CORRELATION OF FLUORIDE IN DRINKING WATER WITH URINE, BLOOD PLASMA, AND SERUM FLUORIDE LEVELS OF PEOPLE CONSUMING HIGH AND LOW FLUORIDE DRINKING WATER IN PAKISTAN

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SUMMARY: A case-controlled study has compared urinary, blood plasma, and serum fluoride (F) levels of people living in endemic areas of the Thar Desert, Sindh, Pakistan, consuming groundwater with F concentrations as high as 4.00–10.00 mg/L with those consuming groundwater with low F levels of 0.30 mg/L. A total of 121 individuals from Samme Jo Tar Village of the Chachro Sub-District, Tharparker, and 121 controls from Gadap Town, Karachi, Pakistan, were selected for this study. Results indicated highly significant differences were present between the mean urinary F (12.90 versus 2.30 mg/L, p<0.001), plasma F (0.61 versus 0.25 mg/L, p<0.001) and serum F levels (0.75 versus 0.29 mg/L, p<0.001) of cases and controls. There was a strong positive correlation between plasma and serum F levels (r = 0.884), while moderate correlations were found between urine plus plasma and between urine plus serum (r = 0.576 and 0.621) F levels of cases, respectively.

Keywords: Fluoride in plasma; Fluoride in serum; Fluoride in urine; Thar Desert, Pakistan.

INTRODUCTION

The Thar Desert in the southeastern part of Sindh province, Pakistan, has recently been identified as one of the most fluoride (F) affected areas, where residents have been consuming groundwater with F concentrations as high as 7–32 mg/L.[1-5] The accompanying fluorosis problem can be observed at various intensity levels in the study area ranging from dental fluorosis to debilitating skeletal fluorosis, along with nonskeletal manifestations and premature aging.

This case-controlled study was designed to compare and correlate urinary, blood plasma, and serum fluoride levels of people age 12 and older living in the endemic F areas of the Thar Desert consuming groundwater with F concentrations as high as 4.00–10.00 mg/L with those who are consuming groundwater with low F levels, viz., 0.30 mg/L.

MATERIALS AND METHODS

Based on a pilot study, a total of 121 cases of fluorosis among residents in Samme Jo Tar Village of Tharparker with high F concentration in groundwater and 121 controls from Gadap Town, Karachi, with low F concentration in groundwater were identified. The two populations were otherwise similar.

The criteria for inclusion were life-long residency in Samme Jo Tar Village and Gadap Town, over age 12, with normal urine detailed report (DR), serum urea, creatinine, and electrolyte levels. Subjects of both genders who consented to participate in the study were included. Anyone who immigrated to or emigrated

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from another area or declined to participate at any stage was excluded. Every fifth resident was included in the study. A list of residents was made according to house-to-house mapping. In cases of nonconsent, the next person on the list was included in the study. Since there is no health care facility in the two remote study areas, all subjects were brought to Karachi for sample collection and analysis at the Pakistan Council of Scientific and Industrial Research (PCSIR) Laboratories Complex.

Early morning urine and blood samples were collected and analyzed by the F ion selective electrode (FISE) method for the F activity concentration in the urine,[6] blood plasma,[7] and serum[7] specimens. Total ionic strength adjustment buffer (TISAB) was used to bring all samples to approximately the same ionic strength, to free F from cation complexes, and adjust the pH.

RESULTS

Table 1 shows the mean F levels in urine, plasma, and serum of cases and controls.

Table 1. Comparison of urinary, plasma, and serum F levels among cases and controls

Specimen	Cases (n=121) Mean (SD) mg/L	Controls (n=121) Mean (SD) mg/L	p value
Urine	12.9 (7.2)	2.38 (1.4)	<0.001
Plasma	0.61 (0.21)	0.25 (0.07)	<0.001
Serum	0.75 (0.24)	0.29 (0.07)	<0.001

There was a highly significant difference ($p<0.001$) between the urinary F levels of cases (mean 12.9 ± 7.2 mg/L) and those of controls (mean 2.38 ± 1.4 mg/L). Similar results were found when comparison was made for serum and plasma F levels. The mean level of plasma F of cases was 0.61 ± 0.21 mg/L, whereas for controls it was 0.25 ± 0.07 mg/L ($p<0.001$). The mean level of serum F among cases (0.75 ±0.24 mg/L) and controls (0.29 ±0.07 mg/L) was also significantly different ($p<0.001$).

When cases were divided into different age groups to see whether there is any age-related increase in urine and blood plasma and serum F levels, no significant difference was found in any of the age groups in all three types of specimens (Table 2). There was also no statistically significant difference between male and female cases in terms of F levels in all three types of specimens (Table 3).

Scatter plots for cases in the Figure (A–C) showed there was a strong positive correlation between serum and plasma F levels ($r = 0.884$), while moderate correlations were found between urine and plasma and between urine and serum F levels ($r = 0.576$ and 0.621), respectively.

Table 2. F specimen levels in cases among different age groups

Age group	Mean urine F level (SD) mg/L	Mean plasma F level (SD) mg/L	Mean serum F level (SD) mg/L
<20 yr	11.4 (8.0)	0.56 (0.2)	0.69 (0.2)
20-29 yr	12.4 (7.9)	0.66 (0.2)	0.80 (0.2)
30-39 yr	13.6 (7.8)	0.57 (0.2)	0.71 (0.2)
40-49 yr	15.8 (5.0)	0.66 (0.1)	0.77 (0.2)
>50 yr	12.7 (3.8)	0.67 (0.1)	0.85 (0.2)

Table 3. Comparison of F specimen levels according to gender among cases

Specimen	Males	Females	p value
Urinary F level mg/L	12.5	14.36	0.20
Plasma F level mg/L	0.62	0.57	0.28
Serum F level mg/L	0.75	0.72	0.51

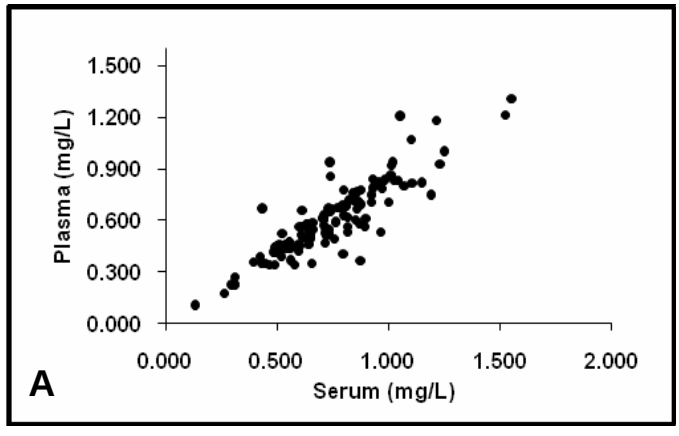

Figure A. Scatter plot between F levels in blood serum and plasma of study cases.

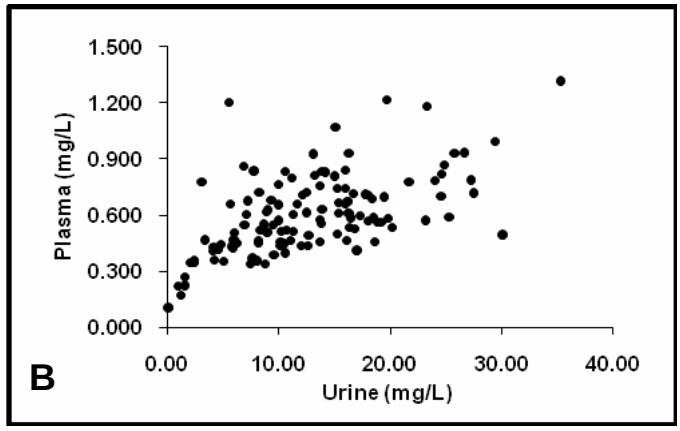

Figure B. Scatter plot between F levels in urine and plasma of study cases.

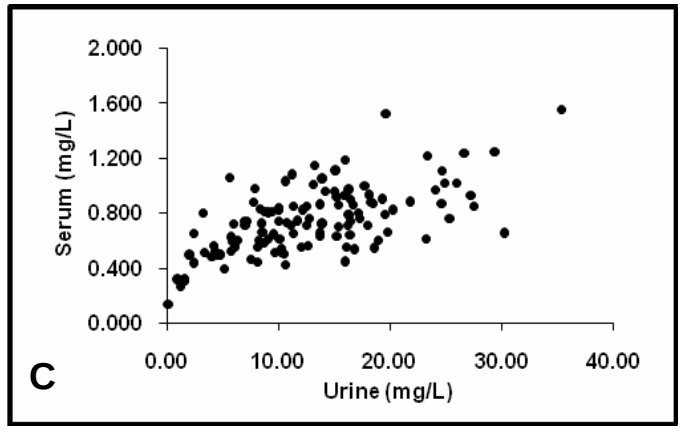

Figure C. Scatter plot between F levels in urine and serum of study cases.

DISCUSSION

Pakistan is among countries where fluorosis is endemic, especially in the Thar Desert areas of Sindh province. The groundwater, especially the water in unconfined aquifers, is the main source of drinking water for people living in the rural desert areas of Sindh. Groundwater is mostly available in dug-wells, generally at the depth of 30 to 75 m, which is brackish and highly contaminated by the presence of F.[2] A high prevalence of fluorosis is present in such areas including dental, skeletal, musculoskeletal and other forms of fluorosis. To monitor F exposure, urinary F levels are commonly used. However, this has not always been found to be a very accurate parameter to reflect the actual F concentration in the drinking water. Therefore, in our study we measured blood plasma and serum F levels together with urinary F levels to determine whether associations exist or not. To further strengthen the findings, we examined an appropriate control group for comparison.

The findings of our study are in good agreement with the international literature, e.g., the report by Ekstrand and Ehrnebo[8] that plasma F levels of adult men are correlated with the F concentration in urine ($r = 0.753$; $n = 70$). Since plasma F levels tend to fluctuate on daily basis,[9] and serum F levels are related to renal function,[10] all three parameters are interlinked, and in order to obtain a realistic

assessment of F exposure, F concentrations in all three specimens should be measured.

Fluorosis is endemic in the entire Thar Desert areas of Pakistan and India. According to Hussain,[11] water F concentrations in the Bhilwara region of the Thar Desert in Rajasthan, India, range from 0.20 to 13.00 mg/L. The minimum concentration was recorded in Negadia village of Asind Tehsil, while the maximum was recorded in Ganesh Pura village of Banera Tehsil. The situation in Pakistan is not much different; almost 78.77% of 424 analyzed groundwater samples[2] have F levels that exceed the WHO recommendation limit of 1.5 mg/L.

Our findings indicate there is a need to re-evaluate the diagnosis modalities for fluorosis using serum, plasma, and urine F levels. Paolillo et al,[12] have recently reported an improved method to measure very low levels of F in biological samples, which could lead to early detection to prevent irreversible damage caused by F in the environment.

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