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Research Article

JOURNAL OF ORTHOPAEDICS AND SPORTS MEDICINE

ISSN: 2688-5115

Epidemiological, Biological, Physical and Radiological Surveys for the Diagnosis of Adult Skeletal Fluorosis in the Rift Valley Region of Ethiopia: A Single Point Prevalence Study

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Abstract

Fluoride is often referred to as a double-edged sword, as insufficient intake is associated with dental caries; excessive intake leads to dental and skeletal fluorosis. The toxic effects of fluoride can be classified as acute and chronic. The acute toxicity of fluoride occurs after a single ingestion of a large amount of fluoride. On the other hand, the chronic toxicity of fluoride is caused by long-term ingestion of the chemical element. Skeletal fluorosis is the result of chronic fluoride toxicity. Fluorosis is an endemic disease in several geographic areas of several countries, including the Rift Valley region of Ethiopia. Nevertheless, there are few epidemiological data on skeletal fluorosis. This study was initiated to determine the prevalence of skeletal fluorosis among adults in the Rift Valley region of Ethiopia. A single-point cross-sectional prevalence study was conducted between January 2023 and February 2023 to determine the prevalence of skeletal fluorosis in adults who met the inclusion criteria. Radiologic, biological (serum and urinalysis), and physical examinations were performed to collect the required data. Physical examinations included assessments of Range of Motion (RMO), muscle strength, and dermatomes of the upper and lower extremities' major joints, muscles, and nerve roots. In addition, the stress tests developed by Susheela and Bhatnagar [1] were used as part of the physical examination to diagnose the disease. After analyzing the musculoskeletal, radiological and biological data of the 42 study participants, the prevalence of skeletal fluorosis was calculated to be 21.4% (n=9). This prevalence rate indicates the importance of immediate intervention, including defluoridation and public education.

Keywords: Serum; Urine; Concentration; Radiology; Biology; Prevalence; Fluorosis

Abbreviations: ROM: Range of Motion; WHO: World Health Organization; OPG: Orthopantomogram; IRB: Institutional Review Board; SPSS: Statistical Package for the Social Sciences; MRC: Medical Research Council scale

Introduction

Fluorine is the most electronegative of all chemical elements and is found primarily in the chemically bound form of fluoride [2]. Fluoride is considered an effective agent in preventing dental caries, but excess fluoride can put bones and teeth at risk of developing fluorosis [3-5]. The minimum limit has yet to be established [6]. Nevertheless, elevated fluoride levels in drinking water (i.e., levels above the World Health Organization (WHO) guideline of

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Citation: Heron Gezahegn. Epidemiological, Biological, Physical and Radiological Surveys for the Diagnosis of Adult Skeletal Fluorosis in the Rift Valley Region of Ethiopia: A Single Point Prevalence Study. Journal of Orthopedics and Sports Medicine 5 (2023): 79-83.

Received: February 22, 2023
Accepted: February 28, 2023
Published: March 02, 2023

1.5 mg/l - WHO 2003) are reported to be toxic [7]. In general, skeletal changes and stained tooth enamel may occur if the fluoride content of drinking water exceeds two ppm [8].

Skeletal fluorosis is a long-term disorder of bone metabolism due to long-term fluoride toxicity. It remains one of the most serious health problems in the world [9]. The disease is prevalent in 50 countries in South Asia, East Africa, North Africa, and Latin America [8]. People in these areas most commonly develop fluoride toxicity from consuming groundwater with high fluoride concentrations [3-5]. Other common forms of toxicity include inhalation of fluoride gases from volcanic activity or industrial exposure from coal burning, brick making, aluminum smelting, and industrial waste. In the United States, skeletal fluorosis is rare and reportedly develops via unusual sources of toxicity, including toothpaste ingestion, excessive tea consumption, voriconazole treatment, and inhalant abuse [6].

The most common manifestations of skeletal fluorosis include osteosclerosis, periosteum formation, and connective tissue and muscle ossification. In patients, symptoms may present as debilitating pain and limitation of movement. Spinal motion restriction is the earliest clinical sign of skeletal fluorosis. The stage at which skeletal fluorosis leads to crippling usually occurs in endemic regions between 30 and 50 years of age [9]. Some cases showed osteosclerosis of the spine and pelvis. Others showed gross trabeculation with cystic changes in the knees and elbows and calcification of the interosseous membrane of the forearm. The hip joint capsule and calcaneus calcification has also been reported [10]. Neurologic complications such as radiculomyelopathy occur in some patients as a result of spinal cord and spinal root compression due to increased bone mineral density and irregular bone deposition in and around the spinal canal [11].

In addition to radiographic findings, most cases of skeletal fluorosis are diagnosed based on clinical and epidemiologic data. Characteristic radiographic imaging features include osteosclerosis, osteophytosis, trabecular blurring or opacities, ossification of tendon attachments or muscles, and ligamentous calcifications. Osteopenia, although less common, may also occur in fluorosis, especially in younger patients at an earlier stage [12]. In addition, the diagnosis of skeletal fluorosis can be confirmed by the detection of excess fluorine in blood, urine, or bone tissue. Blood fluorine levels below 0.05 mg/l are considered normal, whereas levels above 0.2 mg/l are associated with a high risk of bone fluorosis. However, the gold standard remains in quantitative analysis of bone ash fluoride from a bone biopsy [13]. However, the need for a differential diagnosis in the diagnosis of skeletal fluorosis must be emphasized. Accordingly, myelofibrosis, osteoblastic metastases, renal osteodystrophy, ankylosing spondylitis, and Paget's disease should be considered. No cure for fluorosis can be proposed except the elimination of the causative etiologic factor. Treatment of skeletal fluorosis generally focuses on symptom management [14].

Literature indicate that more than 50 countries have high fluoride levels in drinking water [9,15]. The Rift Valley in Ethiopia is one of them. Although the region is considered high-risk, there is insufficient published scientific work on skeletal fluorosis [3-5]. Therefore, this study was initiated to determine the prevalence of skeletal fluorosis among adults living in the Rift Valley region of Ethiopia.

Methodology

The study aimed to determine the prevalence of skeletal fluorosis in adults among the Rift Valley region of Ethiopia. The methodology is aligned with the main objective of the study.

Research Design

A one-time cross-sectional prevalence study was conducted to determine the prevalence of skeletal fluorosis among adults in the Rift Valley region of Ethiopia.

Study period and environment

The study was conducted between January 19, 2023, and February 3, 2023, in Addis Ababa, Ethiopia. Recruited study participants who resided in the Rift Valley region of Ethiopia were brought to Addis Ababa to access high-standard radiological imaging centers. Volunteer study participants were expected to meet the following epidemiologic and clinical inclusion criteria.

Inclusion criteria

- Adults older than 18 years and have mottled teeth (dental fluorosis)
- Have lived or currently live in endemic fluorosis areas
- History of joint pain and limited mobility
- History of muscle weakness
- History of paresthesia
- No history of rheumatology, myelofibrosis, osteoblastic metastases, renal osteodystrophy, ankylosing spondylitis, and Paget's disease.

Sample and sampling method

A purposive sampling method was used in this study. Individuals who met the inclusion criteria were purposively recruited to participate in the study.

Method and instruments of data collection

Relevant data were collected after ethical approval from the Addis Ababa Health Department. Radiological, biological (serum and urinalysis) and physical examinations were performed to collect the required data. A goniometer

Gezahegn H., J Ortho Sports Med 2023
DOI:10.26502/josm.511500083

was used to measure ROMs. Muscle strength was measured based on the Medical Research Council scale (MRC scale) for muscle strength. The MRC scale for muscle strength uses a score from 0 (no muscle contraction) to 5 (normal strength) to assess the strength of a specific muscle group in relation to the movement of a single joint. The Pinprick test (pain sensation) and light touch test (light touch sensation) were used to detect possible sensory loss in study participants. Needles and absorbent cotton were used to test pain or touch sensation (dermatomes). Absence or distortion of any response was considered a neurological deficit or nerve damage. Data collection was performed in three main phases.

First stage: musculoskeletal system assessment

The physical examination at this stage includes an R.O.M. assessment of various joints (e.g., hip, knee, shoulder, and elbow joints). The major muscles (e.g., hip flexors, hip adductors, quadriceps, hamstring, biceps, triceps, deltoid) that attach to these joints were tested for muscle strength. The physical examination also included neurological assessments (dermatomes) and physical exercise tests developed by Susheela et al. [1] as part of the diagnosis of fluorosis [1]. Accordingly, study participants who tested positive on all musculoskeletal assessments and those who volunteered to continue in the study underwent biochemical testing; urinary or serum fluoride concentration tests were carried out based on study participants' preference.

Second stage: Fluoride in urine and serum

Quantitative analysis of fluoride concentration in bone ash from a bone biopsy is the gold standard for diagnosis and can be used to determine the clinical stages of skeletal fluorosis. However, this procedure is expensive and associated with high morbidity in study participants. Therefore, study participants who met the inclusion criteria and responded positively to the musculoskeletal examination at the first stage of the data collection protocol were tested for urine or serum fluoride concentration. Elevated serum or 24-hour urine fluoride levels were considered a positive test to diagnose skeletal fluorosis. Therefore, study participants who had more than the average serum fluoride level-8 μM (0-15 p.p.m.) or a urine fluoride concentration greater than 0.2 mg/l were eventually diagnosed with skeletal fluorosis.

Third stage: Radiological assessment of the calcaneus

Study participants who met the inclusion criteria and who were positive on musculoskeletal testing (ROM, dermatome, and muscle strength) and serum or urine fluoride concentration analysis finally underwent radiological examination of the calcaneus. This radiological examination in anteroposterior and lateral views was intended to confirm the positive physical and biochemical tests for diagnosing skeletal fluorosis. An independent radiologist had interpreted the radiographic films.

Data management, analysis and evaluation

The data were recorded and compiled in an Excel spreadsheet. All results obtained after the various examinations were recorded and analyzed using SPSS statistical software.

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 ethical review board 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 laboratory and radiographic findings of the study participants were kept confidential.

Findings

Findings pertaining to the physical examination

A total of 42 (17 females and 25 males) study participants aged 28 to 69 years participated in this study. Of these, 17, 19, 14, and 22 participants tested positive for muscle strength, ROMs, dermatomes, and physical tests [1]. As shown in Table 1, 11 individuals tested positive on all musculoskeletal tests. Accordingly, the prevalence of skeletal fluorosis based on musculoskeletal testing was calculated to be 26.2% (n=11).

Findings pertaining to biological and radiological examinations

Serum, urine, and radiographic examinations were performed on 11 study participants who tested positive on the musculoskeletal assessment protocols. As shown in Table 2, of these 11 subjects, 10 and 9 tested positive for biological and radiographic examinations, respectively. Of these, 9 (81.8%) tested positive for the above biological and radiographic examinations. Thus, based on the musculoskeletal, biological, and radiographic examinations, the prevalence of skeletal fluorosis was calculated to be 21.4% (n=9).

Discussion

Fluoride concentration in drinking water exceeding the World Health Organization recommended level of 1.5 mg/l has been reported to have toxic effects on the skeletal system [3-5]. This form of chronic intoxication was first described in 1937 in the Indian state of Madras. Today, 20 of the 35 states and union territories of the Indian Republic are affected by the effects of fluoride poisoning. In addition, the disease is designated as a public health problem in more than 50 countries around the world, including Ethiopia [3-5]. The prevalence of skeletal fluorosis in the urban slum areas of Nalgonda, a city in Andhra Pradesh, India, was calculated to

Table 1: Findings of the musculoskeletal tests.

Tests	Results		The total number of study participants tested
	Tested positive	Negative tested for all	
Muscle power (Flexors, extensors, abductors, and adductors).	17	25	42
ROMs (shoulder, elbow, hip and knee)	19	23	42
Dermatomes (upper limbs - C5-T2 and lower limbs L1-S5)	14	28	42
Susheela and Bhatnagar [1] Physical Tests	22	20	42
Individuals tested positive for all tests	11	31	42

Table 2: Findings of the biological and radiological investigations.

Tests	Results		The total number of study participants tested
	Tested positive	Negative tested	
Biologic (analysis of fluoride concentration in serum and urine)	10 (2 serum> 0.15 p.p.m. and 8 Urines> 15 p.p.m.)	1	11
X-ray (X-ray of the calcaneus)	9 (heel spur)	2	11

be 24.9% [16]. Another study conducted in a district endemic for fluorosis, Salem, Tamil Nadu, found a prevalence rate of 24.8% for skeletal fluorosis. In both studies, skeletal fluorosis was found to increase with age [17]. In addition, another study that investigated the association between exposure to drinking water fluoride and skeletal fluorosis in 5 villages of Poldasht district in Iran reported a prevalence rate of 18.1% for skeletal fluorosis. According to the study, the disease was more prevalent in older age groups (54.5%) and in women [18]. Nirgude et al. [16] showed in their study that the prevalence of skeletal fluorosis in Nalgonda was 24.9%. Choubisa et al. [19,20] showed that the prevalence of skeletal fluorosis was 23.9% in individuals with poor nutrition. Similarly, this study found a cumulative prevalence rate of 21.4% after examining the musculoskeletal, radiological, and biological data of 42 study participants. The prevalence rate varied from 21.4% to 26.2%, depending on the study mechanisms used to assess the prevalence of skeletal fluorosis.

On the other hand, a cross-sectional study conducted in the Vidharbha region of Maharashtra, India, found prevalence rates of 56.87% and 43.13% for skeletal fluorosis in male and female study participants, respectively. In this area, the main source of drinking water was reported to be a tube well and the fluoride concentration in the water ranged from 4 to 4.5 ppm [9]. Choubisa et al. [19,20] reported 39.2%, 32.8%, and 36.6% prevalence rates of skeletal fluorosis in different Indian districts with fluoride concentration of 3.2 ppm, 3.7 ppm, and 4.0 ppm, respectively. A study conducted in three endemic fluorotic areas of the Indian state of Punjab found prevalence rates of skeletal fluorosis ranging from 20% to 51% in the different study groups. It was also reported that fluoride concentrations in drinking water ranged from 2.3 to 22.5 mg/L [21]. A study conducted to assess the prevalence of skeletal fluorosis among retired employees of Wonji Shoa sugar settlement in Ethiopia found prevalence rates of 20% and 70.3%, respectively, based on clinical and radiological examinations [22]. In contrast, this study found a comparatively higher prevalence rate on clinical assessment than on radiological examination. This apparent discrepancy between the two studies may be due to the different resolving power of radiological technology and the different fluoride concentrations in water in different areas [23].

Conclusion

Fluorosis is a slowly progressive disease that affects the skeletal system. Several researches have shown that the intake of fluoride in concentrations of 1.5 ppm and above a major risk factor for the development of skeletal fluorosis. This study revealed a significant prevalence rate of skeletal fluorosis among vurnerable adults in Ethiopia. So far, there are no effective therapeutic modalities to cure the condition. The best approach to control the consequences of the disease is prevention. Therefore, a national policy needs to be developed and established to provide drinking water with fluoride levels that do not cause adverse health effects ($\geq$ 1.5 ppm). This can be achieved by finding alternative water sources or by defluoridating water for drinking and cooking.

Conflict of Interest

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

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Citation: Heron Gezahegn. Epidemiological, Biological, Physical and Radiological Surveys for the Diagnosis of Adult Skeletal Fluorosis in the Rift Valley Region of Ethiopia: A Single Point Prevalence Study. Journal of Orthopedics and Sports Medicine. 5 (2023): 79-83.