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Post Exposure Estimation of Urinary Fluoride in Patient with Skeletal Fluorosis and Its Clinical Corelation Atnasipur Village of Birbhum District, West Bengal

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Abstract:- Background-Excretion of fluoride in urine occurs in Skeletal fluorosis.
Aims and Objectives-Discover correlation between urinary fluoride and disease progression.
Result and Analysis-Most common affected age group between 50-60 yrs(42%) with 98% having generalized bone and joint pain and 34 cases clinically graded as gr-II,11 as gr I,and rest as gr III.Fiuoride concentration in urine of 47 cases was >0.5mg/l and analyzed correlation coefficient was+0.89
Conclusion-Patients with higher clinical grading were associated with low level of fluoride in urine and vice versa.
Keyword:- Skeletal fluorosis, Correlation coefficient, Clinical grading

I. Introduction

Serious complication of chronic fluoride contamination is fluorosis.It affects almost every organ of human body and produce deleterious effect[1].Serum and urinary fluoride concentration is recognized as a good indicator of fluoride exposure and provides an important basis for endemic fluorosis[1] control and prevention. Excretion of fluoride in urine appears to be directly related to the daily exposure of fluoride. Quantity of fluoride decreases after exposure gradually because of bone remodeling that's why urinary concentration decreases after exposure. 'Skeletal fluorosis is associated with prolonged accumulation of fluoride resulting in fragile bones having low tensile strength, excessive ossification and joint ankylosis in skeletons[1,2,3].It is well established that prolonged use of fluorides as recommended levels does not produce any harmful physiological effects in the humans.These effects can be classified as acute and chronic intoxication. Fluoride is distributed from plasma to all tissues and organs. Tissue-water-to plasma- water ratio (T/P) ratio of fluoride is 0.4-0.9[4]. This range means that fluoride is able to penetrate cells. (T/P higher than Insulin which is an extracellular marker) but fluoride is not accumulated intracellular as T/P is less than 1. Some exceptions where fluoride cannot penetrate into brain (blood-brain barrier) and adipose tissues in which T/P ratio of fluoride is 0.08 & 0.11 respectively[4,5]. T/P ratio of fluoride in kidney is 4.16. This value does not indicate accumulation but is related to the excretion of fluoride by kidney. Approximately 90% of the fluoride retained in the body is deposited in the skeleton and teeth (calcified tissue). Fluoride exists in both ionic and bound forms in plasma, with the bound form being present in larger quantity. Fluoride in calcified tissues is not irreversibly bound that means, it may be released during normal remodelling of bone.In soft tissues, fluoride has a steady state distribution between the intracellular and extracellular fluids. When the plasma level of fluoride is rising or falling, there is a parallel change in the intracellular fluids. The biological half-life of bound fluoride is several years. Roughly 50% of the absorbed fluoride is excreted in the urine during the following 24 hours. Most of the remaining 50% will become associated with calcified tissue. In children less than three years of age only about 50% of total absorbed amount is excreted, but in adults and children over 3 years - about 90% is excreted. Fluoride also passes through the placenta and also appears in low concentrations in saliva, sweat and milk.

In the year 1978, the World Health Organization dug four deep tube wells in Nasipur, a village of Birbhum district of West Bengal,India and these tube well water was highly contaminated with fluoride. The inhabitants of that area used to consume this water for a long time, and got affected by fluorosis. After 19 years of exposure to contaminated water they were diagnosed incidentally as cases of skeletal fluorosis. Abandoning the sources of contaminated water, provision of alternative safe drinking water and treatment of affected victims was done since 1997.Few affected victims were died and remaining still having features of skeletal,non-skeletal and

Dental fluorosis[6].In this study Weanalyzed post exposure excretion of urinary fluoride and its clinical correlation.

Keyword:- Fluorosis, Skeletal, Dental fluorosis

II. Methods

Study was done in Dept of Orthopaedics, Medical College Kolkata and School of Environmental studies,Jadavpur University**,**starting from January 2014 to July 2014,Fifty diagnosed cases of fluorosis selected from a sample of 210 cases of village Nasipur.Spot urine sample is collected in sterile ion free 10 cc polyethylene bottles of 50 volunteers with clinical features of skeletal fluorosis. Two drop of concentrated hydrochloric acid is added to the sample. Samples were labeled with proper registration number, name, age, and serial no of the patient. Samples were kept in ice with sodium chloride mixture for transportation to laboratory. Samples were stored in ice lined refrigerator. Following required for estimation of fluoride in urine.

a. Spot urine samples
b. Unionized double distilled water
c. ThermoScientificOrion4-StarPluspH/Conductivity Meter[7].
d. Fluoride Ion-Selective Electrodes[8].
e. Total ionic strength adjustment buffer (TISAB) II[9].

III. Result and Analysis

Out of 50 patients, 72% were male and 28% female of different age group starting from 22yrs up to 70 yrs with a median age for male 48.230yrs and female 53.25yrs. 8% are students, 40%labourer, 32% farmers and 20% house wives. Among them 98% having generalized bone and joint pain,68% cases having low back pain stiffness and rigidity of back,22%cases having severe chest symptoms, and dental changes found only 28% cases. There is neurological involvement in 2% cases, 22%cases were of Clinical grade I,68% grade II and 10% were grade III.Grade I patients having Mean urinary fluoride level 1.02mg/l(male) and 1.14mg/l(female).In case of Grade II, mean urinary level of fluoride was 0.997mg/l(male)and 1.003mg/l(female).and Fluoride level of Grade III patients were 0.665mg/l in case of male and 0.723mg/l in case of females.The maximum urinary concentration of fluoride was found in a 45 year male patient with Grade I clinical symptom (2.54mg/l) and the minimum concentration was 0.04mg/l. According to World Health Organization guideline standard of 0.5mg/l of urinary fluoride excretion, three out of 50 cases had <0.5mg/l fluoride. Clinical Grading of these cases done with criteria of Dr S K Gupta, we found 8 males and 3 females have grade I involvement, and 34 case found with Grade II and 5 cases found with Grade III features.

Regression Statistics							
Multiple R	0.891321						
R Square	0.794453						
Adjusted R Square	0.77362						
Standard Error	0.89725						
Observations	49						
ANOVA							
df	*SS*	*MS*	*F*	*Significance F*			
Regression	1	149.3572	149.3572	185.5237	6.2E-18		
Residual	48	38.64276	0.805057				
Total	49	188					
Coefficients varriance	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
0.852	1.689906	0.124069	13.62071	0.03	1.440449	1.939363	1.440449	1.939363

IV. Discussion

R.C.Likin et al1 reported that essentially all absorbed fluoride deposited in the skeletal and dental tissue which is not fixed irreversibly, is shown by its mobilization following a reduction in fluoride intake[10].There was no apparent relation between age and urinary fluoride excretion.This study shows there is a correlation which is the gradual decreasing level of fluoride in urine with advancing age. Our study also reveals a correlation between symptoms and urinary fluoride excretion in the victims. The villagers of Nasipur had stopped ingestion of contaminated water in the year 1997 and were evaluated after 19 years, we found that the patients with higher clinical grading were associated with low level of fluoride in urine and vice versa. Gupta S K et al found that the

neurological complications occur in 3 - 10% of cases of skeletal fluorosis[11]. These complications are mainly due to compression of the spinal cord and the roots by the protruding osteophytes[11,12]. Some of the neurological deficit may also be due to the direct effect of fluorides on neuromuscular enzymes. However, the neurological toxicity of fluorides is yet to be established.The males are affected more than females. The neurological features are in the form of cervical myeloradiculopathy, cervical myelopathy or radiculopathy, dorsal myelopathy, and peripheral neuropathy.The cranial nerve involvement and sensory deficits are rare. In our study, we found one diagnosed patient of skeletal fluorosis had paraparesis with low level of fluoride in urine.

QY Xiang et al,stated that higher serum fluoride level seen in skeletal fluorosis and serum fluoride concentration is recognized as a good indicator of fluoride exposure and provides an important basis for endemic fluorosis control and prevention[13]. Other researchers believe that roughly 50% of the absorbed fluoride is excreted in the urine during the following 24 hours. Most of the remaining 50% fluorides become associated with calcified tissue. In children less than three years of age, only about 50% of the total absorbed amount is excreted, but in adults and children over 3 years about 90% is excreted. Our study emphasized a correlation between the urinary fluoride concentration and age, sex & clinical features of the victims. Results of analysis found that cases having less clinical symptoms excreting higher amount of fluoride in urine.

Susheela A.K. et al found that generation of free radicals, lipid peroxidation and altered antioxidant defense system are considered to play an important role in the toxic effect of fluoride[14]. Investigations reveal that withdrawal of the fluoride source and nutritional supplementation showed improvement in health and a significant reduction in fluoride level in urine and serum of the patients. It is evident from the earlier studies that fluorosis can be prevented through appropriate intervention if the disease is diagnosed early. Consumption of a diet adequate in protein, calcium, vitamin C, vitamin E and other antioxidants can minimize the effect of fluoride toxicity. Ascorbic acid is one of the most important antioxidants in the plasma and is also an anti-stress factor. Ascorbic acid plays a significant role in the amelioration of fluoride-induced toxicity. Earlier studies in patients with fluorosis indicated that drinking water containing high fluoride concentrations reduced the levels of Glutathione and Glutathione peroxidase. With the passage of time, symptoms are either static or increasing but in patients with severe symptoms urinary fluoride level was seen to be decreasing.It may be due to degenerative changes, which may lead to increasing symptoms with advancing age. In our study the victims of fluorosis after 19 years of exposure were found to have reduced level of urinary fluoride.

Biswajit Nayak, Madan Mohan Roy 2009 in the article 'Health effects of groundwater fluoride contamination' says the adverse effects of excess fluoride in a population that used the fluoride-contaminated tube-well water for drinking and cooking[15]. The study was done at the Berhait block of the Sahibganj district of Jharkhand state. A total of 157 cases of fluorosis were studied with history of exposure to contaminated water, physical examination and estimation of fluoride in urine were done in 25 cases. Results shows that 54 patients had chronic low back pain, 18 patients had severe deformity, two patients had paraplegia and five had nodular swelling .Urine reports shows that mean concentration of fluoride in adult urine was 3.21mg/l and 1.48mg/l in children.

V. Summary

Long time after cessation of exposure to fluoride, in the area of village Nasipur, Birbhum district, there is evidence of cases of skeletal fluorosis. Their physical examination including chest expansion and spinal deformity and clinical grading were assessed[16].We collected spot urine sample of 50 cases and with proper precaution and sent them to a laboratory at the School of Environmental Studies,Jadavpur University and analyzed urine samples for fluoride.

There was a correlation between urinary fluoride level and clinical grading with a correlation co-efficient (r) +0.89. So, advanced cases having low level of urinary fluoride in respect to those of mild involvement. Our suggestion is requirement of further study to follow-up those cases where ever concentration of fluoride in urine remains same or decreases and also to find out any element or medication which can eliminate fluoride from body rapidly.

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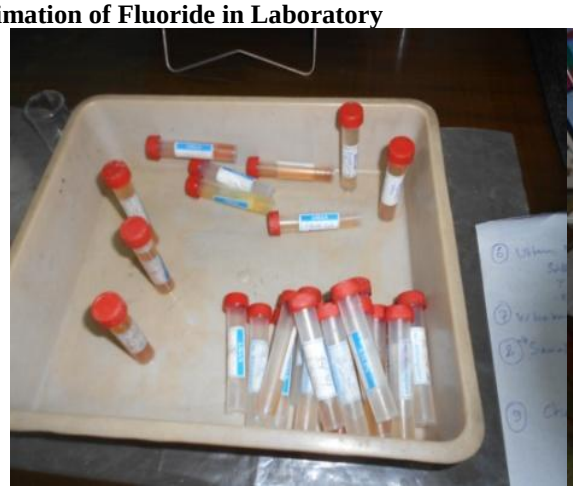
Clinical and Radiological Pictures

Spinal involvement

Estimation of Fluoride in Laboratory

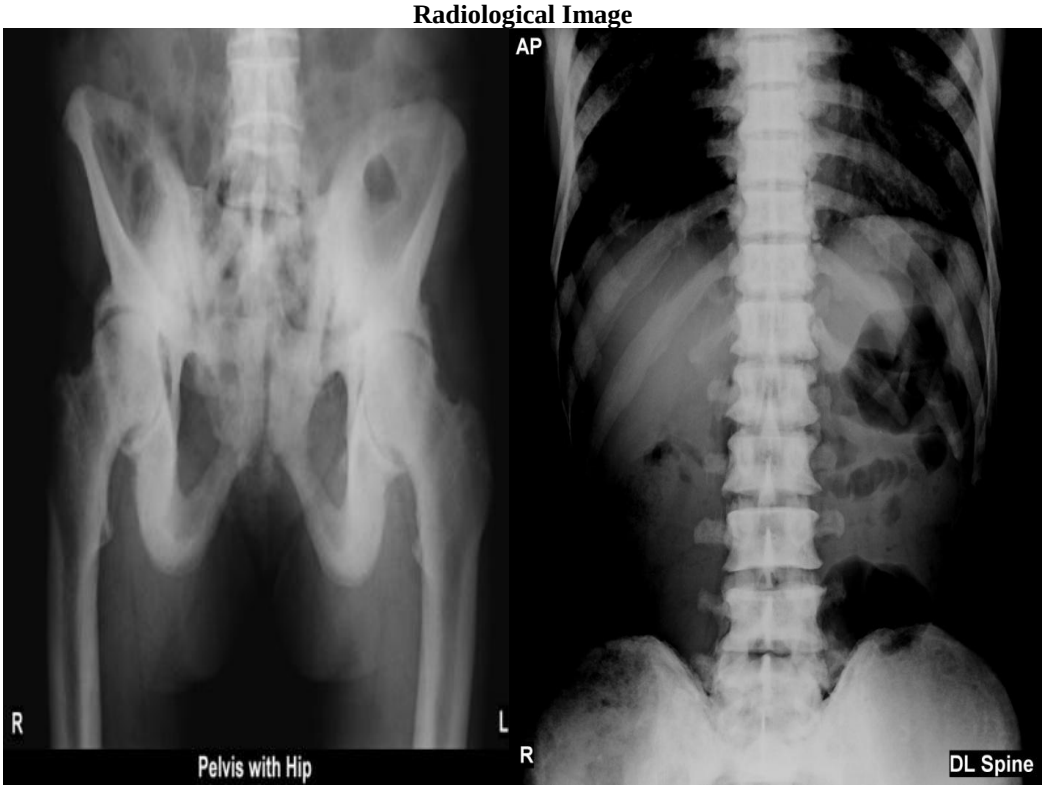


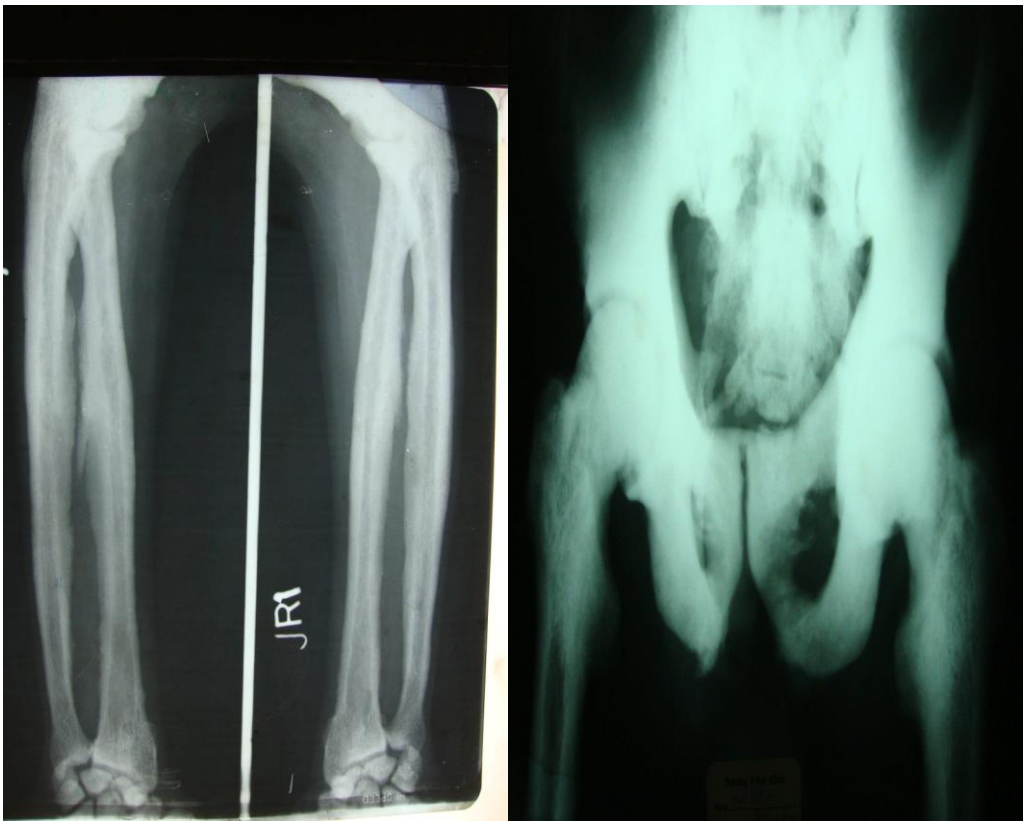
Sample of urine

Instrument Set

Methods of estimation of Fluoride in urine

Radiological Image





ThermoScientificOrion4-StarPluspH/Conductivity Meter

Charts and Diagram

Sl no	Clinical Findings	No of cases	Percentage
1	Pallor	38	76%
2	Icterus	3	6%
3	Edema	20	40%
4	Diminished Chest expansion (< 2.5 cm)	11	22%

Table 1 Distribution of different type of abnormality on General Examination

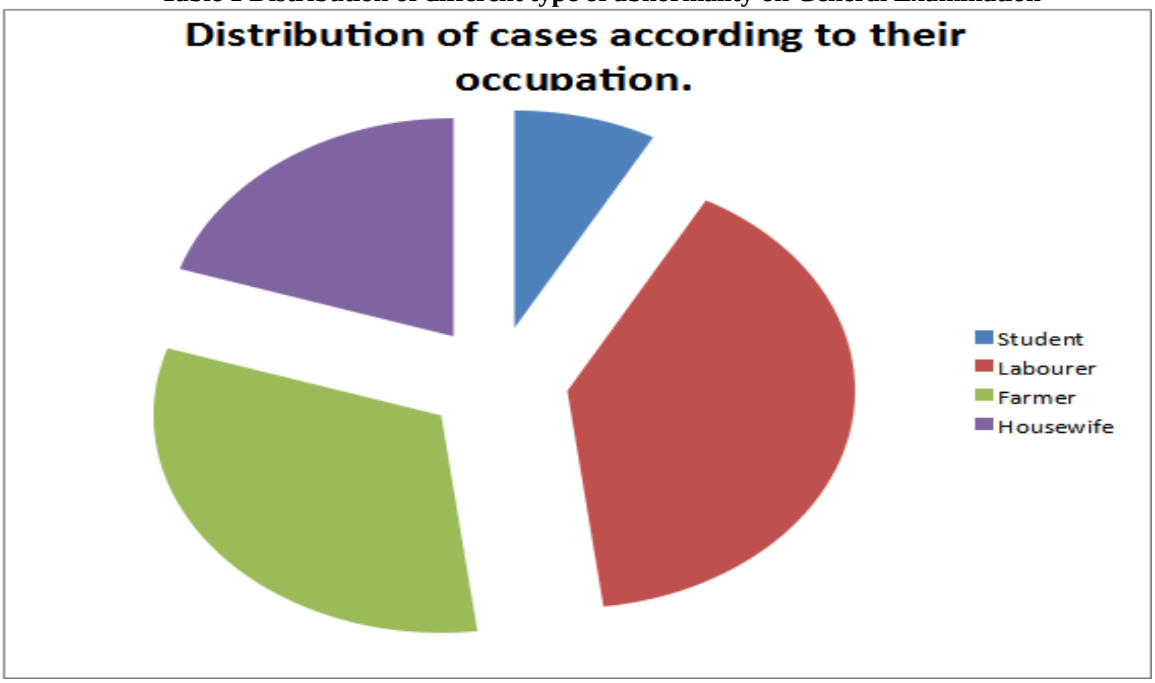


Chart 2 Distribution of cases according to their occupation

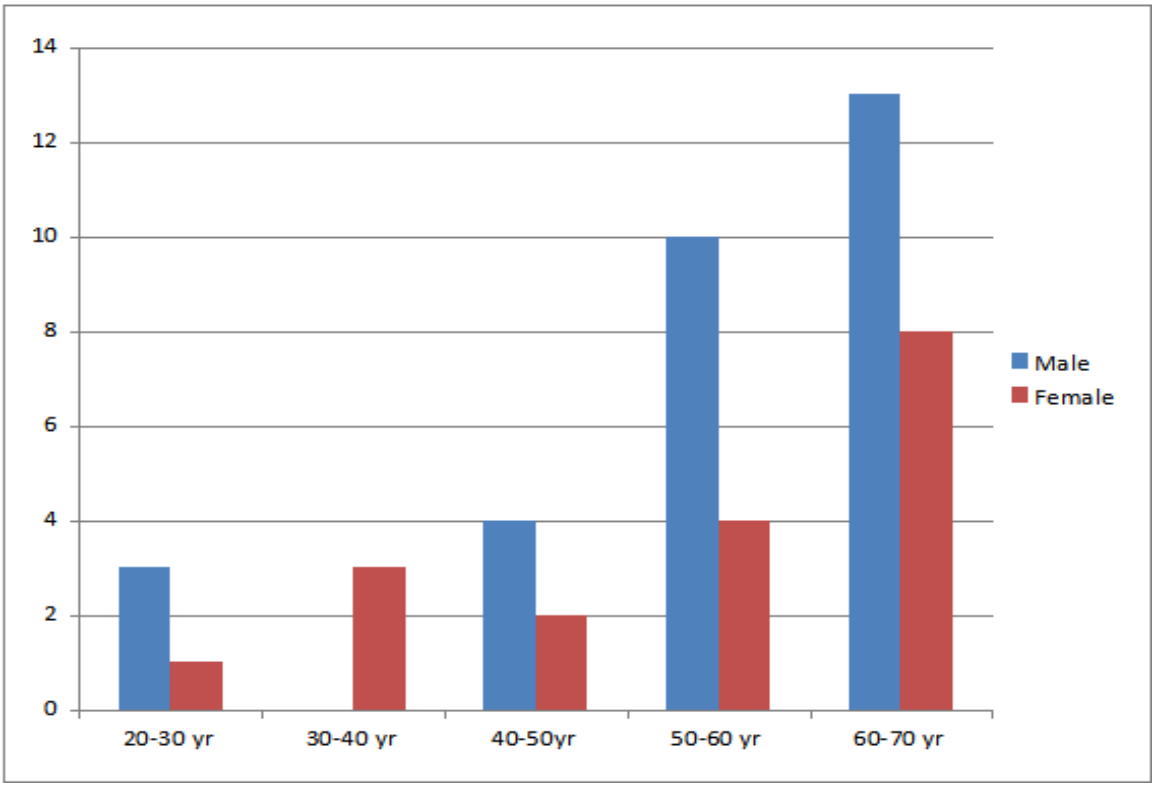


Chart 3 Age wise distribution of cases

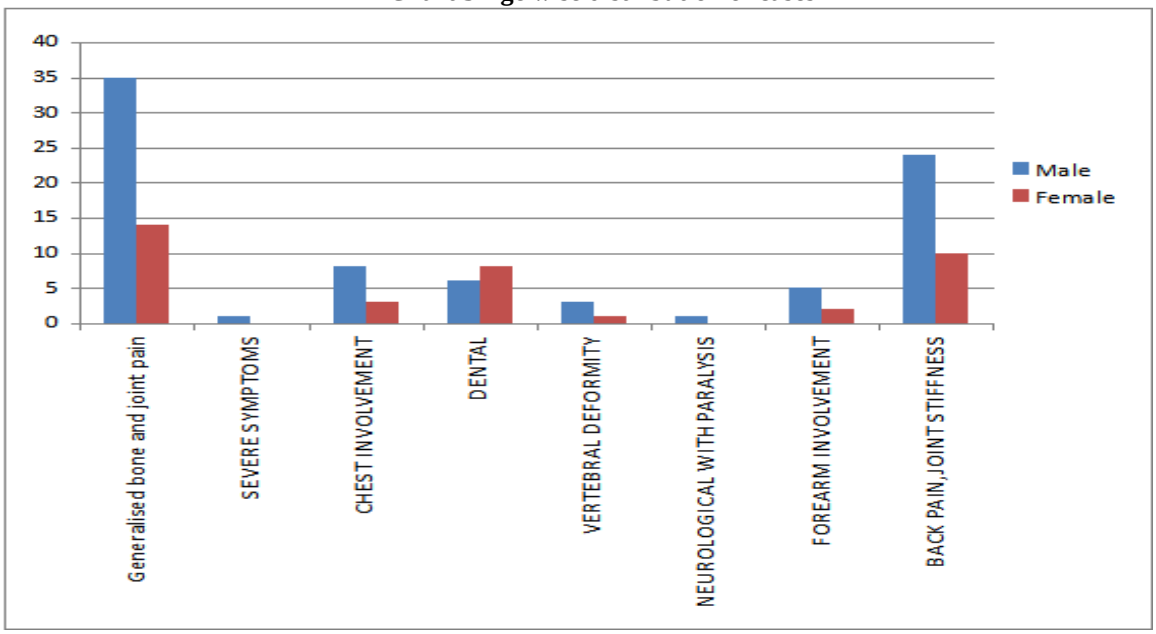


Chart 4 Clinical features

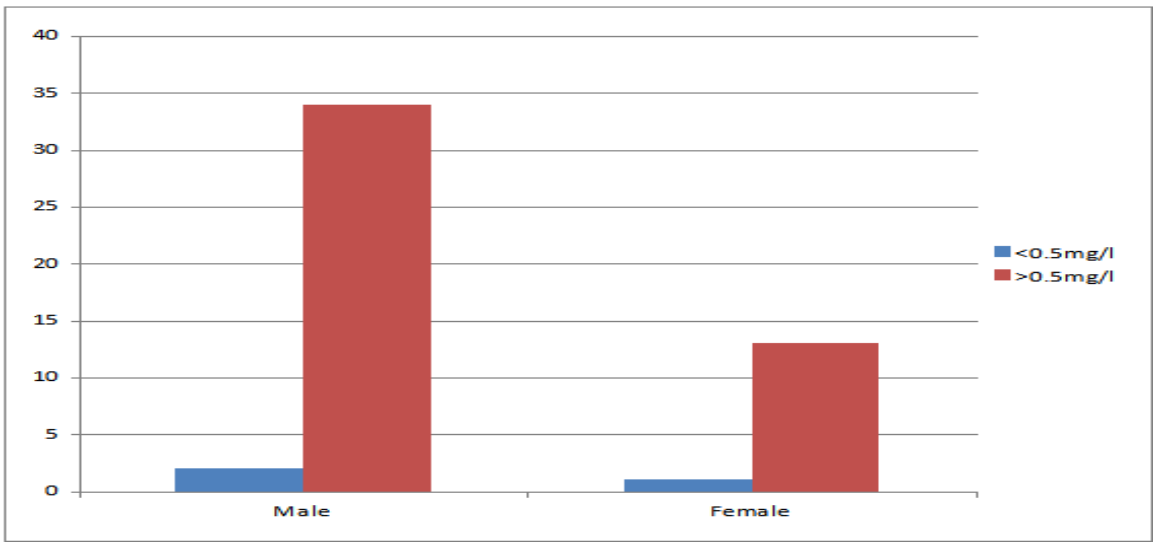


Chart 5 Level of fluoride in urine

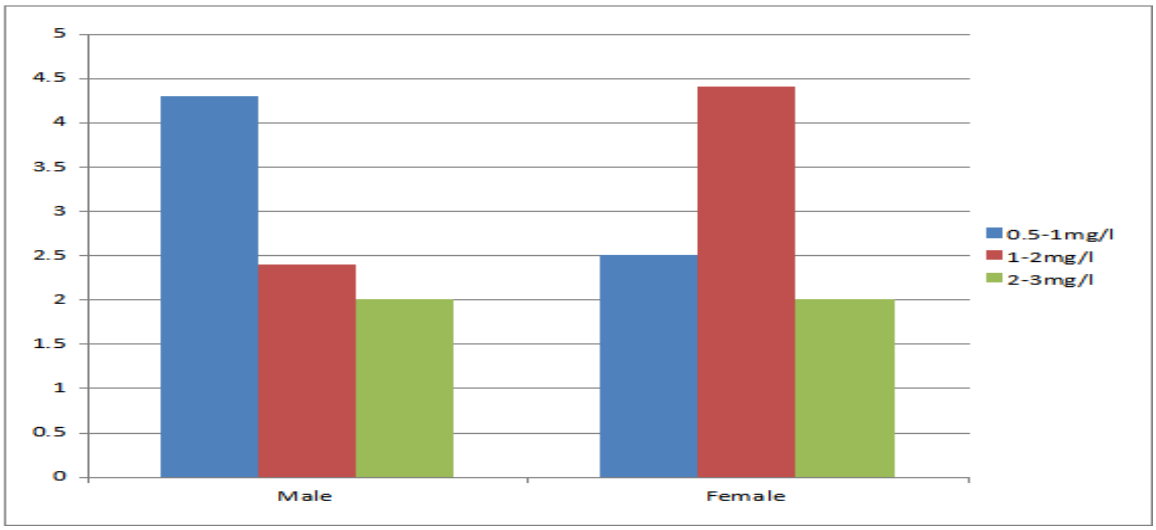


Chart 6- Reports of Urine examination

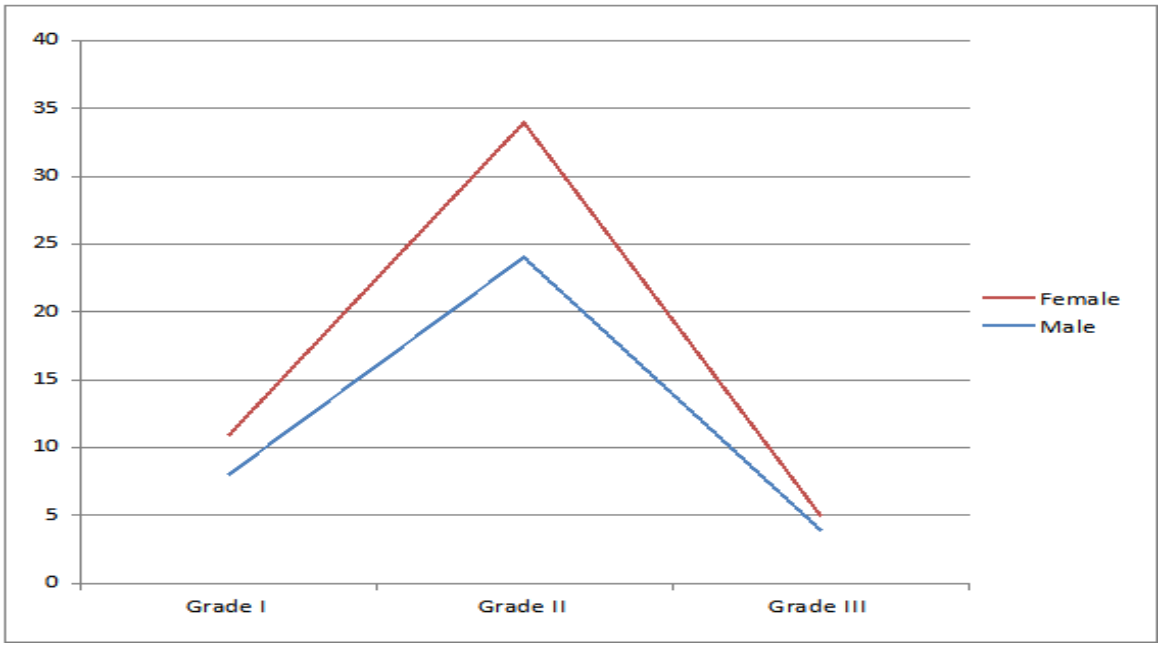


Chart 7 Correlations between Clinical Grading and Sex

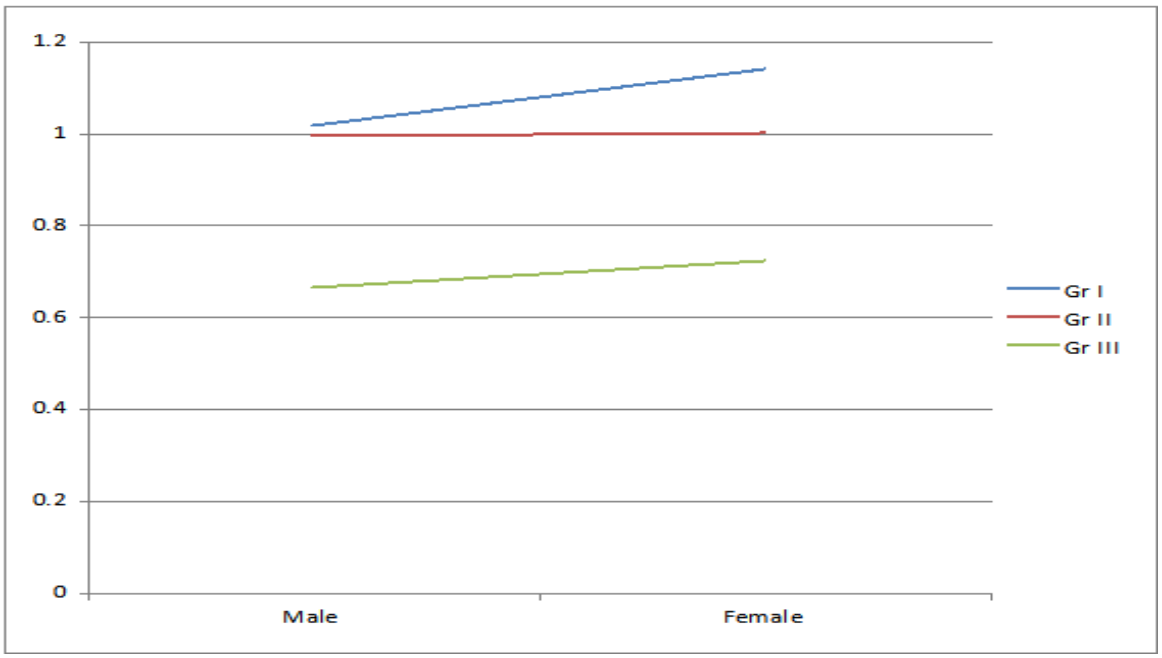


Chart 8 Correlation between Clinical Grading and Urinary Fluoride Concentration