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Effect of Fluorosis On Serum Total Protein Level In A Fluoride Endemic Zone: A Cross-Sectional Observational study

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Abstract: *Fluorosis is a major public health problem in India now a days as most of the population is dependent on ground water. This cross-sectional observational study has been performed in the fluoride endemic zones of Bankura district of West Bengal to evaluate the effect of fluorosis on serum total protein level. This study was carried out in the Hirbandh block of Bankura, on 80 subjects by using simple random sampling among which 42 were cases. The serum samples were collected from the cases and the serum fluoride was estimated by Ion-Meter and serum total protein level was determined by auto-analyzer and were compared with age and sex matched controls. The serum fluoride was found to have a statistically insignificant relationship with serum total protein in the study group. The serum level of fluoride was higher in study group but the total protein level was lower than those of comparison group.*
Keywords: *serum fluoride, total protein.*

I. INTRODUCTION

The disease fluorosis is caused by an element known as fluoride, the 13th most abundant element available in the earth crust. Considering the chemical properties of fluoride, this element of halogen group with molecular weight 19 and atomic number is 9[1]. Fluorosis is identified as a public health problem in 24 other countries around the globe- like Pakistan, Bangladesh, Argentina, United State of America, Morocco, Middle East countries, Japan, South Africa, New Zealand, and Thailand etc[2]. In India the problem also has reached alarming proportion affecting at least 17 states of India. 50-100% districts are affected – Andhra Pradesh, Tamil Nadu, Uttar Pradesh, Gujarat, Rajasthan. 30-50% Districts are affected – Bihar, Haryana, Karnataka, Maharashtra, Madhya Pradesh, Punjab, Orissa, West Bengal.< 30% districts are affected- Jammu and Kashmir, Delhi, Kerala[3]. Fluoride is often called a two-edged sword. Prolog ingestion of fluoride through drinking water in excess of daily requirement is associated with dental and skeletal fluorosis. Similarly inadequate intake of fluoride in drinking water is associated dental carries. World Health Organization (WHO) has set the upper limit of fluoride concentration in drinking water at 1.5 mg/L[4], and the Bureau of Indian Standards , has laid down as 1.0 mg/L as the maximum permissible limit of fluoride with further remarks as " lesser the better" [5]. Intake of fluoride higher than the optimum level is the main reason for fluorosis. In Bankura district of West Bengal out of 22 blocks 17 blocks are fluoride endemic zones, leading to consumption of high levels of fluorides in drinking water with its health consequences, i.e. high incidence of dental and skeletal and non-skeletal fluorosis symptomatic cases[6]. Following ingestion, fluoride accumulates in bones and teeth and disperses toward cardiac muscle, liver, skin, and erythrocytes[7]. In hard tissues it can cause skeletal and dental fluorosis, and in soft tissues it can produce metabolic disturbances and increased free radical activity[8,9].

There is hardly any study on the effect of fluorosis on serum total protein level in human. Few studies have been done on other animals. In Qujeq D et al after 90 days, the average total serum protein level of the rats in the treatment group decreased significantly compared with that in the control after oral treating with sodium fluoride at three doses, 10, 20 and 30 mg/kg daily for 90 days[10]. In Kumar PS et al , biochemical analysis of serum revealed the significant decrease ($P < 0.01$) of serum albumin and total protein content in the affected animals[11]. So aim of the study was to determine the serum total protein levels in patients with endemic fluorosis to check the effect of fluorosis on it.

II. MATERIALS AND METHODS

2.1. Study area: This cross-sectional observational study was conducted in Hirabandh block of Bankura district. The tests were carried out at department of Biochemistry, B.S. Medical College, Bankura (District fluorosis detection laboratory).

2.2. Study subjects: 80 subjects were selected by simple random sampling among them 47 were male and 33 were female. In that particular block, the endemic fluorosis was diagnosed according to the clinical diagnosis criteria, as per described by Wang et al[12]. The criteria for study are (1) people living in the endemic fluorosis region since birth, (2) having mottled tooth enamel, indicating dental fluorosis, (3) consuming water with

fluoride levels above 1.2 mg/L (normal 1 mg/L), and (4) a urine fluoride level greater than 1.5 mg/L. Control subjects living in the same area without showing above mentioned signs were designated as control.
We have chosen the subjects from age 5 to age 65 years.
The exclusion criteria-
1. History of any malignancy,
2. History of any active infection,
3. History of any chronic illness such as chronic kidney disease etc,
4. Pregnant women.
5. Severely malnourished individuals.
6. Any other causes of hypoproteinemia i.e. nephrotic syndrome, chronic liver diseases etc.

The case and the control subjects were screened and physically examined and information regarding demography, nature of illness were collected from them using a predesigned and pretested questionnaire. Informed consent was taken from each of the participant. The study design was approved by institutional ethical committee.

2.3. Study Period: This study was carried out during the period from June 2015 to November 2015.

2.4. Laboratory investigations: The serum samples were collected from the 42 cases and 38 controls and stored at -20ºC before analyzing after doing centrifugation. Serum fluoride level was estimated by Ion Meter (ORION-9609BNWF) and serum total protein level were estimated by auto-analyzer (DS-302).

2.5. Statistical analysis: The data were compiled in MS excel and analyzed by different statistical methods. Data display was done by charts and tables. Data were described by proportion, mean, SD, range etc. Statistical tests like independent 't' test, Pearson's correlation coefficient (r) etc. were used to explore the relationship between variables. P value of <0.05 was considered significant to discard the null hypothesis at 5% precision and 95% confidence interval.

III. RESULTS

Out of 80 participants 33 were female and rest were male (Figure-1).
The average age of the participants was 39.54±6.41 (mean ± SD) years with a range of 60 years. The study group was found to have higher average serum fluoride levels compared to that of the comparison group but lower serum protein level than the comparison group and the difference was statistically robust (Table-1).
The serum fluoride was found to have no statistically significant relationship with serum total protein among the subjects belonged to the study group (Table-2).

IV. DISCUSSION

Fluorosis is an important public health problem in 24countries, including India. Of the 85 million tons of fluoride deposits on the earth's crust, 12 million are found in India[13]. Hence it is natural that fluoride contamination is widespread, intensive and alarming in India. Endemic fluorosis is prevalent in India since 1937[14]. It has been estimated that the total population consuming drinking water containing elevated levels of fluoride is over 66 million[15]. Endemic fluorosis resulting from high fluoride concentration in groundwater is a public health problem in India[16].
The normal upper limit of fluoride in serum is 0.02 mg/l[17] and the normal reference level of serum total protein is 6.4-8.3 G/dL[18]. In our study, the serum total protein level was low in study group than comparison group. AQ study done by Cenesiz S et al showed that the serum total protein level was low in case than in control[19] and the study was done on Tuj sheep. Serum total protein level was also reported to decrease in rats[20] children[7] and sheep[21,22] with chronic fluorosis which were similar to our study findings.
Fluorosis can inhibit protein synthesis by weakening the beginning of the peptide chain and by preventing the production of peptide chains in ribozomes[23,24].

V. CONCLUSION

Our study suggested that the increased serum fluoride concentration can lower the serum total protein level. Hence proper remedy and health education should be implemented for the people residing in fluoride endemic zones and more studies should be conducted for establishing the association between fluorosis and serum total protein level in human being as most studies were done on the animals other than human being.

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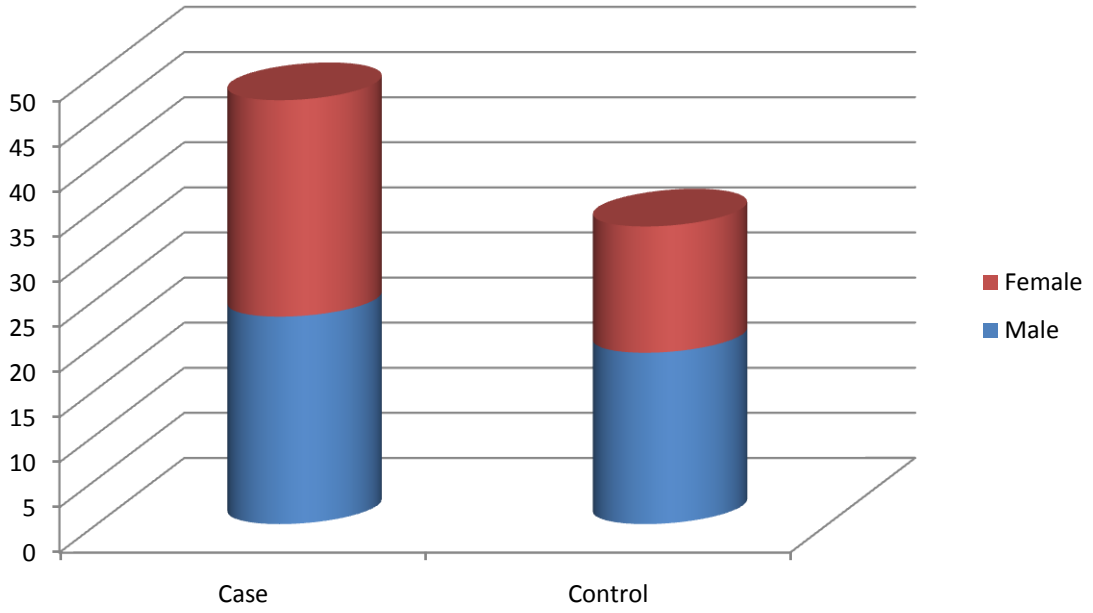

Figure-1: Distribution of case and control according to gender

Sl.No	Parameter	Fluorosis subject (n=42) (Mean± SD)	Control (n=38) (Mean± SD)	*P* Value	Significance
1	Serum fluoride (mg/l)	0.2473±.0087	.0338±.0038	0.001	Significant
2	Serum total protein (G/dL)	5.43±0.98	8.55±0.29	0.004	Significant

Table No-1: Serum levels of total protein and Fluoride in Cases and control

Parameter	Group	Correlation coefficient (r)	Significance (p value)
Serum fluoride Vs Total protein	Study	0.118	0.455*

* Correlation is insignificant (2-tailed).

Table No-2: Relationship between the serum parameters among study group