# Vitamin D Insufficiency Risk Score for Screening for Vitamin D Insufficiency

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## Abstract

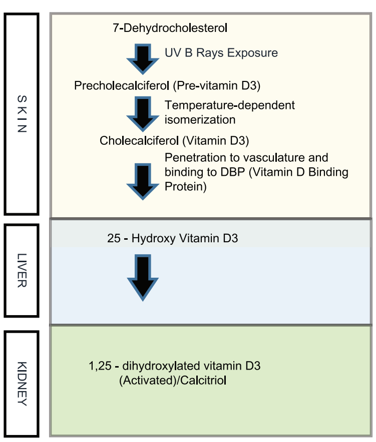
**Background and Aims:** Vitamin D Deficiency/Insufficiency (VDD/VDI) is now recognized as a pandemic. Vitamin D is a versatile yet crucial factor which is vital for many metabolic functions in our body. Till now there is no screening tool for VDD/VDI. The aim of this study is to develop and validate a screening tool Vitamin D Insufficiency Risk Score (VDIRS). **Methods:** This study was a rural community based cross-sectional study. It was done during May 2016 to April 2017 among 197 adults residing in rural West Bengal. After a thorough literature review and discussion with the field experts, four characteristics (BMI, Physical activity, Daily Sun exposure, Diet) were considered for VDIRS. Data was collected after taking informed consent. After interviewing every individual was examined for height, weight and blood was collected for vitamin 25-(OH) D. Weights were given to VDIRS characteristic according to Adjusted Odds' Ratio. Receiver Operating Characteristics (ROC) curves were utilized to validate and find out optimum cut off for VDIRS using Youden's index for VDD/VDI with the use of R software. **Results:** Only 133 (67.5%) had Vitamin D insufficiency. On ROC curves for VDIRS for VDI and VDD, AUC was 0.83 and 0.77 which signifies VDIRS as a good screening and predictive tool. A score of VDIRS ≥14 had sensitivity of 78.2% and specificity of 75.0% for VDI. **Conclusion:** Use of the VDIRS can make mass screening for undiagnosed VDI/VDD in India more cost effective. Researchers strongly believe and perceive a necessity of such validated score in the present scenario.

**Keywords:** India, receiver operating characteristic curve, Vitamin 25-(OH) D, Youden's index

## Introduction

Vitamin D is a fat soluble vitamin which has been traditionally known as anti-ricketic factor or sunshine vitamin.[1,2]

**Flow of Vitamin D in body[1]:**

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Quick Response Code:

Website: www.ijem.in

DOI: 10.4103/ijem.IJEM_539_19

Activated vitamin D leads to multiple biological responses and regulates cell differentiation by binding to vitamin D receptors (VDR) in several body tissues.[3,4]

Usually 50-90% of vitamin D is produced by sun exposure and the remainder comes from the diet. As with recent progress, it is now clear that Vitamin D has its effect on overall health, besides its effect on bone health such as on glycemic control, on immunity, on various malignancies, on lipid profile, on cardio-vascular diseases, increasing neuromuscular function and improving mood, protecting the brain against toxic chemicals, and potentially reducing pain and on various other aspects of health.[5-7] Also, now it is known that level of vitamin D in the pregnant lady has effects on birth weight,

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**How to cite this article:** Garg S, Dasgupta A, Paul B, Maharana SP. Vitamin D insufficiency risk score for screening for Vitamin D insufficiency. Indian J Endocr Metab 2019;23:552-6.

baby's vitamin D level and health.[8-10] According to a published research, if the vitamin D level of person remains in adequate range then the chances of mortality will decrease by 26%.[11]

VDD is now recognized as a pandemic. It is a major public health problem worldwide in all age groups.[12-16] It was believed previously that vitamin D deficiency are uncommon problems in India because of abundant sunshine.[17] Actually it is not uncommon even in the sunny land of India. VDD prevails in epidemic proportions all over the Indian subcontinent, with a prevalence of 70-100% in the general population.[7]

Vitamin D status is tested by blood tests which are costly and not feasible in the field setting. Till now there is no screening tool for detecting VDD and VDI, which can predict VDD/VDI and give health system an opportunity to intervene early long before any deleterious effects of VDD/VDI occur.

With this background, we have developed and validated a new screening tool Vitamin D Insufficiency Risk Score (VDIRS) for predicting VDD/VDI among adults (≥18 years).

## Methods

This study was a rural community based cross-sectional study. It was done during May 2016 to April 2017 among adults residing in a rural block of West Bengal, India. Pregnant and lactating women who had not given written informed consent, who were critically ill, and who had vitamin D supplementation within the last 6 months, were excluded.

As this kind of study i.e., study on VDD/VDI has not been conducted in this part of the country on a community basis, reference of a study done in Mangalore has been considered for sample size calculation where the prevalence of VDI was 80%.[18] After taking confidence interval of 95%, relative error as 10% and design effect as 2. The minimum sample size was 197.

Rural Health Unit and Training Center, Singur (RHUTC) is the rural field practice area of All India Institute of Hygiene and Public Health (AIIHPH), Kolkata, which serves 64 villages through two of its Union Primary Health Center (UPHC). Each UPHC serves 32 villages. Multi-stage sampling was used to recruit the study participants. In the first stage, 3 villages were selected randomly from the 32 villages of each UPHC. Line listing of all the adults from selected villages was done and number of participants from each village was calculated by Population Probability to Size Sampling. Required number of participants were drawn from the list of each village by Simple Random Sampling (SRS). If the selected individual was found to be as per exclusion criteria or could not be contacted even after two visits, SRS was done again without replacement.

Due permission of the Institutional Ethics Committee of AIIHPH was taken. Data was collected by the researcher himself after obtaining written informed consent by interviewing the respondents with the help of a structured pre-tested pre-designed schedule. After a thorough literature review (deductive technique) and discussion with the field experts (inductive technique), four characteristics (BMI, Physical activity, Daily Sun exposure, Diet) were considered for VDIRS and a schedule was prepared to collect data on these characteristics.

The Schedule had four parts:

a. Socio-demographic characteristics,
b. Sun exposure,
c. Physical Activity; Short International Physical Activity Questionnaire (IPAQ),[19]
d. Diet

a. Socio-demographic characteristics: Age, sex
b. Sun exposure: Each individual was asked about the usual daily sun exposure in hours.
c. Physical Activity: Each individual was asked about their various activities in last seven days.
d. Diet: Dietary intake of at least 100 Grams (gms) of milk/dairy products OR at least 100 gms fish or 1 egg with yolk for four or more days in the last seven days.

After interviewing every individual was examined for height and weight and blood was collected for vitamin 25-(OH) D. Blood was collected from cubital vein and transported to biochemical laboratory for serum vitamin 25-(OH) D levels. Height was measured in standing position against a hard wall with occiput, shoulder blades, buttocks and heel touching the wall without any footwear and head-gear with non-stretchable measuring tape with the precision of 0.1 cm. Weight was measured with properly calibrated digital weighing scale with precision of 0.1 kilograms with participants standing in straight position with minimum respectable clothing.

### Operational definition

- Vitamin D Insufficiency: VDI is defined as serum vitamin D 25-(OH) level <30 ng/ml.[18]
- BMI: Each individual was classified into different BMI categories as per South Asian WHO criteria.[20]
- High Sun Exposure: An optimum cut-off for daily sun exposure was found using ROC curve for vitamin D sufficiency. Individuals with daily sun exposure more than equal to this cut off were stated as having high sun exposure.

### Statistical analysis

Recorded data was analyzed using R: A language and environment for statistical computing. ROC curves were utilized to find out optimum cut off for daily sun exposure using Youden's index (J = sensitivity + specificity – 1). Each characteristic under VDIRS was coded as 'Zero' for preferable condition i.e., BMI <25 kg/m$^2$, Health Enhancing Physical Activity (HEPA), High sun exposure (≥1.75 hours) and adequate dietary intake and as 'One' with counterpart. Multivariable logistic regression was run after taking VDI as outcome variable and characteristics of VDIRS as predicting variable. Weights were given to VDIRS characteristic according to Adjusted Odds' Ratio (AOR). ROC curves were utilized to validate and find out optimum cut off for VDIRS using Youden's index for VDD/VDI.[21-23]

## Results

Mean (SD) age of the participants was 42.8 (15.3) years. Most prevalent age group was 36-44 years with 44 (22.3%) participants. Among them, 102 (51.8%) were females.

Among the study participants, 31 (15.7%) had VDD and 102 (51.8%) suffered from VDI [Table 1]. Mean (SD) minutes of daily sun exposure was 90 (75) min./day. On asking about the time usually spent under sunlight, 85 (43.14%) adults replied 30 minutes or less, only 1 stated that he did not spend any time under sunlight. Only 9 study participants were reported to have daily sun exposure of more than 3 hours.

On ROC for daily sun exposure for vitamin D sufficiency (Vitamin D ≥30 ng/ml), AUC (area under the curve) was 0.7846 which signifies daily sun exposure as a good screening tool. With Youden's method as well with Closest to top-left method, optimum cut-off of daily sun exposure was found to be 1.75 hour/day. At this cut-off, an individual had minimum vitamin D level of 30 ng/ml with a sensitivity of 75% and specificity of 77.44% [Figure 1].

All the preferable scenarios were coded as 'Zero'. Out of all 59.4%, 40.6%, 64.5% and 39.6% had preferable BMI (<25 kg/m2), HEPA active physical activity, adequate diet and high daily sun exposure, respectively. Proportions of vitamin D insufficiency across categories of all the explanatory variables of VDIRS differed statistically significantly. On multivariable analysis BMI, sun exposure and diet retained their significance [Table 2].

**Table 1: Vitamin D level among study participants (*n*=197)**

| Vitamin D Level | No. (%) | Status of Vitamin D |
|---|---|---|
| Vitamin D Deficient (<20 ng/ml) | 31 (15.7) | Vitamin D insufficiency (Vitamin D <30 ng/ml) |
| Vitamin D Insufficient (20-29.99 ng/ml) | 102 (51.8) | |
| Vitamin D Sufficient (≥30 ng/ml) | 64 (32.5) | Vitamin D Sufficiency |
| Total | 197 (100) | |

After considering score for physical activity as "1", other variables were weighted according to their AOR. Hence, "sun exposure" was weighted maximum with a value of "nine". After weighing each variable of VDIRS maximum attainable score is 18 with minimum score of 0 [Table 3].

On ROC for VDIRS for vitamin D insufficiency (Vitamin D <30 ng/ml), AUC was 0.83 which signifies VDIRS as a good screening and predictive tool. With Youden's method and Closest to top left method, optimum cut-off of VDIRS was found to be 8.5. At this cut-off an individual will have a Vitamin D level <30 ng/ml with a sensitivity of 78.2% and specificity of 75.0% [Figure 2].

On ROC for VDIRS for vitamin D deficiency (vitamin D <20 ng/ml) AUC was 0.77 which signifies VDIRS as a fair screening and predictive tool. With Youden's method and Closest to top left method, optimum cut-off of VDIRS was found to be 13.5. At this cut-off an individual will have a Vitamin D level <20 ng/ml with a sensitivity of 71.0% and specificity of 80.1% [Figure 3].

Finally, AUC for ROC curves showed VDIRS as a good predictive tool for VDI and VDD. Individuals with VDIRS upto 8 will have sufficient vitamin D level while those with VDIRS more than equal to 14 will have vitamin D deficiency [Table 4].

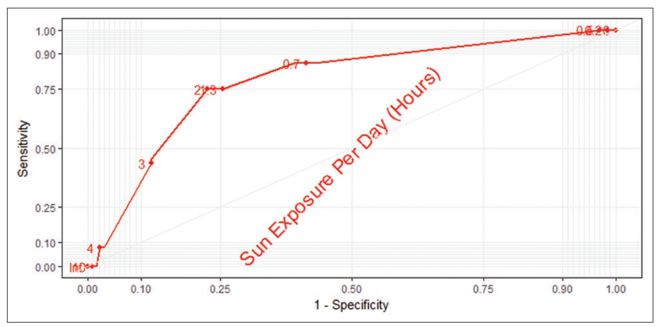


**Figure 1:** Receiver Operating Curve (ROC) for Time of Sun Exposure per day for Predicting Vitamin D Sufficiency (Vitamin D ≥ 30 ng/ml) (*n* = 197)

**Table 2: Variables for Vitamin D Insufficiency Risk Score (VDIRS) and Vitamin D Insufficiency among study participants (*n*=197)**

| Variables | Insufficiency No. (%) (*n*=133) | OR (95% CI) | AOR (95% CI) |
|---|---|---|---|
| Obesity | | | |
| BMI <25 kg/m$^2$ (*n*=117) | 66 (56.4) | Ref. | Ref. |
| BMI ≥25 kg/m$^2$ (*n*=80) | 67 (83.7) | 3.98 (1.98-7.99) | 2.42 (1.09-5.41) |
| Physical Activity | | | |
| HEPA active (*n*=80) | 39 (48.8) | Ref. | Ref. |
| Non-HEPA active (*n*=117) | 94 (80.3) | 4.29 (2.28-8.10) | 0.90 (0.36-2.25) |
| Diet | | | |
| Adequate (*n*=127) | 71 (55.9) | Ref. | Ref. |
| Inadequate (*n*=70) | 62 (88.6) | 6.11 (2.70-13.81) | 4.40 (1.77-10.28) |
| Daily Sun Exposure | | | |
| ≥1.75 h (*n*=78) | 30 (38.5) | Ref. | Ref. |
| <1.75 h (*n*=119) | 103 (86.6) | 10.30 (5.13-20.67) | 7.61 (3.03-19.16) |
| Total | 133 | | |

*$P$<0.05 for all

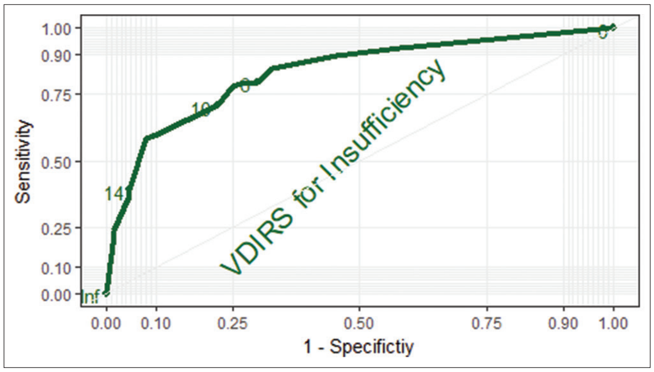


**Figure 2:** Receiver Operating Curve (ROC) for VDIRS score for Predicting Vitamin D Insufficiency (Vitamin D < 30 ng/ml) ($n$ = 197)

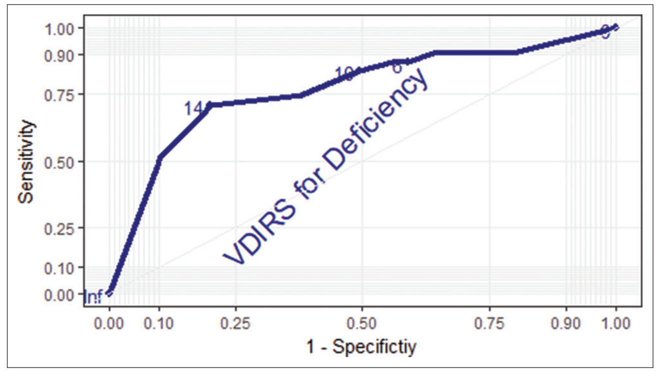


**Figure 3:** Receiver Operating Curve (ROC) for VDIRS score for Predicting Vitamin D Deficiency (Vitamin D < 20 ng/ml) ($n$ = 197)

**Table 3: Vitamin D insufficiency risk score**

| Variables | Code (Initial) | AOR | Weight | Score (Final) |
|---|---|---|---|---|
| Physical Activity | | 0.90 | 1 | |
| HEPA active ($n$=80) | 0 | | | 0 |
| Non-HEPA active ($n$=117) | 1 | | | 1 |
| Obesity | | 2.42 | 2.7≈3 | |
| BMI <25 kg/m$^2$ ($n$=117) | 0 | | | 0 |
| BMI ≥25 kg/m$^2$ ($n$=80) | 1 | | | 3 |
| Diet** | | 4.40 | 4.9≈5 | |
| Adequate | 0 | | | 0 |
| Inadequate | 1 | | | 5 |
| Daily Sun Exposure | | 7.71 | 8.6≈9 | |
| ≥1.75 h ($n$=78) | 0 | | | 0 |
| <1.75 h ($n$=119) | 1 | | | 9 |

** Dietary intake of at least 100 Grams (gms) of milk/ dairy products OR at least 100 gms fish or 1 egg with yolk for four or more days in the last seven days was considered Adequate

**Table 4: Recommended cut-offs for vitamin D insufficiency risk score to predict vitamin D levels**

| VDIRS | Vitamin D Level |
|---|---|
| 0-8 | Sufficient |
| 9-13 | Insufficient |
| 14-18 | Deficient |

## Discussion

Among the study participants, 31 (15.7%) had VDD. About two third participants i.e., 67.5% had VDI. Mean (SD) minutes of daily sun exposure was 90 (75) min/day and 85 (43.14%) adults replied 30 minutes or less. Only 9 study participants were reported to have daily sun exposure of more than 3 hours. With Youden's method on ROC curve, optimum cut-off of daily sun exposure was found to be 1.75 hours/day (105 minutes) for vitamin D sufficiency at 30 ng/ml with a sensitivity of 75%.

Proportions of vitamin D insufficiency across of all categories of the four variables of VDIRS differed statistically significantly. Multivariable logistic regression was performed for each VDIRS variable with vitamin D insufficiency and individual AOR was reported. Minimum AOR was for "Physical activity" and maximum for "Sun Exposure". On multivariable regression, physical activity lost its significance but still considered into VDIRS as it was found to be significant in univariate regression as done during the development of IDRS (Indian Diabetes Risk Score) by Mohan *et al*.[24] After weighing each variable of VDIRS maximum attainable score is 18 with minimum score of 0. On ROC Curve for VDIRS for vitamin D insufficiency, AUC was 0.83 and for vitamin D deficiency was 0.77 which signifies VDIRS as a good screening and predictive tool. With Youden's method, optimum cut-off of VDIRS for vitamin D insufficiency was found to be 8.5. Similarly optimum cut-off for vitamin D deficiency was 13.5.

In this study, we have devised a new screening tool i.e VDIRS for identifying newly diagnosed vitamin D insufficient subjects in our country. This is of great significance as use of such scoring system could prove to be a cost effective tool for screening of VDI/VDD. Further, use of such a risk score would be of great help in developing countries like India where there is a marked explosion of VDD/VDI with exponential growth of non-communicable diseases and most of the cases remain undiagnosed till the condition worsens.

VDIRS uses four simple easily obtainable factors. In addition, the study is conducted on a representative sample of a block in rural India, the demographic of which is similar to the rest of the India. Hence the results can be extrapolated to the whole of India. However, the main limitation is that the findings are based on a cross-sectional study and needs further validation in prospective studies.

VDIRS can help in cost effective screening for vitamin D insufficiency and deficiency as it uses simple, safe and inexpensive measures. Moreover it would help to do selective screening instead of universal screening. For example, if we were to screen a population of 1,00,000 adults in a city using serum vitamin 25-(OH) level, assuming the cost of one vitamin D estimation including blood collection to be Rs. 500/-, the cost would work out to Rs. 500,00,000. For the same population, if a two-step procedure is used for screening for vitamin D insufficiency and deficiency, i.e. use VDIRS first and then screen only those likely to have vitamin D insufficiency and deficiency, only 55% of the population who have a score of more than 8, will have to be screened. This would capture over 75% (Sensitivity) of the undiagnosed subjects. If the screening test is carried out on all these individuals then the cost would work out to Rs. 27,500,000. Even if we add a cost of Rs. 100,000 for collecting information on VDIRS, the overall cost would only work out to Rs. 27,600,000. Thus there would be a cost saving of almost 45%, which in this case is Rs. 22,400,000/-.

## Conclusion

About two-third of the participants, i.e. 133 (67.5%), had VDI. After weighing each variable of VDIRS maximum attainable score is 18 with minimum score of 0. On ROC Curve for VDIRS for vitamin D insufficiency, AUC was 0.83 and for vitamin D deficiency was 0.77 which signifies VDIRS as a good screening and predictive tool.

In conclusion, this study provides a Vitamin D Insufficiency Risk Score for identifying undiagnosed vitamin D insufficiency and deficiency among adults in India. This is the first study to our knowledge to have evolved a Vitamin D Insufficiency Risk Score, which has categorized the risk factors based on their severity. Use of the VDIRS can make mass screening for undiagnosed VDI/VDD in India more cost-effective. Researchers strongly believe and perceive a necessity of such validated score in the present scenario when vitamin D deficiency has become a pandemic, which can screen high risk individual without going for expensive blood investigation. This will provide us the important lead time to intervene and prevent clinical consequences of vitamin D deficiency among the population at large.

### Acknowledgments

We would like to thank the Officer-in-charge and staff of RHUTC, Singur for their help and cooperation in conducting the study. We would also like to thank the health workers for helping us during our field visits. We sincerely thanks to all the developers of R software.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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