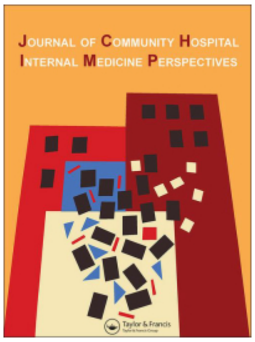

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Effect of drinking high fluoride water on liver enzymes a comparitive cross-sectional study

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ABSTRACT

Objective: The aim of this study is to determine the effects of drinking water with high fluoride level on liver functions.

Method: This is a descriptive comparative cross-sectional study conducted at *Sammu rind* village where the drinking water has increase fluoride content. The comparative area was *Gadap* town where the drinking water has normal fluoride level. Sampling was done randomly and sample size was calculated by WHO calculator and found to be 121 each for exposed and unexposed population. Blood samples taken for liver functions included bilirubin, AST, ALT, Alkaline phosphate, Gamma GT, total protein, albumin and globulin. SPSS version 16 was used for analysis. Mean and SD calculated for quantitative variable and the two comparative groups were cross-tabulated. To check the statistical significance t-test was applied.

Results: There was no statistically significant difference with consideration to serum bilirubin, ALT, and AST. However, statistically significant difference was established with respect to alkaline phosphatase, Gamma GT total proteins and A/G ratio between two groups.

Conclusion: In our study, there was no evidence of impaired liver function tests in subjects drinking water with high fluoride content.

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Fluoride; ALT; AST; liver enzymes; Gamma GT

1. Introduction

Fluoride is the thirteenth most ample ingredient found in the earth's crust. Fluorosis is a condition originate by fluoride deposition or cumulation in the body [1]. Fluoride can cause the rearrangement of the production of collagen and results in the degradation of collagen in bone, tendon, muscle, skin, cartilage, lungs, kidney and wind pipe [2]. Sources of fluoride in the atmosphere are water (both surface water and underground water), food (seafood, animal meat, tea) [3], drugs (such as fluoroquinolones, anti-cancer, anti-malarial) [4], air [5] (released during manufacture and use of phosphate fertilizers, burning of fluoride laden coal), cosmetics, toothpaste, mouth rinses, etc.

Fluorosis causes a variety of negative health impacts for individuals who are exposed to it. It is associated with many complications in which dental defects such as white coloring, yellowish and brownish stains, black discoloration, pitting, etc are most common [6]. Other common disorders include the musculoskeletal system with arthralgic symptoms, painful and restricted joint movements, limb deformities, hip fractures etc [7].

The liver is a key metabolic organ, which take necessary part in regulating the metabolism of the biochemical plus trace elements, and swallowing of enormous quantities of fluoride can spoil the liver tissue. Fluoride ingestion not only damages bones and teeth but also impairs organ function. Fluoride has been known to slow down or trigger countless enzymes such as transaminases and phosphatases [8]. Several research groups have observed irregular activity, metabolism and histopathological changes in the liver of goats, cattle, rats and mice. An increase in the activities of serum transaminases is a delicate marker of destruction to the cytoplasmic and mitochondrial membrane. The familiar biomarkers of liver function, serum transaminases and phosphatases, have been documented to be significantly upraised in adults and little one with fluorosis [9], suggesting liver damage and compromised liver function [10]. Studies have revealed that excessive fluoride intake results in extensive degenerative changes in the liver [11]. While other studies have also demonstrated histopathological variation in the hepatic parenchyma in reaction to large quantity of fluoride exposure [12].Jackson et al. (1994) documented that there was a significant elevation in hepatic biochemistry in test subjects taking 23 mg of fluoride a day for 18 months, but the enzyme level were nevertheless within the conventional range[13].

The highly affected area by fluoride is Thar Desert of Pakistan in Sindh province, where population have

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been utilising undergroundwater with concentrations of fluoride as enormous as 7–12 mg/dL. World Health Organization (WHO) has set the upper limit of fluoride concentration in drinking water at 1.5 mg/L.The current study was planned to assess the variation in enzymes of liver biochemistry in patients exposed to large fluoride in drinking aqua.

2. Subjects and methods

It was a descriptive comparative cross-sectional study to evaluate the consequence of high level of fluoride in water on liver biochemistry and synthetic function test. The exposed subject were taken from village '*Sammo Rind* 'which is located 40 km in the south east of *Chachro Tow*n in Thar. The well water utilized by the community of *Sammo Rind* has been examined for its fluoride content and was establish to be 6–8 mg/dL. The unexposed subjects were taken from *Gadap town* situated at north–west *Karachi* with *Hub River*. Initially, a pilot study was carried out. Ethical approval was taken prior to study.

Probability systemic technique was used with every fifth villager being selected after taking written informed consent. In case of denial of consent, the villager next to was chosen. Sample size was calculated using WHO sample size calculator and comes out to be 121 in each group (n = 242)[12]. Permanent resident of '*Sammu Rind*' village of greater than 15 years regardless of gender who are willing to participate in study were included while those who are immigrant are excluded from the study. One out of thirty residents from *Gadap t*own above 12 years of age were selected as unexposed and they were gender and age matched. Nutritional history was also taken from both exposed and unexposed subject. Both groups have adequate calcium intake.

Prior to data collection ethical approval was acquired by the institutional review board. As there was limited facilities in the remote area so the research participant moved to tertiary care hospital at Karachi for sampling and analysis. Venous blood samples were acquired under aseptic condition. The sample was investigated for serum bilirubin, AST, ALT, alkaline phosphate, Gamma GT, total , and globulin by institutional laboratory using automated analyzers. Demographic variable including age, sex, were recorded, data was analyzed using SPSS version 20. Mean median and Standard deviation were calculated for quantitative variable. T-test was applied to calculate p value. P value of less than 0.05 was considered as statistically significant.

3. Results

The fluoride content of water sample from the village *Sammo rind* was high and that of the representative sample from *Gaddap* town taken from underground tank and tap water was having normal fluoride content.

Of gross 242 subjects, the number of exposed and unexposed subjects were 121 each. The mean age of exposed subjects was 33.82 ± 14.10 years while the mean age of the unexposed subjects was found to be 33.33 ± 11.67 years, the overall males in exposed subjects were 90 while the total number of males in unexposed group was 84, which constituted about 74.4% and 69.4% of the subject in these group respectively.

Among liver function test (LFT), the mean total bilirubin comes out to be 0.57 ± 0.25 mg/dL in exposed, whereas in unexposed it was established to be 0.61 ± 0.45 mg/dL, respectively Table 1. Independent t-test was applied to compare mean and statistically different results was found for gamma GT and alkaline phosphate, also the result was statistically different for synthetic liver function

Table 1. Comparison of LFT in exposed and unexposed population.

	Exposed				Unexposed				
	Minimum	Maximum	Mean	Std. Deviation	Minimum	Maximum	Mean	Std. Deviation	p value
Serum total bilirubin (mg/dl)	0.14	1.46	0.56	0.24	0.15	2.81	0.6114	0.44	0.332
Serum direct bilirubin (mg/dl)	0.08	0.71	019	0.09	0.1	0.54	0.1707	0.09	0.098
SGPT (ALT) (u/l)	10	331	27.45	36.67	10	292	34.02	36.17	0.163
SGOT(AST) (u/l)	10	131	25.36	19.14	10	127	28.37	20.9	0.24
Alkaline phosphatase (u/l)	58	551	130.46	67.21	34	525	103.83	57.64	0.001
Gamma GT(u/l)	10	204	18.24	20.16	10	350	30.18	35.71	0.002
Total proteins (g/dL)	6.4	9.27	8.0518	0.59	4.02	9.55	7.1309	0.98	<0.005
Albumin (g/dL)	3.6	5.64	4.6146	0.37	2055	5.4	4.00	0.51	<0.005
Globulins(g/dL)	1.68	4.4	3.42	0.46	1.32	5.36	3.125	0.62	<0.05
A/G ratio	0.9	1.98	1.36	0.19	0.64	2.12	1.3228	0.23	0.164

4. Discussion

Fluorosis has always been an interesting subject for clinical research. According to WHO, the highest prevalence of fluoride in groundwater worldwide has been identified in India and China [14]. It has been reported that the concentration of fluoride in the ground and underwater in Pakistan is continuously rising. Among the conducted studies on the Pakistani population in 16 different cities of Pakistan water, fluoride content was detected between the range of 1.6 to 25 mg/l [15]. This amount of fluoride is considerably higher than the safe limit declared by WHO [16]. In addition, studies conducted on well water samples of the Thar Desert revealed fluoride levels of 7–12 mg/l which are relatively hazardous, while studies conducted on groundwater in the same area revealed alarming levels of fluoride between 7 and 19 mg/l [17]. Fluoride has dynamics variation on the working of important organs of the body, including the liver and kidney. A study done in non-human subjects suggested that fluorosis hampers the protein formation mainly due to deterioration in initiation of peptide chain [18] and by impeding with peptide chains on ribosomes hence disrupting protein synthesis[19].

Shivashankara et al. demonstrated impaired liver biochemistry among subjects with skeletal fluorosis, with a two-fold increase in alkaline phosphatase, ALT and AST [9]. A study done by Shashi in India among regions where fluorosis was endemic in 2011 also identified changes in liver enzymes, with alkaline phosphatase levels increasing in correlation with serum fluoride levels while AST and ALT were found higher in females affected from fluorosis [20]. Similarly in 2016, a study carried by Suman Chatterjee on the Indian inhabitant living in fluorosis area has also shown the elevated liver enzyme activity among subjects with fluorosis [21]. The observed findings were statistically significant in regards to impairment of gamma GT and Alkaline phosphatase, it is valuable highlighting that the divergent range was not demarcated in the study. Also, the mean values of exposed and unexposed were within normal limits, so clinically, no difference was noticed. Furthermore, the extrahepatic release of alkaline phosphatase can also be blameworthy for the inconsistency in statistical analysis [22].

This study explained no statistically significant difference of hepatic biochemistry by Fluorosis. Liang et al.also reinforced in his study that there is no established significant changes in hepatic function tests carried between six different fluorides endemic regions [23]. A research conducted by Wan et al. also showed no change in LFTs although the quantity of fluoride in aqua was as high as 23 mg/L [24]. Lastly, a research performed in the USA also showed no associated with plasma or water concentrations with hepatic enzyme derangements, a finding synchronizing with our study results[2].

5. Conclusion

In our study, there was no evidence of impaired LFTs in subject drinking high flouride water with respect to bilirubin, ALT and AST, However, larger studies are required for further elaboration of hepatic derangements in fluorotic endemic areas.

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Disclosure statement

The research article is a part of thesis entitled 'health impact of flurosis in a village: the Thar desert pakistan, submitted by principal investigator to DUHS karachi for the award of degree of doctor of philosophy.

No potential conflict of interest was reported by the authors.

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