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The Association Between Genetic Factors and Temporomandibular Disorders: A Systematic Literature Review

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ADMINISTRATIVE INFORMATION

Support - King Khalid University.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202440063

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 April 2024 and was last updated on 16 April 2024.

INTRODUCTION

Review question / Objective The main aim of this study was to explore and critically appraise the existing evidence of the role of genetic factors in the development of TMD. In addition, this study will investigate the different genetic variants and the risk of developing TMD.

Condition being studied Temporomandibular disorders (TMDs) are multifaceted conditions affecting the temporomandibular joint (TMJ), masticatory muscles, and related structures. TMDs clinically manifest through orofacial pain, limited jaw movement, joint sounds, and dysfunction. In addition, they significantly affect public health, with a higher prevalence among women and middle-aged subjects.

The aetiology of TMDs is multifaceted, involving various factors, broadly categorized into risk factors and contributors to the onset and development. Risk factors include genetic predisposition, anatomical factors like joint morphology and muscle attachments and psychosocial factors, including stress and anxiety. On the other hand, contributors to the onset and development may include trauma, parafunctional habits like bruxism and clenching, and occlusal factors, which trigger the TMD symptoms onset. In addition, other factors, like inflammatory processes, muscle hyperactivity, and central sensitization, may escalate the progression of TMDs and the signs and symptoms severity.

In addition, other essential biological processes like bone metabolism and cartilage formation genes may also potentially influence TMD development, including growth differentiation factor 5 (GDF5), frizzled-related protein (FRZB), and lumbar-disc degeneration (LDD) gene (ASPN). These relationships between genetic factors and

TMD onset and development are based on the assumption that genetic variations may impact an individual's susceptibility to TMD signs and symptoms development. These genetic factors may also influence the severity and progression of TMDs.
Research has yielded inconclusive results on the association between genetic factors and TMD. This study will investigate the relationship through a systematic review and meta-analysis of the role of genetic factors in the onset and progression of TMDs. In addition, it will provide a quantitative synthesis of the existing evidence of the relationship.

METHODS

Search strategy A comprehensive database search was conducted via ScienceDirect, PubMed, Cochrane Library, Dimensions, and Emerald. The following keywords were used in different combinations to optimize the search results for different databases: Genetic, gene, genome, temporomandibular disorder, and musculoskeletal disorder.

Participant or population Human subjects with TMD.

Intervention Not applicable.

Comparator Different gene variants and other genetic factors influencing TMD development.

Study designs to be included This study included original research articles on the influence of genetic factors on TMD development. It also included only studies on human subjects, studies with more than eight participants, and studies with access to the full text.This study preparation and conduction was according to the Preferred Reporting of Items for Systematic Reviews and Meta-analysis (PRISMA).

Eligibility criteria Studies published in English.

Information sources The literature search yielded 851 articles, of which 72 duplicates were removed. Further, 697 articles were excluded following title and abstract screening. The remaining 82 articles were sought for retrieval, after which 19 studies that met the eligibility criteria were included.

Main outcome(s) TMD onset and development, demonstrated by different signs and symptoms, including myofascial pain and bruxism.

Additional outcome(s) Genetic factors significantly influenced TMD signs and symptoms, and gene polymorphisms significantly influenced TMD onset and progression. Further research should be conducted in more diverse settings with larger sample sizes to verify and validate these findings.

Data management Data were systematically extracted from the included studies and tabulated in an Excel Workbook for analysis. The extracted data included the authors, study design, settings, duration, sample characteristics, size, mean age, study purpose, gene type, outcome measures, and the findings.

Quality assessment / Risk of bias analysis The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for non-randomized experimental studies was used to assess the methodological quality of the eligible studies. The extracted data were analyzed and reported according to the predominant themes regarding the association between genetic factors and TMD onset and development.

Strategy of data synthesis A comprehensive database search was conducted via ScienceDirect, PubMed, Cochrane Library, Dimensions, and Emerald. The following keywords were used in different combinations to optimize the search results for different databases: Genetic, gene, genome, temporomandibular disorder, and musculoskeletal disorder.
This study included research on the role of genetic factors in the onset and development of TMD. Articles fulfilling the modified PICOS criteria were selected.

Subgroup analysis The data was compiled from a variety of articles:
• Author(s), year of publication, country, study design.
• Total number of patients/datasets.
• Training/validation datasets.

Sensitivity analysis Not Applicable.

Language restriction Only articles in English.

Country(ies) involved Saudi Arabia.

Keywords Genetic Factors, Genes, Polymorphism, Temporomandibular Disorders.

Dissemination plans All the Data will be shared after the publication of the article.

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