Skeletal Fluorosis-Induced Morphological Changes of the Temporomandibular Joint and Associated Functional Limitations among Adults in Ethiopia

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Abstract
Skeletal fluorosis is a chronic metabolic bone and joint disease caused by ingesting large amounts of fluoride. The clinical manifestations of the disease range from mild joint pain to severe bone deformities. Joint pain, stiffness of joints, and abnormal growth of the upper and lower extremities are some of the symptoms of the disease. In its severe form (crippling fluorosis), the disease can cause a rigid, stiffened spine that renders the patient virtually immobile. However, the adverse effects of skeletal fluorosis are not limited to the spine and the upper and lower extremities of the body. The joints and bones in the anatomical region of the oro-skull are also similarly affected by the condition. Despite that, there are insufficient data on the biological effects of skeletal fluorosis in this essential anatomical region.

A one-point, investigative, cross-sectional study was conducted to determine possible skeletal fluorosis-related morphologic changes in the T.M.J. and associated functional limitations among individuals diagnosed with skeletal fluorosis. The study included 9 participants with skeletal fluorosis and was conducted between February 4, 2023, and March 20, 2023. A two-dimensional orthopantomogram was used to rule out possible skeletal fluorosis-related morphological changes in the temporomandibular joint. The TheraBite TMJ ROM scale was used to evaluate the R.O.M. of the T.M.J. by measuring the distance between the maxillary and mandibular cutting edges (interincisal open distance). The temporomandibular joint was auditioned to with a stethoscope for possible noises. Radiographs of the 8 study participants showed morphologic changes such as ossification of various joint structures, osteophytosis, osteophytes, and hyperostosis. In addition, 6 study participants had varying degrees of temporomandibular joint ankylosis. Of these, 4 participants showed low-intensity crepitus sounds on stethoscope auscultation. The results of this study suggest that skeletal fluorosis should be considered as the first differential diagnosis in patients complaining of pain, abnormal sounds, and stiffness related to the temporomandibular joint.

Keywords: Skeletal fluorosis; Temporomandibular joint; Morphology; Functional limitations

Abbreviations: ROM: Range of Motion; TMJ: Temporomandibular Joint; OPG: Orthopantomogram; IRB: Institutional Review Board; SPSS: Statistical Package for the Social Sciences

Introduction
Long-term and excessive fluoride consumption leads to impaired bone homeostasis and several chronic systemic diseases, including dental and
skeletal fluorosis. Dental fluorosis, first described by Trendley Dean in 1937, is caused by excessive fluoride intake, which leads to multiple changes in developing tooth enamel and alters its structure [1,2]. Similarly, skeletal fluorosis is caused by toxic osteopathy characterized by massive fluoride incorporation into the bones [3]. The main pathological features of skeletal fluorosis include joint pain, stiffness, muscle weakness, and skeletal deformities [4,5]. Fluoride directly affects bone through two main mechanisms [6]. In mineralized tissues, fluoride is incorporated into apatite crystals by ion exchange, forming fluorapatite [7]. Such transformation leads to changes in crystallinity and decreased mechanical properties [8]. In bioactive tissue, fluoride also stimulates osteoblasts and osteocytes in a concentration-dependent mechanism [5].

The severity of skeletal fluorosis has been reported to range from mild joint pain to crippling disability and severe bone deformity [9]. Typical signs and symptoms include pain, limited joint motion, knock knees, leg flexion, and spinal curvature [10]. Recurrent joint pain, axial osteosclerosis, radiculomyelopathy, myelopathy, and joint stiffness are typical musculoskeletal problems associated with the disease [11]. Skeletal fluorosis may be completely asymptomatic in the early stages, and the only method to detect it earlier is a radiographic examination [12]. Most cases of skeletal fluorosis are diagnosed based on epidemiological data associated with radiographic findings [13]. However, skeletal fluorosis is not clinically noticeable and may be confused with other rheumatologic diseases [14]. Radiological changes can be seen in earlier stages of the disease, with irregular thickening and high density of bone on radiographic examination [15]. Radiographic presentation is mainly characterized by bone changes with osteocondensation and later ossification of many ligaments and interosseous membranes [16]. Accordingly, characteristic imaging features include osteosclerosis, osteophytosis, and ligamentous calcifications, primarily in the pelvis and spine [17]. Trabecular blurring or opacities, calcification or ossification of tendon attachments or muscles, hypertrophic ruts at bone margins with areas of relative radiolucency, and a coarse trabecular pattern [1,18].

In general, skeletal fluorosis can lead to significant and crippling deformities, including kyphosis, restricted spinal and thoracic motion, and deformities of the extraspinal joints, especially the hips, which are prone to hip osteoarthritis [18]. In addition, several studies reported a high incidence of genu valgum deformities [19]. Neurologic complications may also occur in 10% of patients diagnosed with skeletal fluorosis [20]. These are primarily due to mechanical compression of the spinal cord and nerve roots resulting from osteophytosis, gross reduction in the anteroposterior diameter of the spinal canal and intervertebral foramina, sclerosed spine, and ossified ligaments [21]. Myelopathy due to ossification of the posterior longitudinal ligament and/or ligamentum flavum has also been reported in patients with skeletal fluorosis, usually localized to the lower thoracic portion of the spinal cord [22]. Progressive radiculomyelopathy of fluorosis is characterized by muscle atrophy, atrophy, and spastic paraparesis or quadriparesis, often in flexion and fasciculation. Urinary incontinence, flexion spasms, and signs of long tract involvement have also been reported [23].

Although the most pronounced changes are seen in the spine, the orofacial skeletal tissues are not free from the adverse effects of skeletal fluorosis [18]. Cranial nerve palsies can occur due to skeletal fluorosis, usually the eighth nerve, with progressive high-frequency perceptual hearing loss due to nerve compression in the sclerosed auditory canal [1,15]. There are also reports of skeletal fluorosis-induced morphological changes in the jaw bones and temporomandibular joints [4]. However, there is limited data on skeletal fluorosis's effects on the T.M.J. [10]. This study was initiated to identify possible skeletal fluorosis-related temporomandibular joint morphological changes and associated functional limitations in adults in the Rift Valley region of Ethiopia.

Methodology

This study aimed to determine possible skeletal fluorosis-related morphologic T.M.J. changes and associated functional limitations in Ethiopian adults diagnosed with skeletal fluorosis. Accordingly, the methodology section focuses on the study's primary objective.

Research Design

A one point cross-sectional study was conducted to identify possible skeletal fluorosis-induced morphologic T.M.J. changes and associated functional limitations in adults diagnosed with skeletal fluorosis.

Study period and sample

The study was conducted between February 4, 2023, and March 20, 2023, in Addis Ababa, Ethiopia. Study participants diagnosed with skeletal fluorosis were included in this study. The diagnosis was based on epidemiological, clinical, biological, and radiological examination results.

Method and instruments of data collection

The relevant radiological data were collected after ethical approval by the Addis Ababa Health Department. Further radiological examinations were performed to rule out possible skeletal fluorosis-related morphological changes of the temporomandibular joints in the study participants. The jaw R.O.M. scale of TheraBite was used to assess the R.O.M. of the temporomandibular joint by measuring the distance between the maxillary and mandibular cutting edges (interincisal open distance) when the mouth was opened.
T.M.J. Assessment

Measurement of temporomandibular joint R.O.M., evaluation of temporomandibular joint sounds, and radiographic examination of the temporomandibular joint were considered relevant to assessing the temporomandibular joint. The physical examination focused primarily on determining the mobility and sounds of the T.M.J.

Evaluation of the jaw range of motion

Interincisal open measurement.

T.M.J. Noise Investigations

Auscultation of temporomandibular joint sounds with the stethoscope.

Radiologic orofacial assessment

A two-dimensional panoramic radiograph or orthopantomogram was used to rule out possible skeletal fluorosis-related morphologic changes in the temporomandibular joint. A bilateral radiographic examination of the temporomandibular joints was performed on each subject who participated in the study. An independent radiologist interpreted the radiographs. The range of motion of the temporomandibular joint was assessed to rule out potential functional limitations. In addition, the temporomandibular joint was examined with a stethoscope for possible sounds. It should be noted that differential diagnoses such as myelofibrosis, osteoblastic metastases, renal osteodystrophy, ankylosing spondylitis, and Paget’s disease were considered to avoid confusion of findings.

Data management, analysis, and evaluation

The IBM SPSS (Statistical Package for Social Sciences) Statistics, version 29 version was used to analyze the collected data. Descriptive statistical analysis was applied to describe and present the findings of the study in simple and compact forms.

Ethical considerations

Ethical assurance (approval number: A/A/H/8415/227) was provided by the Addis Ababa Health Bureau Institutional Review Board (I.R.B.), the ethics committee, after a review of the submitted study proposal. Study participants were adequately informed of the nature of the research project. In addition, verbal informed consent was obtained from each volunteer participant. The right of study participants to make decisions about themselves was respected. They were also free to interrupt or discontinue the study. The radiographs of the study participants and their respective interpretations were kept confidential.

Findings

Initially, 42 study participants were screened epidemiologically, biologically, clinically, and radiographically to be diagnosed with skeletal fluorosis. Of these, 9 were found to present skeletal fluorosis. Those 9 patients (three women and six men) underwent further radiographic investigation (O.P.G.) to rule out possible skeletal fluorosis-related morphologic changes of the temporomandibular joint. The age of the study participants ranged from 41 to 69 years (Table 1). Various morphologic changes (n=11) were seen on the radiographs of the 8 study participants (3 females and five males). Three study participants (1 female and two males) had two morphologic changes each (bilateral skeletal fluorosis-induced T.M.J. lesions). The remaining 5 study participants had a single skeletal fluorosis-induced T.M.J. lesion. In general, ossification of various joint structures, osteophytosis, osteophytes, and hyperostosis were noted as skeletal fluorosis-related morphologic changes in the T.M.J.s. In addition, 6 study participants were found to have varying

<table>
<thead>
<tr>
<th>Number of cases of skeletal fluorosis</th>
<th>Mouth opening by millimeters</th>
<th>NOITULP Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>&gt; 40mm</td>
<td>Class 1</td>
</tr>
<tr>
<td>2</td>
<td>20-40mm</td>
<td>Class 2</td>
</tr>
<tr>
<td>1</td>
<td>1-20mm</td>
<td>Class 3</td>
</tr>
<tr>
<td>-</td>
<td>Locked jaw</td>
<td>Class 4</td>
</tr>
<tr>
<td>6</td>
<td>Total number of cases of skeletal fluorosis with ankylosis</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Skeletal fluorosis-induced morphological changes of the temporomandibular joints.

<table>
<thead>
<tr>
<th>Study participants who had morphological changes in the temporomandibular joint</th>
<th>Radiologically identified morphologic changes</th>
<th>Radiography used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (n=3)</td>
<td>Ossification of ligaments and fibrous tissue; osteophytes in particular disc; multifocal periarticular calcifications; multifocal periarticular calcifications.</td>
<td>Panoramic imaging (O.P.G.) Side view</td>
</tr>
<tr>
<td>Male (n=5)</td>
<td>Ossification of the temporomandibular ligament; ossification of the joint capsule; Osteophytes in the mandibular condyle; ossification of the interosseous membrane; osteophytes in the soft tissue attachments; periarticular calcifications; ossification of the mandibular fossa.</td>
<td>Panoramic imaging (O.P.G.) Side view</td>
</tr>
</tbody>
</table>

Table 2: Skeletal fluorosis cases with different levels of mouth opening status (NOITULP grade).

degrees of temporomandibular joint ankylosis (limitation of temporomandibular joint mobility). Of these, 4 participants exhibited low-intensity crepitus sounds on auscultation with a stethoscope (Table 2).

**Discussion**

Fluoride is strongly associated with hard tissues in humans [24]. The chronic toxic effects of fluoride on the skeletal system were described in 1937 in the Indian state of Madras [25]. Skeletal fluorosis is a slowly progressive disease [26]. Clinical symptoms do not appear for decades and mainly affect the musculoskeletal system [27]. Patients with skeletal fluorosis often present with symptoms of varying degrees, primarily involving muscles, joints, nerve roots, intra-articular tissues, and bones [28]. Typical symptoms include vague joint pain, weakened muscles, stiffness of joints, muscle contractures, numbness, paresthesias, narrowing of the joint interior, and various types of bone deformities [22]. Some claim that the bones and joints of the upper and lower extremities, the muscles and nerve roots of the upper and lower extremities, and the spinal cord are the central anatomical regions affected by skeletal fluorosis [18]. However, several studies have described, albeit to a limited extent, the consequences of skeletal fluorosis on the oro-craniofacial anatomic complex, including the temporomandibular joint [4,6].

The temporomandibular joint is a joint with an articular head (both a hinge and a gliding joint) that harmonizes with various structures such as the bilateral mandibular condyle, meniscus, glenoid fossa, articular ligaments, and associated musculature [25,29]. Temporomandibular disorders (TMD) represent a group of conditions that cause pain or dysfunction in the temporomandibular joint and the muscles that control its movement [4]. Several studies have found that approximately 50-75% of the population is affected to some degree and shows signs of TMD [30]. Several RISK factors, including skeletal fluorosis, have been reported to promote the development of TMD [4,31].

Asawa et al. [4] studied the association of T.M.J. signs and symptoms with dental fluorosis and skeletal manifestations among residents of Dad, Bokarsal, and Deotalab villages in Dungarpur district, Rajasthan, India. Analysis of the study revealed a significant association between signs and symptoms of T.M.J. and skeletal fluorosis. Cracking was the most prominent symptom (21.4%) suggestive of T.M.J. disorder in patients diagnosed with skeletal fluorosis. A study by Harbrow et al. [6] examined the effects of chronic fluoride administration on rat condylar cartilage. Based on morphometric and histochemical techniques, this study showed changes in the cartilaginous layer of the rat temporomandibular condyle after chronic exposure to fluoride (100 parts per million sodium fluoride in drinking water).

Similarly, in this study, morphological changes caused by skeletal fluorosis were observed in 11 of 16 temporomandibular joints examined. The morphologic changes seen on the radiographs of the 8 study participants were ossification of various joint structures, osteophytosis, osteophytes, and hyperostosis. In addition, 6 study participants had varying degrees of temporomandibular joint ankylosis. Of these, 4 participants exhibited low-intensity crepitus sounds on auscultation with a stethoscope.

**Conclusion**

Fluoride in various chemical forms, doses, and exposures has physicochemical and biological effects on cells and tissues. Long-term fluoride exposure can alter the function, differentiation, and proliferation of osteoblasts, osteoclasts, and chondrocytes and lead to skeletal fluorosis by disrupting the balance between bone formation and resorption. Such physiological disruption leads to morphological changes in bones and various joints, including T.M.J. In this study, the morphological changes caused by skeletal fluorosis and the associated functional limitations in 11 temporomandibular joints were described. Significant functional impairments were reported, which could potentially by roughened and irregular articular surfaces of the temporomandibular joints. Therefore, clinicians must consider skeletal fluorosis when examining and treating patients with T.M.J. symptoms. At the same time, in addition to ensuring a preventive strategy against fluorosis, it is essential to thoroughly investigate the complex pathogenesis of skeletal fluorosis and explore new targeted therapies at the molecular level to treat the disease effectively.

**Conflict of Interest**

The author declares no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**References**


