Prevalence of Vitamin D Deficiency, Metabolic Syndrome and Association Between the Two in a South Asian Population

Ramesh Reddy Allam1*, Rashmi Pant1, Chengappa K Uthappa2, Manjunath Dinaker3, Ganesh Oruganti1,3 and Vijay V Yeldandi1,3,4

1Department of Health Research, SHARE India, Hyderabad, India
2The National Institute of Health (US), New Delhi Office, India
3GYD Diagnostics and Reference Laboratories (P) Ltd., Secunderabad, India
4College of Medicine, University of Illinois at Chicago, USA

Abstract

Background: The etiological role of vitamin D in the metabolic syndrome among Asian Indians with good exposure to sunlight is not well understood. The objective of this was to estimate the prevalence of metabolic syndrome and vitamin D deficiency and to determine the association between vitamin D status and metabolic syndrome in an Asian Indian population from Hyderabad, India.

Methods: 299 normal individuals were randomly selected, for this cross sectional study, from individuals who voluntarily participated in a health camp. Anthropometric measures were taken along with 25-hydroxyvitamin D, fasting blood glucose, complete lipid profiles were also assessed. Socio-demographic data such as sex, age, smoking status, physical activity and diet were also collected. Data was analyzed using t-tests and chi-square test of association.

Results: 81.6% had 25 (OH) D deficiencies, 13.4% had insufficiency and 44% had metabolic syndrome. Females had lower levels of mean 25 (OH)D 18.33 ± 12.9 nmol/l as compared to males. 34.4% had 25 (OH)D deficiency as well as metabolic syndrome. A significant (p=0.02) association was observed between serum 25(OH)D and metabolic syndrome. Participants with 25(OH)D insufficiency had 4.6 (p-value=0.023) times higher odds of metabolic syndrome versus those with 25(OH)D >100 nmol/l, whereas those with deficiency had approximately 2 times higher odds.

Conclusion: Vitamin D deficiency has become a pervasive problem with implications for cardiovascular health across age and gender groups. Our research indicates that women are at a higher risk of having metabolic syndrome than men if they have deficiency or insufficiency of vitamin D. Timely translational research needs to develop the appropriate interventions to stem this.

Keywords: 25(OH)D; Metabolic syndrome; Metabolic risk; Lifestyle modification; Hypovitamnosis D

Introduction

Vitamin D is an important hormone for the functioning of the skeletal and non-skeletal systems of the body. Therefore the biochemistry and physiology of vitamin D in humans is extensively researched and documented [1,2]. Advances in medical diagnostics have made it possible to measure vitamin D levels more accurately and these are now best ascertained through serum concentration of 1, 25-hydroxyvitamin D [3,4]. The major source of vitamin D for the human body is through exposure to sunlight (UVB rays) leading to synthesis by the skin and then used for cell metabolism. Studies have shown low vitamin D levels in some populations despite adequate sunlight exposure [5].

Optimal levels of this steroid hormone in the body vary depending on the individual's geographical location, skin colour, age, sex and other factors [6,7]. Deficiency of the vitamin is associated with a multitude of conditions such as musculoskeletal, autoimmune and cardiovascular problems [8] and respiratory disorders [9]. Over the past decade vitamin D deficiency has been recognized as a widespread problem and the public health implications of this deficiency have become a cause of concern especially in low and middle income countries.

There is now also an active interest in understanding the role of vitamin D as a mediator or moderator of metabolic outcomes [10]. This stems in part from the fact that a greater prevalence of metabolic syndrome (MS), as defined by the International Diabetes Federation (IDF) [11], has been recognized increasingly across the world [12]. Studies in different settings have shown an association between vitamin D, measured as serum 25(OH) D levels, and metabolic risk factors. However most of these studies have been in developed countries, at higher latitudes and primarily with urban populations [13-16].

To obtain better ethnic and geographic estimates of the relationship between serum 25(OH) D and metabolic syndrome including constituent metabolic risk outcomes, evidence from Asian populations...
living in latitudes with sufficient sunlight exposure needs to be evaluated. This study aims to add to the sparse evidence in this area [17,18] with the objective to estimate the prevalence of MS as defined by the International Diabetes Federation [19] and to assess the association between vitamin D levels and metabolic syndrome in an Asian Indian population from Hyderabad in south India.

**Methods**

**Study design and sample size determination**

This is a cross-sectional study. The protocol of the study was approved by the institutional ethics committee of the Department of Health Research at SHARE INDIA prior to the start of the study, and written informed consent was obtained from all study participants.

The study sample consisted of N=299 individuals in the age group of 18-75 years randomly selected from an ostensibly healthy population registered for a health awareness camp at Padmarao Nagar, Secunderabad, Telangana, India (17° 27' N, 78° 33' E). A random number generator was used to select subjects from among those registered for the health camp. The sample size was chosen so as to have at least 80% power to detect an odds ratio of 2, at 5%-level, for risk of metabolic syndrome among individuals with vitamin D deficiency- assuming a population prevalence of vitamin D deficiency of 50% [20].

Subjects were ostensibly healthy and were attending the camp for the purpose of routine health evaluation/screening and information motivation counseling campaign for lifestyle modifications. Pregnant women, lactating women, and those who did not fast for at least 10 hours prior to the camp and individuals who did not consent for the study were excluded. Individuals having history of thyroid dysfunction, on hormonal replacement therapy, on vitamin D supplementation, physically or mentally challenged and non-cooperative in nature were also excluded from the study.

**Measurements**

The research staff administered a structured questionnaire, which included questions on demography, smoking, diet, physical activity, and health history to all eligible participants. Details about smoking were obtained for type (cigarettes, bidis, and hookah), frequency (number of days), and years of smoking. Anthropometric measurements (height, weight, and waist circumference (WC)) and blood pressure were measured using standardized techniques [20] and calibrated equipment by trained research staff. Height and weight were measured using a stadiometer and a calibrated spring weighing scale. WC was measured using a non-expandable measuring tape.

Resting blood pressure with 5-min interval between each measurement was recorded using an automatic sphygmomanometer (Omron Healthcare). An average of up to two brachial systolic (SBP) and diastolic blood pressure (DBP) readings was used for the SBP and DBP values. A certified phlebotomist drew fasting (at least 10hr overnight) morning blood samples from the examinee's arm for the lipid (total cholesterol, HDL-C, and TGs), vitamin D and glucose assays. The samples were tested at a laboratory certified by the National Accreditation Board for testing and calibration Laboratories (NABL).

**Laboratory assays**

Venous blood was collected in evacuated tubes after an overnight fast of 8-12 hr (Vacuett, Greiner Bio-One GmbH, Vienna, Austria). Serum, EDTA, and plasma samples were separated by centrifugation within 1hr of sampling. Fasting venous plasma glucose was assayed using Dimension RXL Automated Clinical Chemistry Auto Analyzer (Dade Behring Inc., Newark, DE). Serum values were estimated using reagents and standards from Siemens and controls from BioRad Laboratories, Ltd. Estimation of HDL-C levels was carried out by the homogenous direct HDL-C method using reagents from Siemens and controls from Bio-Rad Laboratories, Ltd. All lipid assays were carried out on Dimension RXL Clinical Chemistry Auto Analyzer (Dade Behring Inc., Newark, DE). The serum concentration of 25(OH)D, regarded as the “gold standard” to measure the vitamin, was estimated using end point method [21]. LDL Cholesterol was calculated from the Friedewald equation.

**Metabolic syndrome criteria**

To identify the presence of MS, we used the IDF definition specified for a South Asian population [19]. Abdominal obesity as defined by WC of ≥ 94 cm for men and ≥ 80 cm for women is a mandatory feature of this definition which is specific to Asians. In addition, any of the two features as defined in NCEP ATP III [22] with a fasting glucose cutoff of ≥ 100 was used to define MS by this criterion.

**Vitamin D levels**: Definition of deficiency was levels of 25(OH)D <25 nmol/l, insufficiency levels of 25<25(OH)D ≤ 49.9 nmol/l and sufficiency i.e. level of 25(OH)D D >50 nmol/l [3].

In addition, individuals who reported current use of antihypertensive or statins or other-lipid lowering medications were classified as having high blood pressure and individuals currently taking insulin or oral hypoglycemic medication were classified as having diabetes. Individuals with a prior physician’s diagnosis of hypertension or type 2 diabetes who did not report medication use were not classified as having high blood pressure or diabetes but were screened for high blood pressure and diabetes.

BMI was calculated by dividing weight by height squared (kg/m²). Weight categories were created based on the Indian government’s consensus guidelines [23] which have reduced the diagnostic cutoffs for BMI for the Asian Indian population. The recommended categories used in this analysis were: Normal weight (BMI 18-22.9), overweight (BMI 23-24.9), and obese (BMI 25 or greater). Generalized obesity was defined as BMI greater than or equal to 25 kg/m², and central obesity was defined as WC greater or equal to 90 cms for males and 80 cms for females.

**Statistical analysis**

A descriptive analysis of risk factors is stratified by gender (Table 1). For each gender, a comparison between those determined to have MS versus those not having MS. The overall comparison of characteristics between the genders was done using t-tests (assuming unequal variances in groups) for quantitative variables for which test assumptions were met. Variables that were found to have a skewed distribution (triglycerides and fasting blood sugar), were compared using non-parametric Mann-Whitney U-test.
### Table 1: Physical, biochemical and general characteristics of the study population.

The association between MS and vitamin D is tested using chi-square (Table 2). We also present the risk, using odds ratios and 95% confidence intervals, of MS in vitamin D deficient and insufficient subjects versus those with normal levels of 25(OH)D. We calculated the prevalence of risk of MS and MS across all categories of vitamin D. The lowest category represents the most deficient group. For each category, the prevalence of MS, abdominal adiposity, high triglycerides, hypoglycaemia and high blood pressure was calculated as a percentage (Table 3). All p- values presented are two tailed at 5% level.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Males (n=189)</th>
<th>Females (n=110)</th>
<th>Total (n=299)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic Syndrome</td>
<td>No MS (122)</td>
<td>MS (67)</td>
<td>p-value&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No MS (46)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.2 ± 14.7</td>
<td>54 ± 12.9</td>
<td>0.0016</td>
<td>38.7 ± 13.</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>161.7 ± 7.56</td>
<td>159.62 ± 7.94</td>
<td>0.079</td>
<td>147.9 ± 9.2</td>
</tr>
<tr>
<td>Weight (Kgs)</td>
<td>68.3 ± 12.4</td>
<td>75.2 ± 9.6</td>
<td>&lt;0.001</td>
<td>59.6 ± 11.2</td>
</tr>
<tr>
<td>BMI(Kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>26.1 ± 4.4</td>
<td>29.6 ± 3.9</td>
<td>&lt;0.001</td>
<td>27.4 ± 5.6</td>
</tr>
<tr>
<td>Waist circumference(cms)</td>
<td>76.5 ± 20.8</td>
<td>104.7 ± 37.6</td>
<td>&lt;0.001</td>
<td>80.6 ± 18.5</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>205.5(171,235)</td>
<td>203(172,242)</td>
<td>0.868</td>
<td>195.5(171,225)</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>159(108,247)</td>
<td>173(130,244)</td>
<td>0.977</td>
<td>99(82,132)</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>36(29,44)</td>
<td>36(31,43)</td>
<td>0.539</td>
<td>49(37,57)</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>127.5(97,158)</td>
<td>123(95,163)</td>
<td>0.78</td>
<td>122(111,151)</td>
</tr>
<tr>
<td>BP Systolic (mmHg)</td>
<td>129.2 ± 14.8</td>
<td>137.2 ± 14.6</td>
<td>&lt;0.001</td>
<td>120.6 ± 18.1</td>
</tr>
<tr>
<td>BP Diastolic (mmHg)</td>
<td>79.7 ± 10.3</td>
<td>81.3 ± 9.9</td>
<td>&lt;0.001</td>
<td>75.2 ± 6.6</td>
</tr>
<tr>
<td>Fasting Blood Sugar (mg/dL)</td>
<td>104(97,136)</td>
<td>112(104,154)</td>
<td>0.711</td>
<td>95(69,104)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Values for continuous risk factors and outcomes are expressed as mean±standard deviations. For non-parametric variables values are reported as median (25th, 75th) percentile

<sup>2</sup>As defined by International Diabetes Federation definition

<sup>3</sup>p-values are for two-sided t-tests, assuming unequal variances, for comparison of means between males diagnosed with MS versus those not having MS and are significant at 0.05 level.

<sup>4</sup>p-values are for two-sided t-tests, assuming unequal variances, for comparison of means between females diagnosed with MS versus those not having MS and are significant at 0.05 level.

<sup>5</sup>p- values are for two-sided t-tests, assuming unequal variances, for comparison of means between males and females and are significant at 0.05 level.

<sup>6</sup>p-values are for non-parametric Mann-Whitney U test for comparison of medians

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**Table 1:** Physical, biochemical and general characteristics of the study population. The association between MS and vitamin D is tested using chi-square (Table 2). We also present the risk, using odds ratios and 95% confidence intervals, of MS in vitamin D deficient and insufficient subjects versus those with normal levels of 25(OH)D. We calculated the prevalence of risk of MS and MS across all categories of vitamin D. The lowest category represents the most deficient group. For each category, the prevalence of MS, abdominal adiposity, high triglycerides, hypoglycaemia and high blood pressure was calculated as a percentage (Table 3). All p- values presented are two tailed at 5% level.

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Serum Vitamin D</th>
<th>Metabolic Syndrome&lt;sup&gt;*&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No MS</td>
<td>MS</td>
</tr>
<tr>
<td></td>
<td>142(58.2)</td>
<td>102(41.8)</td>
</tr>
<tr>
<td></td>
<td>15(37.5)</td>
<td>25(62.5)</td>
</tr>
<tr>
<td></td>
<td>11(73.3)</td>
<td>4(26.7)</td>
</tr>
<tr>
<td></td>
<td>168(55.9)</td>
<td>131(44.1)</td>
</tr>
</tbody>
</table>

<sup>6</sup>p-value<sup>6</sup> for chi-square test of independence. (Null hypothesis is there is no relationship between MS and Vitamin D in our target population).
Odds ratios and p-values from logistic regression models adjusted for age, sex, BMI, physical activity and diet.

Definition of MS as given by International Diabetes Federation Guidelines for South Asians.

Table 2: Relationship between metabolic syndrome (MS) and serum 25-Hydroxyvitamin D.

<table>
<thead>
<tr>
<th>Categories of vitamin D (nmol/l)</th>
<th>Metabolic syndrome</th>
<th>Abdominal adiposity 1</th>
<th>Hyperglycaemia 2</th>
<th>High triglyceride 3</th>
<th>High BP 4</th>
<th>Low HDL-C 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (n=189)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deficiency (&lt;25)</td>
<td>33.6</td>
<td>37.4</td>
<td>47.1</td>
<td>52.9</td>
<td>50.9</td>
<td>64.5</td>
</tr>
<tr>
<td>Insufficiency (25-49.9)</td>
<td>52.2</td>
<td>56.5</td>
<td>65.2</td>
<td>69.6</td>
<td>30.4</td>
<td>56.5</td>
</tr>
<tr>
<td>Sufficiency (&gt;49.9-150)</td>
<td>50</td>
<td>50</td>
<td>33.3</td>
<td>50</td>
<td>33.3</td>
<td>50</td>
</tr>
<tr>
<td>Toxicity (&gt;250)</td>
<td>0</td>
<td>0</td>
<td>60</td>
<td>100</td>
<td>40</td>
<td>80</td>
</tr>
<tr>
<td>Ptrend</td>
<td>0.138</td>
<td>0.13</td>
<td>0.774</td>
<td>0.287</td>
<td>0.674</td>
<td>0.897</td>
</tr>
</tbody>
</table>

Females (n=110)

| Deficiency (<25)                | 56.2              | 100                    | 44.9             | 34.8               | 24.7      | 68.5        |
| Insufficiency (25-49.9)         | 76.5              | 100                    | 41.2             | 47.1               | 47.1      | 70.6        |
| Sufficiency (49.9-150)          | 25                | 100                    | 25               | 25                 | 0         | 75          |
| Toxicity (>250)                 | 0                 | 100                    | 0                | 0                  | 0         | 0           |
| Ptrend                          | 0.978             | 0.746                  | 0.746            | 0.154              | 0.321     |

P\text{trend} is p-value from a test of linear trend of proportions.

1 Abdominal adiposity is defined as waist circumference >90 cms (Males) and >80 cms (Females)

2 Hyperglycaemia is defined as fasting blood sugar >110 mg/dl

3 High triglyceride is defined as triglyceride >150 mg/dl

4 High BP is defined as Systolic BP >130 mmHg and diastolic BP >85 mmHg

5 Low HDL-C is defined as HDL <40 mg/dl (Males) and <50 mg/dl (Females)

Table 3: Prevalence of metabolic syndrome and its components across categories of vitamin D.

All analyses were done using STATA 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Results

The study sample was pre-dominantly male (63.2%, 189/299) and the mean age was 47.5 ± 14.6 years. Subjects with mean abdominal adiposity (86.9 ± 14.3 cms), median fasting blood sugar 107 mg/dl IQR-(97,136) that is higher compared to normal waist circumference of ≤80 cms and fasting blood sugar lower than ≤110 mg/dl respectively (Table 1). A significant difference was observed in anthropometric measures between males and females: height (p <0.0001), weight (p<0.0001) and BMI (p =0.004)). Significant differences in lipid profiles were observed between males and females: triglycerides (p<0.001), HDL-C (p=0.002), LDL-C (p=0.008), diastolic BP (p=0.042) and systolic BP (p=0.0013).

Among males there was no significant difference in total cholesterol (p=0.87), HDL-C (p=0.54), LDL-C (p=0.78), triglycerides (0.98), diastolic BP (p=0.30) and fasting blood sugar (p=0.71) between those with MS and those without MS (Table 1). Systolic blood pressure was significantly different in males with MS versus those without MS (p<0.001). In females, we found a significant difference (p<0.01) between those who had MS versus those who did not, in all lipid, blood pressure and fasting glucose measures except LDL-C (p=0.17).

The prevalence of MS in our sample was 44.1% (131/299) (Table-2). Also 81.6% (244/299) of the participants had vitamin D deficiency (25(OH) D <25 nmol/l), 13.4% (40/299) have insufficiency (25<25(OH) D ≤ 49.9 nmol/l) and only 5% are identified as sufficient (15/299).
Table 2 presents the bivariate association between vitamin D levels and MS. It explores the null hypothesis that there is no relationship between 25(OH) D and MS. It shows that 34.4% of the sample had 25(OH) D deficiency as well as MS. The association was significant (p=0.02) indicating that there is a relationship between MS and vitamin D that cannot be attributed to chance alone. After adjusting for age, sex, BMI, physical activity and diet, the risk (odds) of MS in vitamin D deficient subjects was found to be 1.9 times higher than that of subjects with normal levels and 4.6 times higher risk for those with insufficiency.

Prevalence of MS and associated components was calculated for different categories of vitamin D levels separately for males and females (Table 3). For males, the highest prevalence and metabolic risk (Prevalence: MS-52.2%, abdominal adiposity-56.5%, high triglycerides-69.6%) was shown for subjects who had insufficiency in vitamin D. Males who had deficiency in vitamin D had high prevalence of High BP (50.9%) and Low HDL-C (64.5%). Females with vitamin D insufficiency had a high prevalence of MS (76.5%), central obesity (100%), high triglycerides and high BP (47.1% each and low HDL-C (70.5%). The p-values for trend in prevalence (P trend) are greater than 0.05, indicating there is no uniformly increasing or decreasing trend in prevalence of MS and its components across vitamin D categories.

Discussion

This paper explores the prevalence and relationship of two rapidly emerging conditions in the Indian sub-continent; metabolic syndrome and vitamin D deficiency. The prevalence of MS in India varies between 10-30% and the criteria used for defining MS are not uniform [24]. We used the International Diabetes Federation guidelines to determine presence of MS [14]. The overall prevalence of MS in the current study was 44%. Like other studies our data also showed significant gender-specific differences. While some studies [25] show that males are at higher risk of MS as compared to females, our study like other studies in similar settings [24,26], showed higher (2.5 times) prevalence among females. Older subjects had higher odds of developing MS (Age≥ 46 had 1.9 times higher odds than Age≤46). Studies in other populations like Bali [27], Korea [28], Norway [29] have indicated an increasing prevalence of the MS with age.

Studies have reported a prevalence of 70-100% of vitamin D deficiency in the Indian subcontinent [24,26] which is much higher than the prevalence range reported globally 30-50% [5,7,13]. There is a continued debate in the published literature with respect to the uniformity cut-off for 25(OH) D. For the purpose of maintaining uniformity, we used the categories used in studies based in South Asia [17,18,26]. Our study reports a prevalence of 25(OH)D <25 mmol/l as 82% and 25(OH)D <50 mmol/l as 95%. This is despite the fact that the subjects belong to a low latitude area that have abundance of sunlight, hence sunlight exposure is expected to be adequate in our sample.

The key finding of this study augments the evidence of association of low vitamin D status and MS. The impact of poor vitamin D status on health with evidence of increased disease risk is steadily accumulating. Our study has shown a statistically significant relationship between MS and vitamin D with lower 25(OH) D levels showing higher odds of MS. A meta-analysis of 28 studies conducted between 1990 and 2009 [30] investigated the effects of vitamin D on the risk of CVD, diabetes and the metabolic syndrome. Eight of the studies reported prevalence of MS as the outcome. All of the eight studies reported a significant association between high 25(OH) D levels and reduced MS prevalence (OR=0.49, 95% CI: 0.38-0.64). Very few of these studies accounted for diet and physical activity in their models. In this study we assessed diet through a seven day recall and physical activity by the duration of intense physical work and exercise. We included diet, physical activity and smoking status in our model to make the association between MS and vitamin D more discriminating. We found that after adjusting for age, sex, smoking status, diet, physical activity and other metabolic risk factors, 25(OH)D deficiency was associated with a clinically high odds (OR=3.5) of having MS.

Conclusion

Our study indicates high prevalence of vitamin D deficiency among those with metabolic syndrome and women are especially vulnerable. The results from this study have shown a significant association between MS and vitamin D levels. However a proportionally greater risk of MS with the lowest levels of vitamin D as compared to mere insufficiency could not be demonstrated as a clear “dose response” relationship. Those with insufficiency were shown to be at five times greater risk and those with deficiency were at 2 times greater risk than those who were vitamin D sufficient. Perhaps insufficiency of the vitamin poses a greater risk of developing MS than deficiency due to other concomitant factors. Hence this evidence warrants further research in this area to identify better predicates of association. Policymakers should take note that vitamin D deficiency has become a pervasive problem with implications for cardiovascular health across age and gender groups. Timely translational research can be used to develop the appropriate interventions- such as food fortification, supplementation, improvements in environment and behavior change to mitigate potential problems attributable to Vitamin D deficiency.

Limitations of the study

This is a cross-sectional study and does not include long term follow-up to understand the causal pathway through which vitamin D deficiency may lead to metabolic syndrome or its components in Asian Indians. A longitudinal design would also have enabled the capture of seasonal variation in 25(OH) D levels by testing at multiple time points.

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Competing Interests

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.

References


