack of standardized reporting of outcomes in some studies may hinder the synthesis of data and interpretation of results.

Conclusion:

In conclusion, chorea poses significant clinical challenges in Kingdom of Saudi Arabia, with diverse etiologies, limited prevalence clinical presentations, and treatment approaches. Sydenham type chorea predominates, with a slightly higher prevalence in males and a greater impact on children than adults. Genetic factors significantly contribute to Huntington's chorea and chorea-acanthocytosis, while other types may stem from different causes. Symptoms vary but typically include involuntary movements and slurred speech. Huntington's chorea is associated with progressive dementia. Treatment options remain limited, with penicillin and sodium valproate showing efficacy in treating Sydenham's chorea. However, there is no effective treatment for Huntington's chorea. The diversity of associated diseases underscores the need for individualized treatment plans.

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