

## REVIEW ARTICLE

# MULTIPLE ETIOLOGIES OF TEMPOROMANDIBULAR JOINT DISORDERS – A REVIEW

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### ABSTRACT

Temporomandibular joint (TMJ), is a synovial joint, involves two bones particularly mandible and temporal bone. Since TMJ involve muscles of mastication and jaw movement therefore, its disorders damages surrounding tissues and minimizes its function. The etiology of TMJ disorders is complex and multifactorial including genetic, traumatic, inflammatory, degenerative and idiopathic disorders as well as behavioral factors (parafunctional habits). Generally females are more affected because of increased level of estrogen hormone affecting bone and cartilage; moreover, emotional factors (anxiety, stress and depression) are also higher in females compared to males. Genetic disorders of TMJ include many genes, which contribute in bone formation and inflammation mediation.

This article is focused on etiology of temporomandibular joint disorders and involvement of certain genes and other predisposing factors leading to pathophysiology of its development. Information regarding TMJ disorders was retrieved through PubMed, Medline and other authentic search engines available in the University, information was collected through reviews, research, and epidemiological studies published up to 2016.

This review article concludes urgent management is sought in 1-2% young children, 5% teenagers and 5-12% adults. In order to avoid any iatrogenic injury it is mandatory to do prior extensive and detailed physical examination of TMJ.

**Keywords:** TMJ Disorders; Genes; Bruxism; Malocclusion; Estrogen.

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### INTRODUCTION

Temporomandibular joint (TMJ) is a synovial type that allows significant movement by two bones each with an articulating surface, covered by hyaline cartilage. The two bones are particularly a skull bone (temporal bone) and a jawbone (mandible). TMJ articulation has two joints, superior and inferior, separated by an articular disc present between temporal bone and condyle<sup>1</sup>. The superior joint is for gliding movement and inferior joint for rotatory or hinge movement<sup>2</sup>. There is coordination between muscles and jaw for movement of the mandible, which limits damage to surrounding tissues and maximizes its function. TMJ disorders are a group of conditions including TMJ and muscles of mastication, that lead to pain and dysfunction in the mandible<sup>3</sup>.

A number of conditions such as myoarthropathy of the TMJ, occlusomandibular disturbance, myofascial pain dysfunction syndrome, stressed pain dysfunction syndrome and temporomandibular pain dysfunction syndrome are included<sup>4</sup>. Some clinicians suggest the term craniomandibular disorders for these conditions because according to them the symptoms are not only associated with TMJ, whereas, it involves the etiology of pain, which is not related to dental region. However, its adds confusion, for that reason, the American Dental Association (ADA) has opted the terminology "temporomandibular joint disorders" (TMD)<sup>5</sup>. It can also be associated with different types of pains and ailments such as ophthalmologic, otolaryngology and other chronic disorders<sup>6</sup>.

From various studies it is apparent that prevalence of TMD in general populations is very common

about 60-70%, however, only 25% patients recognize the development of this disorder<sup>7</sup>. Urgent management is sought in 1-2% young children, 5% teenagers and 5-12% adults<sup>8</sup>. In order to avoid any iatrogenic injury it is mandatory to do prior extensive and detailed physical examination of TMJ, which is

shown in the following Table 1.

This article is focused on etiology of temporomandibular joint disorders and involvement of certain genes and other predisposing factors leading to pathophysiology of its development.

**Table 1: Elements to be examined in TMJ.**

TMJ EXAMINATION	
EXAMINATION ELEMENT	OBSERVATIONS
Inspection	Facial symmetry/swelling, masseter and temporal muscle hypertrophy, opening pattern (corrected and uncorrected deviations, uncoordinated movements, limitations)
Assessment of range of movements	Maximum opening with comfort, with pain and with clinical assistance
Palpation	Masticatory muscles TMJ Neck muscles and accessory muscles Parotid and submandibular area Lymph nodes
Provocation test	Pain in joint or muscle with tooth clenching Reproduction of symptoms with chewing
Intraoral Examination	Signs of parafunction (cheek and lip biting, occlusal wear, scalloped tongue borders, tooth mobility, sensitivity to percussion, fractures of enamel, restorations)

**DISCUSSION**

The etiology of TMJ disorders is complex and multifactorial comprising genetic, traumatic, inflammatory, degenerative and idiopathic disorders. These can be initiating, perpetuating, predisposing and systemic factor such as bruxism, micro-trauma and macro-trauma, orthodontic treatment, orthopedic instability, occlusal abnormalities, factors like poor nutrition and health, exogenous estrogen and joint laxity. However, a single factor in some cases can be a contributory cause to the pathology. Therefore, accurately identifying and treating the causative factors are the focus of this review which is crucial for their successful management<sup>9,10</sup>.

**Initiating Factors**

Adverse loading and trauma of the masticatory system primarily leads to the onset of initiating factors<sup>11</sup>. Trauma may include injuries to the lower jaw and chin especially in pediatric patients, because of frequent falling<sup>12</sup>. Other related injuries are due to sports, motor vehicle accidents, forceful intubation, third molar extraction, physical abuse etc.<sup>13</sup> Ankylosis can also result from prolonged immobilization and closed reduction<sup>14</sup>.

**Perpetuating Factors**

Perpetuating factors include Social factors (could affect response to pain), Behavioral factors (clenching, grinding, bruxism and abnormal head posture), cognitive factors (hopelessness and discouragement can negatively affect management) and Emotional factors (anxiety and depres-

sion). Compared to men, more severe problems are observed in women who seek treatment for TMJ (ratio Male:Female1:8)<sup>15</sup>. Detailed overview is as follows:

**Prevalent in Females**

Since, TMJ disc is made up of collagen and elastin and female hormones metabolically affect its cartilage cells. Estrogen along with progesterone, increases cytokines synthesis and has a role in remodeling and degenerative function affecting bone<sup>16,17</sup>. Estrogen acts via its receptors, estrogen receptor alpha(ERα) and estrogen receptor beta(ERβ); ERα is particularly recognized in TMJ, cartilage and growth plate. Some studies have shown correlation of estrogen receptor polymorphisms with TMJ disorders. Studies have shown that PX ERα haplotype has 3.9 and 5.9 fold higher risk of medium to high intensity pain compared with Px and px haplotype subjects<sup>18,19</sup>. Patients with homozygous and heterozygous for PX haplotype also need rigorous treatment like occlusal stabilization splint or physical therapy along with pharmacotherapy. Psychological factors also have a vital role in development of TMD such as stress, anxiety and depression which is more common in females<sup>20</sup>. For physiological and psychological markers, haplotypes of beta-2 adrenergic receptor (ADRB2) are reported to be associated with TMD<sup>9, 21</sup>.

**Bruxism (Serotonergic Neurotransmission):** Clinical studies and examinations have shown bruxism is a genetic factor and it may be associated with some hereditary conditions like Down's syndrome, noctur-

nal frontal lobe epilepsy, Cerebral palsy, Prader-Willi syndrome, Rett syndrome and Huntington's disease<sup>22</sup>. In Down's syndrome, prevalence of bruxism has been reported to be 18% to 70%. There is a higher chance of bruxism in children with Trisomy 21 and it is more common during daytime due to spasticity<sup>23</sup>. Genes related to serotonergic neurotransmission are SLC6A4, HTR1A, HTR2A and HTR2C. The researchers have found that the C allele of HTR2A SNP rs6313 (C102T) was related significantly with greater risk of sleep bruxism. These findings show the genetic involvement in sleep bruxism and their ultimate relationship with TMD<sup>24</sup>.

### Predisposing Factors

The predisposing factors influencing masticatory system enhance the probability for development of TMD. These include structural processes besides psychological and pathophysiological factors that are already discussed above. Structural processes can be discussed under the heading of occlusal factors<sup>9, 21</sup>.

### Occlusal Factors

One of the most important etiologic factors in TMD is disturbed occlusion. Pullinger et al. showed lower correlation of occlusion with following structural factors such as unilateral lingual cross-bite, multiple absent posterior teeth (more than 5), ill-fitting prosthesis and faulty restorations, open-bite, over-jet > 6-7 mm and retruded intercuspal position > 4 mm l l.

Costen concluded that deep-bite is the one of reason of developing symptoms in many patients with TMD. For which he adopted bite raising dental procedures but was unsuccessful in relieving symptoms<sup>25</sup>. The symmetry of intensity of occlusal contacts distribution in the posterior occlusion is more significant than their numbers related to TMJ function<sup>26</sup>. Patients with lesser occlusal contacts reported frequent headaches. Pullinger et al. also found that 10-20% causes of TMD are due to occlusal factors that differentiate between healthy persons and patients with TMD<sup>27</sup>. Ting Wong et al. showed an association for the genes ectodysplasin A (EDA) and X-linked ectodermal dysplasia receptor (XEDAR) in dental crowding present in malocclusion patients. However, multiple researches did not significantly show heritability for occlusal traits<sup>28</sup>.

### Polymorphism of ESR1 Gene and ENPP1 Gene

Nicot et al. studied 13 genes SNP in development of TMD and surgical outcome in dentofacial deformities. AA genotype of SNP rs1643821 (ESR1 gene) reported as a risk factor while TT genotype of SNP rs858339 (ENPP1 gene) is identified as a protective factor for dysfunctional deterioration after orthognathic surgery. However, the heterozygous genotype AT is also a risk factor for TMD. These elements are significant in devising novel screening tests and methods as well as new treatments in future<sup>29</sup>.

### Systemic Factors (Autoimmune Disorders)

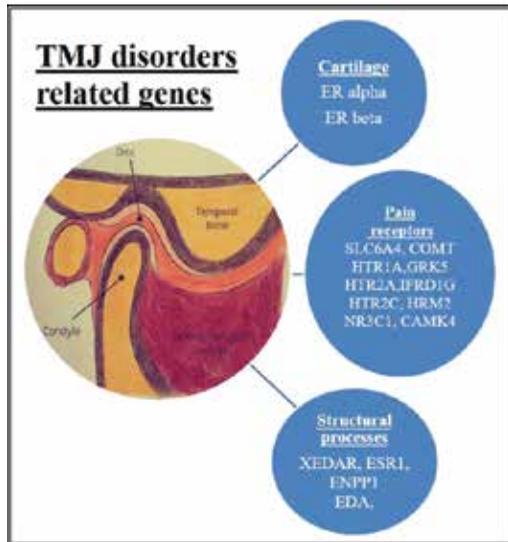
Some systemic factors (autoimmune disorders) that contribute to TMD are due to imbalance of pro-inflammatory cytokines leading to free radical formation and eventually joint damage<sup>30</sup>. The disorders include systemic lupus erythematosus (SLE) and rheumatoid, psoriatic and juvenile arthritis. Other systemic factors that may be included under this heading are genetic susceptibility, joint hypermobility and hormonal fluctuations of estrogen and progesterone as discussed above. Ehlers-Danlos syndrome has generalized joint laxity and hypermobility which is also reported to be less associated with TMJ disorders<sup>31</sup>.

### Pain Related Genes in TMD

Pain is an important phenomenon seen in TMD, Laskinproposed the term "Myofacial Pain Dysfunction Syndrome (MPDS)" after extensive research and clinical observations. However, the approved terminology is 'Temporomandibular joint disorders' with the features of restricted joint movements, pain and joint sounds along with contributions of psychophysiological disorders<sup>4</sup>. Multiple pains related genetic loci contribute to TMD. A study by Shad et al. reported number of genes related to pain in TMD including Glucocorticoid receptor gene (NR3C1), Calcium/calmodulin-dependent protein kinase (CAMK4), Cholinergic receptor muscarinic 2 (CHRM2), Interferon related developmental regulator 1 (IFRD1), G protein-coupled receptor kinase 5 (GRK5), 5-Hydroxytryptamine receptor 2A HTR2A and Catechol-O-methyltransferase (COMT). Many other genes have been reported but their effect is not very significant. The serotonin transporter gene (SLC6A4) polymorphism involving affective pathway in orofacial pain has a significant role in sharp pain. The T102C and A218C single nucleotide polymorphism (SNP) of the serotonin receptor HTR2A have also been shown to differ significantly between TMD cases and controls<sup>32</sup>.

### Disc Defects

Patients with decreased disk (eminence ratio) have advanced stages of temporomandibular joint dislocation. In flat eminence, there is minimum posterior rotation of disk during depression of mandible and when the steepness increases there is greater movement of the disk on condyle during function. Exaggerated movement of condyle may also elongate the ligament and lead to dislocation disorders. Some dental procedures such as complete root canal treatment in one sitting, orthodontic treatment or relapse can initiate and predispose to disc defects leading to TMD<sup>33</sup>. Females are more commonly affected than males due to high stress ratio as well as estrogen and progesterone receptors playing an important role in the pathophysiology. Genes associated in pain perception; TMJ development; anatomical structures and response to immune system have a crucial role in TMD as depicted in Figure 1.



**Figure 1: Genes involved in TMJ disorders.**

**CONCLUSION**

Disorders of temporomandibular joint are common, affecting both children and adults. It has multifactorial causes but much of the fundamental pathophysiology remains poorly understood. Factors include genetic, traumatic, inflammatory, degenerative and idiopathic disorders as well as structural disorders such as malocclusion. TMJ disorders are a concern for dental practitioners and public health that calls for special attention to future research initiatives because every person has a distinctive genetic makeup. Accurate timely identification is vital for the appropriate treatment. It is compulsory to understand the pathophysiological mechanism of genetics modulating TMD. This understanding will lead to improved innovative therapies against TMD.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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