Short Report

Micronutrient Selenium: A Pan-India Report on Borderline High

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ABSTRACT

Aim: Selenium is an essential micronutrient and like other nutriments has detrimental health effects in low as well as high levels in the human body. Selenium toxicity is a recorded phenomenon and in this report we aim to present the picture of borderline high selenium levels recorded in a Pan-India cohort. **Materials and Methods:** Whole blood selenium analysis was done in a cohort of 529,461 individuals inclusive of 284,189 males and 245,272 females respectively. Technology of Inductively Coupled Plasma Mass Spectrometry was used to derive selenium values. Average blood selenium levels were also analyzed. The reporting range of blood selenium is 60 - 340 μg/L. For analysis in this report, 1SD value of > 225 μg/L was considered to be borderline high. **Result:** The total frequency of borderline high detected in our study was 3.5%. The average blood selenium levels in the borderline high cohort was detected to be 256 +/- 33 μg/L. Geographic prevalence analysis highlighted maximum to be from the North and North-Western region. **Conclusion:** Our report is one of the few to highlight not alone the frequency of borderline selenium in Pan-India level, but also identify geographical regions of concern. Such analysis will aid in devising region-specific Action plans to prevent overdosing as well as monitor deficiency.

Key words: Selenium, Borderline High, Asian, Indian, Mass Spectrometry.

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INTRODUCTION

Selenium (Se) is a naturally occurring micronutrient essential for human health and has the narrowest ranges between dietary deficiencies at < 40 μg/day to toxicity at > 400 μg/day according to a WHO report of 1996. Dietary source of Se for humans include plants grown in selenium-rich soil the presence of which varies in different geographies depending on rainfall levels, floods, irrigation water availability, etc.[1]

Dietary sources of Se and the diet pattern in humans together affect its availability and quantification of bioavailability remains a challenge because of its complex forms in food stuffs.[2] Vitamin E deficiency has also been linked with Se toxicity and high intake has been associated with increased risk for cancer of pancreas and skin, as well as high risk of type-2 diabetes, as effect of high Se on insulin signaling has been proven.[3] Outbreak of endemic human selenosis have been reported from many regions of the world, like certain provinces of China in the 1960s, wherein the reason was determined to be intake of high-Se crops grown on soil derived from coal. Data records over 50% morbidity in the peak prevalence period 1961 to 1964 in the worst affected villages among population of subsistence farmers.[4,5] Thus, identifying and stratifying populations of low and high Se becomes crucial to determine supplementation or modification of dietary sources.

Selenium analysis and quantification has undergone rapid advancements due to advanced analytical technologies which bear very low detection limits. Technologies like Atomic Fluorescence Spectrometry (AFS), Gas Chromatography (GC), Inductively Coupled Plasma Mass Spectrometry (ICP-MS), exhibit high sensitivity and low detection limits. In humans, Se can be analyzed using samples of blood, plasma, serum, hair, toenail as well as urine.[6]

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Our report is an attempt to present prevalence of borderline high Se along with geographical prevalence as not many reports exist on the same. The large pan-India cohort analyzed by the advanced ICP-MS technology for blood Se levels becomes an efficient source to record pattern as well as prevalence.

MATERIALS AND METHODS

Whole blood Se analysis was done on a pan-India cohort of 529,461 inclusive of 284,189 males and 245,272 females respectively. The average age-group of males and females in the cohort was 45 +/- 14 years. States like Maharashtra, Delhi and Southern parts contributed for over 50% of the total cohort size analyzed. This study presents a retrospective analysis and the data was generated from a reference lab and not hospital-based. This study deviates from need for informed consent as no participant identity apart from age and gender has been considered.

Whole blood EDTA samples were used for analysis of Se levels. A 2ppm gold solution with 0.5% nitric acid and was used for sample preparation and 1ppm Yttrium was used as internal standard for assessing extraction efficacy as well as sensitivity of the analysis. The prepared samples were then subjected to analysis by mass calibrated ICP-MS (i CAP Q, Thermo Fisher Scientific) analyzer. ^{78}Se isotope of Se was standardized and quantified.

Certified reference material, Seronorm™ Trace Elements Whole Blood (SERO) was run before every batch of sample analysis apart from linearity checks. The quality control was prepared in the same way as samples before the ICP-MS analysis. Linearity for selenium was assessed between 40-500 µg/L. For further quality assessment, Se analysis was also enrolled for CAP (College of American Pathologists) proficiency testing program.

RESULTS

Whole blood Se levels of 60-340 µg/L was the analytical reference range. However, since this range was detected to be fairly wide for analysis, the 1SD value of 225 µg/L calculated as per Se levels distribution of our cohort was considered as cut-off for borderline high values. Further analysis of borderline high Se levels was done considering the value of >225 µg/L.

Frequency analysis for borderline high based on 1SD distribution value of > 225 µg/L was detected to be 3.5%. The frequency among males was detected to be higher at 4.2% in comparison to females in the cohort at 2.7% and the difference was found to be statistically significant by the at $p < 0.05$.

Table 1: Top 10 States with average selenium levels (This study).

State	Frequency (%)	Average selenium levels (µg/L)
Goa	8.2	265 +/- 44
Punjab	6.7	272 +/- 53
Jammu & Kashmir	6.1	263 +/- 38
Assam	5.8	256 +/- 30
Kerala	5.7	265 +/- 53
Uttarakhand	5.6	258 +/- 43
Delhi, Gujarat & Rajasthan	5.4	256 +/- 32
Haryana & Tripura	4.9	255 +/- 28
Chandigarh	4.8	258 +/- 32
Uttar Pradesh	4.7	257 +/- 30

The average whole blood Se levels for the study cohort were calculated to be 165 +/- 60 µg/L. In case of females in the cohort, the average levels were found to be slightly lower at 160 +/- 58 µg/L in comparison to males at 168 +/- 61 µg/L. In case of borderline high whole blood Se levels, the cohort exhibited average levels of 256 +/- 33 µg/L.

Geographical distribution analysis to identify State-wise prevalence in the country was also done. The top 10 states have been enlisted in Table 1. The prevalence has been drawn in relation to the sample contribution from each of the States and the incidence of borderline high.

DISCUSSION

Identification of Se toxicity or high levels of exposure requires preliminary investigations to understand soil Se levels from regions of major agricultural produce in the country apart from areas wherein man-made contribution exists. An Indian study which documented Se status in soils from northern districts of India identified parts of soil from Rajasthan as well as southern parts of Haryana to have above normal selenium levels as these are drier lands receiving low rains and have less irrigation water available.[1] Our study evaluated the prevalence of borderline high Se levels across different regions of India, identified states of Rajasthan and Haryana to rank among the top states with higher than 3.0% frequency.

The same Indian study which analyzed soil Se levels from some Northern regions of the country identified some districts of Punjab and Himachal Pradesh like Amritsar and Khannuri to harbor normal to low Se levels. In our analysis, though the state of Punjab was detected as one of the highest in prevalence in relation to cohort contribution, further region-based analysis detected no case of high selenium to be from Amritsar.

The reason as mentioned in published literature would be availability of good irrigation water source and sufficient river water availability in comparison to the state of Haryana. Floods have also been proven to affect soil Se levels, reducing them considerably.[1]

Our analysis of the top states majorly lists regions from North India, with just one from the southern part; Kerala. This can be attributed to the fact that recent publications from this region on impact of rare earth mining and processing on soil along the coastal regions detected Se along with many other elements in the contaminated soil.[7] Some studies have also documented accumulation and distribution of Se among vegetable crops from Punjab grown in selenate-Se clay loam soil. This greenhouse experiment detected Se levels to be high in both the edible and inedible portions of all the grown crops; potato (*Solanum tuberosum*), radish (*Raphanus sativus*), cauliflower (*Brassica oleracea* var. *Botrytis*), turnip (*Brassica rapa*), brinjal (*Solanum melongena*), tomato (*Lycopersicum esculentum*), pea (*Pisum sativum*), spinach (*Spinacea oleracea*) with an increase in levels of Se applied to the soil.[8]

With reference to mean blood Se levels, one study from the year 1996, published blood Se levels of Indians from Delhi area in a cohort of 40 individuals including 20 males and females respectively. This study detected mean blood Se levels to be 169 +/- 40 ng/mL and 161.2 +/- 46.2 ng/mL among males and females respectively.[9] Our study detected the average blood Se levels among males and females to be comparable with this published study at 168 +/- 61 μg/L and 160 +/- 58 μg/L.

Acute Se toxicity connected to dietary supplementation and outbreaks of acute Se poisoning have also been recorded in literature. One such from the year 2010 documented the identified cause of the outbreak to be liquid Se supplementation containing 200 times the labeled concentration of the same.[10] Though our study detected borderline high Se to be 3.5% frequency overall, the geographical evaluation adds a significant touch. Further, considering borderline high analysis in a country like India, would also aid to highlight concern areas wherein remediation measures can be devised before onset or outbreak of episodes of selenosis.

CONCLUSION

In India, though toxic elements like lead, arsenic, mercury, etc. have been added to the concern list, Se continues to be evaded because of it being both nutritional and toxic albeit at different levels. Fortification and supplementation are the major drivers to tackle nutritional deficiencies in any country, but devising a region specific program is necessary to avoid development of toxicities. This report is an attempt to bridge that gap in presenting the whole Se picture in India.

CONFLICT OF INTEREST

None

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ABBREVIATIONS

AFS: Atomic Fluorescence Spectrometry; **CAP:** College of American Pathologists; **EDTA:** Ethylenediamine-tetraacetic acid; **GC:** Gas Chromatography; **ICP-MS:** Inductively Coupled Plasma Mass Spectrometry; **Se:** Selenium; **SERO:** Seronorm™ Trace Elements Whole Blood; **WHO:** World Health Organization.

SUMMARY

Selenium is a nutritional as well as toxic element depending on its levels in the human body. This report studies levels of high blood selenium across a Pan India cohort.

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