

## Original Article

## Fluoride levels and osteosarcoma

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## Abstract

**Context:** Osteosarcoma is a rare malignant bone tumor; commonly occurring in the age group of 10 to 24 years. Recent reports have indicated that there is a link between fluoride exposure and osteosarcoma. **Aims:** The present study was planned to analyze serum levels of fluoride in patients of osteosarcoma and fluoride content of their drinking water. **Settings and Design:** The present study was carried out comparing 10 patients of osteosarcoma and 10 healthy volunteers (who served as controls). **Materials and Methods:** Serum and drinking water fluoride levels were estimated by ion selective electrode. **Statistical analysis used:** The data were computed as mean  $\pm$  SD and Student's t test was applied. **Results:** Both, the serum and drinking water fluoride levels, were significant by higher in patients with osteosarcoma as compared to controls ( $P < 0.05$ ,  $P < 0.001$ , respectively). **Conclusions:** These results suggest a link between fluoride exposure and osteosarcoma.

**Key words:** Fluoride, osteosarcoma, serum, water

## Introduction

Osteosarcoma is a rare malignant bone tumor, commonly occurring in the age group of 10 to-24 years. Bone is the principal site of fluoride accumulation.<sup>[1,2]</sup> In several parts of India, particularly Haryana, incidence of fluorosis is high in certain areas.<sup>[3]</sup> Recent reports have indicated that there is a direct link between fluoride exposure and osteosarcoma.<sup>[4,5]</sup> Studies have also linked high incidence of bone cancer to fluoridation in drinking water.<sup>[5-7]</sup> On the other hand, a few reports have also indicated that fluoride exposure has no role in osteosarcoma.<sup>[2,8,9]</sup>

To the best of our knowledge, we could not come across any study where fluoride levels have been estimated in serum and drinking water of osteosarcoma patients. Hence, the present study was planned to analyze serum levels of fluoride in patients of osteosarcoma and fluoride content of their drinking water.

## Materials and Methods

The present study was conducted in 10 patients of osteosarcoma and 10 healthy volunteers, who served as

controls. 2 ml venous blood was collected aseptically from antecubital vein, and serum was separated by centrifugation. Also, 10 ml drinking water samples brought by these subjects from their home were also evaluated. Serum and fluoride levels were estimated by ion selective electrode.<sup>[11]</sup> The data were computed as mean  $\pm$  SD and Student's t test was applied.

## Results

Serum fluoride levels were significant by higher in patients with osteosarcoma as compared to controls ( $P < 0.05$ , Table 1). Also, drinking water fluoride levels were significantly higher in osteosarcoma group as compared to controls ( $P < 0.001$ , Table 1). There was also a positive correlation between drinking water fluoride and serum fluoride levels in the osteosarcoma group patients ( $r = 0.855$ ,  $P < 0.01$ ).

## Discussion

Fluoride influences bone growth by acting as mitogenic agent for Osteoblasts.<sup>[12]</sup> Recent studies have indicated relationship of high fluoride levels in drinking water with incidence of osteosarcoma.<sup>[4]</sup> There are no reports available in literature where serum and drinking water fluoride levels have been correlated in osteosarcoma. We have recently reported on serum fluoride and sialic acid levels in osteosarcoma.<sup>[13]</sup>

In the present study, significantly higher serum fluoride levels were documented in osteosarcoma patients as compared to healthy controls (Table 1,  $P < 0.05$ ). Also, samples of drinking water from the homes of these patients also showed a higher fluoride content.

Fluoride gets incorporated into bone lattice by forming fluoroapatite, which is more stable than hydroxyapatite.

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**Table 1: Fluoride levels in two groups (mean ± SD, mg/L)**

	Control group	Osteosarcoma patients	P value
Serum fluoride	0.042 ± 0.035	0.183 ± 0.105	< 0.05
Water fluoride	0.475 ± 0.243	1.302 ± 0.760	< 0.001

During periods of rapid skeleton growth, fluoride uptakes in bone increases since hydroxyapatite crystal are extremely small in young age. Also, fluoride has been reported to increase calcium absorption in intestine,<sup>[14]</sup> and this property is exploited in treatment of osteoporosis.

We showed a correlation between drinking water fluoride and serum fluoride in osteosarcoma patients. However, a Chinese report documented no correlation between drinking water fluoride and serum fluoride (correlation coefficient was 0.855) where fluoride in drinking water is safe and reasonable.<sup>[15]</sup>

*In vitro* studies have shown that exposure to fluoride causes osteoblast proliferation and malignant transformation.<sup>[16]</sup> Optimal dose of between 10-100 µmol/L is required to stimulate bone cell proliferation and differentiation.<sup>[16]</sup> Also, a link between p53 mutations and fluoride bone content has been reported in tissue samples from osteosarcoma patients.<sup>[17]</sup>

Finding of high serum fluoride levels in osteosarcoma patients along with high drinking water fluoride level in our patients suggest a link between fluoride and osteosarcoma.

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## NEWS

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