CUT OFF FOR HYPOVITAMINOSIS D BASED ON PARATHYROID HORMONE LEVELS AMONG A POPULATION OF PREGNANT MOTHERS IN COLOMBO DISTRICT

K. Anusha*[1], U.P.K. Hettiaratchi[1], S. Prathapan[2], G. Liyanage[3]
[1]Department of Biochemistry, Faculty of Medical Sciences, University of Sri Jayewardenepura, [2]Department of Community Medicine, Faculty of Medical Sciences, University of Sri Jayewardenepura, [3]Department of Paediatrics, Faculty of Medical Sciences, University of Sri Jayewardenepura
*Corresponding author (email: anushakanesh@yahoo.com)

Introduction

Countries near to equator receive more sunlight throughout the year. However, sun-seeking behavior is uncommon in these populations due to hot climate. Epidemiologic studies from our neighboring country, India, have shown high prevalence (70%) of low vitamin D (< 20 ng/mL) in all age groups; neonates, preschool and school children, pregnant women and adult males. Rodrigo *et al.,* has reported 56% of premenopausal women having vitamin D level ≤14ng/mL, in Southern coastal belt of Sri Lanka [1]. In recent years, another study has shown vitamin D level of <20 ng/mL among 35% preschoolers[2].

Lack of a standard definition for optimal level and lack of consensus on the cut-off values for vitamin D levels has led to the terminologies; sufficiency, insufficiency and deficeincy. Further, comparison of published data on vitamin D status among diverse populations and regions has become difficult due to different reference values and methods that have been used to assess vitamin D. Hence, standardising the measurements will benefit policies on supplementation and food fortification programmes. Importantly, such policies or guidelines should consider national and cultural variations and food availability. Thus, this present study was undertaken to determine the cut off for hypovitaminosis D based on parathyroid hormone (PTH) levels among a population of pregnant mothers in the Colombo District.

Materials and Methods

The study was carried out as a descriptive analytical study among a population of pregnant mothers (28 weeks to 40 weeks) from all the MOH areas in the Colombo district. The inclusion criteria were, uncomplicated pregnancy, single intrauterine pregnancy, gestational age 28 weeks and above and mothers who permanently reside in the Colombo district. The sample was selected to represent the pregnant mothers in the Colombo district. The study was carried out with statistically analysed sample number of 393 pregant mothers to describe the prevalence of vitamin D deficieny in the Colombo District. Sampling

was carried out as a stratified random sampling method. According to the population basis, samples were recruited from each MOH area. However, the Colombo Municipal Council (CMC) area is providing the calcium supplementation along with vitamin D as a product called "Kalzana". Thus, all the 6 MOH areas functioning under CMC were not considered in the sample recruitment as the vitamin D supplementation is one of the exclusion criteria for the recruitment process.

A pre tested interwiewer administered questionnaire was used in data collection. A venous blood sample was collected for the analysis of vitamin D, PTH, serum calcium, inorganic phosphorous and alkaline phosphatase (ALP).

The following laboratory methods were used in the sample analysis
• Serum vitamin D: The LIAISON 25 OH Vitamin D TOTAL assay kit
• PTH: The LIAISON N-TACT PTH Gen II assay kit
• Calcium, inorganic phosphorous and ALP: colorimetric method using Konealab analyzer

Participant's outdoor activities over the previous week in terms of duration (in minutes) and frequency (per week) were recorded in the questionnaire and the sun exposure (hours/week) was calculated.

Statistical analysis was performed using SPSS (version 15.0) software package. Correlation analysis and regression analysis were carried out to find out the relationship between serum vitamin D and other biochemical parameters. The Receiver operating curves (ROC) were used to find out the possible and suitable cut off for hypovitaminosis D based on PTH values.

Results and Discussion
Mean age of the maternal population was 29±6 years. Majority of the mothers were Sinhalese (75.3%), house wives (76.6%) and had secondary education (76.8%). The mean gestational age at birth was 32.9±3.5 weeks. The biochemical parameters of the study population are given in the Table 1.

Table 1. Biochemical parameters of the population

Blood biochemical Parameters	Blood biochemical parameters	
	Mean ± SD	Median (IQR)
Corrected calcium (mmol/L)	2.37±0.20	2.38 (2.46-2.32)
Inorganic phosphorous (mmol/L)	1.20±0.15	1.21 (1.31-1.09)
Total ALP (IU/L)	151.4±66.6	136.0 (181.3-105.8)
Bone specific ALP (IU/L)	79.2±27.5	74.0 (95.0-62.0)
PTH (pg/mL)	26.5±11.5	23.8 (31.1-18.4)
Vitamin D (ng/mL)	18.63±7.55	17.9 (22.9-13.1)

SD: Standard deviation; IQR: Inter quartile range

Serum inorganic phosphorus was within the normal range for the population. However, the corrected calcium was found to be low (normal 2.15- 2.57 mmol/L) among 07 mothers (1.8%). Total ALP (heat labile & heat stable) was above the cut off (>240 IU/L) in 10.2% (n=40). PTH levels above the cut off (>66.5 pg/mL) was observed only among 0.8% (n=03) of the population. Correlation analysis was carried out to find the association between serum vitamin D and other biochemical parameters. Only the serum corrected calcium (r=0.102;p=0.044), inorganic phosphorous (r=0.165;p=0.001) and PTH (r=-0.220;p=0.000) had a significant correlation with serum vitamin D levels. Then the regression analysis was performed to eliminate the effect of confounding factors such as age of the mother, occupation, monthly income, gestational age, and BMI. PTH levels and amount of sunlight exposure only had a significant association to serum vitamin D levels [3, 4].

The ROC was performed and corresponding area under the curve (AUC) was calculated. The figure 01 shows the ROC curve for the serum vitamin D levels based on the manufacturers recommendation for PTH cut off levels 66.5 pg/mL. AUC for the serum vitamin D levels was 0.933 at the level of 95% CI (p=0.010). Newer cut off value proposed to detect the hypovitaminosis D with highest accuracy, sensitivity (96.1%) and specificity (66.7%) is 8.1 ng/mL. This value is quite lower than the Institute of Medicine (IOM) cut off values. Prevalence of hypovitaminosis D according to newer cut off among pregnant mothers in the Colombo District is 4.1%.   (n=16). Similar analysis had been carried out in another study from North India and had derived higher cut off value (22.5 ng/mL)[5]
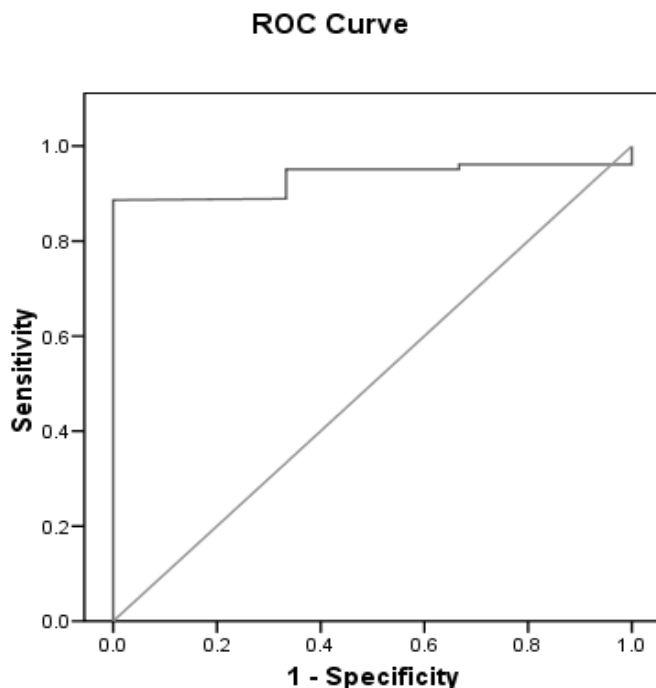
ROC Curve

Figure 1. ROC for serum vitamin D levels based on PTH

Conclusions and Recommendations

The ROC curve between serum vitamin D and PTH yielded a cut of for vitamin D value, which is less than the cut off value recommended by IOM (20 ng/mL). There were no reported studies in Sri Lanka on serum vitamin D with bone biochemical, diet and sunlight exposure among pregnant mother. A larger sample size would have been more useful in finding out the cut off for hypovitaminosis D among a representative sample of Sri Lankan population. Larger randomized control trials are needed to investigate the need of vitamin D supplementation and safe dose.

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