Original Research Article

Is Vitamin A Deficiency a Growing Concern? A Pan-India Retrospective Study of 15,000 Individuals

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ABSTRACT

Introduction: Vitamin A deficiency is a very huge clinical burden; both subclinical as well as clinical. In the Indian scenario, it also forms a major aspect of the broad micronutrient deficiency. Absence of symptoms does not rule out deficiency and that is what makes diagnosing sub-clinical deficiency of Vitamin A imperative. **Methods:** Data from a total of 15,116 specimens analyzed for serum Vitamin A levels were studied for this report. The cohort consists of all age-groups, from infants to old adults and includes 8,226 males and 6,890 females respectively. Serum Vitamin A levels were analyzed using the superior platform of Liquid Chromatography - Mass Spectrometry. **Results:** The clinical reference range for Vitamin A levels vary as per age, but to understand the prevalence of borderline low and high Vitamin A scenario among Indians, 1SD values of less than 387 ng/mL and > 748 ng/mL was considered for further analysis. The total frequency of borderline low was detected to be 9.8%, while that for high was 10.6%. Geographical distribution analysis identified significant number of cases to be from North India and certain Southern States wherein it is a public health issue and a concern needing action as well as regions wherein deficiency is likely to exist. **Conclusion:** Our study is one of the few to assess a huge cohort of over 15,000 samples and present a detailed pan-India picture of low Vitamin A levels.

Key words: Vitamin A, India, Deficiency, Micronutrient, Liquid Chromatography Mass Spectrometry, Serum.

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INTRODUCTION

Micronutrient deficiency is a growing clinical concern in India. A report by FLAIR (Forum for Learning and Action with Innovation and Rigour) highlighted death of more than 15 lakh children below the age of five in India mainly due to malnutrition. India alone has been estimated to account for 22% of under-five deaths occurring world over, as stated by a UNICEF report.[1]

Vitamin A Deficiency (VAD) is generally fueled due to poor dietary intake and preventable complications like xerophthalmia in children, blindness, etc. can be diagnosed by measuring levels of Vitamin A in serum; lower levels of which generally indicates dietary deficiency.[2] However, for positive conclusion of VAD, ocular symptoms are generally noted followed by biochemical investigations for the same.[3]

To tackle the growing number of exophthalmia cases, the government-initiated programs in the 1970s, to prevent blindness due to keratomalacia; one such National Prophylaxis Programme against Nutritional Blindness due to Vitamin A Deficiency (NPPNB) sponsored by the Central government. Vitamin A Supplementation programme (VAS) is a continuous activity in the present wherein month-long intensive drives are also planned once every six months to achieve maximum coverage.[4]

India has been documented to harbor highest number of subclinical and clinical VAD cases among all South Asian countries with 62% of preschool children being affected, highlighting a high mortality rate of 330,000.

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Global statistics indicate more than 250,000 children to go blind in Asia due to VAD of which around 52,500 cases per year is recorded from India.[5]

Hypervitaminosis caused due to over-consumption, supplementation or even abnormal transport and distribution is characterized by joint ache, alopecia, vomiting, skin desquamation, etc.[6] Our report is an attempt to study incidence of low as well as high Vitamin A prevalence in a Pan-India mode and also highlight the average serum levels of Vitamin A.

MATERIALS AND METHODS

Sample cohort

Data from a total of 15116 individuals tested for serum Vitamin A levels was included for analysis. This cohort included 8226 males (42 +/- 16 years) and 6890 females (42 +/- 16 years) respectively. The data was generated from routine screening in our reference laboratory and not in a hospital-based setting. The need for informed consent was deviated from as apart from age, gender and geography no other patient identifiers were included for analysis.

Estimation of Vitamin A

Serum Vitamin A levels were measured using the analytical platform of Liquid Chromatography – Mass Spectrometry (LC – MS/MS; Shimadzu Corporation, Kyoto, Japan). The prepared samples were subjected to High-Performance Liquid Chromatography (HPLC) separation (Nexera UHPLC) in C_8 column (Kinetix, 50X4.6 mm). Clinicheck lyophilized serum (Recipe, Germany) was utilized as quality control material. The parent ion and daughter ion transitions validated and analysed was the 269.25>95.10.

RESULTS

Serum Vitamin A levels from a total of 15,116 pan-India individuals were analysed inclusive of 8,226 males and 6,890 females respectively. The total frequency of low Vitamin A levels detected was 9.8%. The frequency among males and females was detected to be 6.8% and 13.3% respectively and this difference was found to be statistically significant at $p < 0.0001$. The average Vitamin A levels was detected to be 327 +/- 55 ng/mL in the borderline low cohort. When studying borderline low as per geography of the country, the Northern States contribute towards the maximum detected.

The total frequency of high Vitamin A was detected to be 10.6% in our study. The frequency among males and females was detected to be 14.4% and 6.1% respectively and this difference was found to be statistically significant at $p<0.0001$. The average Vitamin A levels in the borderline high cohort was detected to be 886 +/- 140 ng/mL. Geographical prevalence analysis for borderline low and high has been summarized in Table 1.

There have also been some high-risk states which have been classified into four different groups according to their under-five mortality rates and the extent of VAD.[7] This has been summarized in Table 2, with the number of cases detected from each group in our study.

DISCUSSION

Our analysis detected the total deficiency frequency to be 9.8% and the difference between the 13.3% females and 6.8% among males was found to be statistically significant. Maximum cases were detected from the priority III states wherein VAD is likely to exist. In case of high Vitamin A level cases, the total frequency was detected to be 10.6% and the difference between males at 14.4% and females at 6.1% was found to be statistically significant. This also raises a concern about the need to monitor supplementation programs. A very significant highlight to this point could be the Assam incident in the year 2001, when twenty children died due to excess Vitamin A supplementation in a campaign.[8]

In case of the Indian scenario, few individual studies have recorded frequency of subclinical deficiency in small cohorts of under-five across different regions. The highest frequency was recorded in the state of Hyderabad at 80.1% (n=126) followed by 77% in Mumbai (n=196), 70.8% in Madurai (n=130) and many such more. However, all these studies have considered serum retinol levels of < 0.70/L as cut-off.[9]

Table 1: Top 10 States for Borderline Low and High Vitamin A.

Borderline Low State	Frequency (%)	Borderline High State	Frequency (%)
Jharkhand	21.7	Kerala	23.2
Bihar	18.5	Chandigarh	17.3
Madhya Pradesh	17.2	Jharkhand	15.7
Andhra Pradesh and West Bengal	16.9	Bihar	15.4
Uttar Pradesh	15.8	Uttar Pradesh	14.3
Chhattisgarh	13.6	West Bengal	13.4
Chandigarh	11.8	Uttarakhand	12.9
Delhi	9.7	Maharashtra and Assam	12.5
Assam	9.6	Andhra Pradesh	12.4
Uttarakhand	9.5	Chhattisgarh, Punjab and Gujarat	12.3

Table 2: State-wise distribution of number of border-line low cases (This study).

Type	States	VAD status	Number of cases (This study)
I	Uttar Pradesh, Madhya Pradesh, Jharkhand, Odisha, Chhattisgarh, Arunachal Pradesh, Rajasthan, Assam, Bihar, Meghalaya	Is a serious concern and needs action	325
II	Nagaland, Andhra Pradesh, Gujarat, West Bengal, Tripura, Uttaranchal, Karnataka, Mizoram, Haryana, Punjab, Jammu and Kashmir	Is a public health issue	518
III	Maharashtra, Delhi, Manipur, Himachal Pradesh, Sikkim, Tamil Nadu, Goa	Likely to exist	550
IV	Kerala	May or may not be a public health issue	14

Another recent publication documented prevalence of VAD to be high at 77% in Mumbai, followed by 63.8% in Orissa, 52.3% in Andhra Pradesh, between 30-80% in Hyderabad and 17-70.8% in Tamil Nadu.[10] However, our current report has analysed the borderline low levels instead of the clinical reference ranges highlighting the areas which need action even before development of clinical VAD.

Vitamin A supplementation trials have recorded the mode to have a significant bearing in reducing the frequency of maternal mortality by 40% in females who received Vitamin A and 49% in those who received beta carotene.[11] Among the High Priority Districts (HPDs), since vulnerability of VAD is definitely high, a recent cross sectional Indian study evaluated utilization of the VAS programme in 10 HPDs from Bihar region of the country with respect to utilization and outcome. The correct use of the recommended spoon for VAS stood at 80.66% and the frequency of centers which made an effort to record the age of the child before administration stood at 79.55%. The Due List (DL) which is crucial to identify coverage and beneficiaries was detected only at 30.85% sites, while the MCP cards important to avoid re-administration within 6 months to prevent hypervitaminosis was only found at only 30.11% sites. This observational study identified crucial gaps between input and implementation, reinforcing the need for better programme management in the Indian scenario.[12]

CONCLUSION

VAD has risen to become a global concern as it becomes one of the major contributors of under-five mortality. Our study highlights the need for awareness regarding VAD and also reiterates the fact that identifying sub-clinical deficiencies in young age due to any causative factor is very important to prevent the long-term adverse health effects.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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ABBREVIATIONS

DL: Due List; **FLAIR:** Forum for Learning and Action with Innovation and Rigour; **HPLC:** High Performance Liquid Chromatography; **HPD:** High Priority Districts; **LCMS:** Liquid Chromatography Mass Spectrometry; **NPPNB:** National Prophylaxis Programme against Nutritional Blindness due to Vitamin A Deficiency; **VAD:** Vitamin A Deficiency; **VAS:** Vitamin A Supplementation Programme.

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