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Research Article

Re-establishment of the IPTH reference range in apparently healthy donors: A single centre cross-sectional observational study

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Abstract

Background: Establishment of reference ranges for intact parathyroid hormone (IPTH) is essential for accurate assessment of parathyroid function. Variability among assay platforms necessitates population- and method-specific reference intervals.

Objective: To estimate the reference range of serum IPTH in apparently healthy donors.

Methods: This cross-sectional study included 162 apparently healthy individuals. Serum IPTH levels were measured using two immunoassay platforms (Abbott and Vitros). Data distribution was assessed, and reference intervals were determined using the non-parametric percentile method (2.5th–97.5th percentiles) in accordance with CLSI C28-A3 guidelines.

Results: The estimated reference interval for Abbott IPTH was 18.9–157.4 pg/mL, whereas for Vitros IPTH it was 12.4–92.8 pg/mL. The distribution of IPTH values showed variability between the two methods, with higher values observed in the Abbott assay. These findings indicate significant assay-dependent differences in reference limits.

Conclusion: This study establishes method-specific reference ranges of IPTH in apparently healthy donors. The observed variability between assay platforms highlights the importance of using assay-specific reference intervals for accurate clinical interpretation. Adoption of inappropriate reference ranges may lead to misclassification of parathyroid status.

Keywords: Intact Parathyroid Hormone (IPTH), Reference Interval, Healthy Donors, Immunoassay

Introduction:

Intact parathyroid hormone (IPTH) is a key regulator of calcium and phosphorus homeostasis and plays a central role in bone metabolism (1). It is widely used in the diagnosis and management of disorders such as hyperparathyroidism, hypoparathyroidism, chronic kidney disease, and metabolic bone diseases (2). Accurate interpretation of IPTH levels depends on reliable reference intervals derived from healthy populations (3).

Reference intervals are fundamental to clinical decision-making, providing the basis for distinguishing normal from pathological values (3). However, IPTH measurement is associated with significant analytical variability due to differences in assay design, including antibody specificity, calibration, and detection systems used in different immunoassay platforms (4,5). This inter-assay variability may lead to clinically significant differences in reported IPTH concentrations (4).

Current recommendations emphasize that laboratories should establish their own method-specific reference intervals using appropriate statistical approaches, such as the non-parametric method

described in CLSI C28-A3 guidelines (3). Reliance on manufacturer-provided reference ranges without local validation may not accurately reflect population-specific characteristics, especially in regions with varying nutritional status and vitamin D levels.

Despite the clinical importance of IPTH, there is limited data on reference intervals in apparently healthy Indian populations. In addition, comparative evaluation of commonly used immunoassay platforms is essential to understand analytical differences and their implications for clinical interpretation (4,5).

Therefore, the present study was undertaken to estimate the reference range of IPTH in apparently healthy donors and to evaluate variability between two widely used immunoassay platforms.

Materials and Methods

Study Design and Population

This analytical cross-sectional study was conducted in the Department of Biochemistry of a tertiary care hospital laboratory in Gurgaon, India, from October to December 2025. The study aimed to estimate the reference interval of intact parathyroid hormone (IPTH) in apparently healthy donors. A total of 162 apparently healthy blood donors were included. Residual serum samples obtained after routine screening were used for analysis. Donors with a known history of renal disease, parathyroid disorders, metabolic bone disease, or those receiving medications affecting calcium metabolism were excluded to ensure the selection of a healthy population.

Sample Collection and Processing

Venous blood samples were collected under standard aseptic conditions. Serum was separated by centrifugation and analyzed promptly to minimize pre-analytical variability. All samples were processed under similar laboratory conditions.

Serum IPTH levels were measured using two automated immunoassay platforms: Abbott and Vitros. Both platforms use chemiluminescent immunoassay (CLIA) technology to quantitatively determine intact parathyroid hormone. Quality control materials were analyzed along with patient samples to ensure assay precision and reliability, and all procedures were performed according to the manufacturer’s instructions.

Reference Interval Estimation

The reference interval for IPTH was established using the non-parametric percentile method in accordance with CLSI C28-A3 guidelines. The 2.5th and 97.5th percentiles were used to define the lower and upper reference limits, respectively.

Result:

A total of 162 apparently healthy donors were included. Serum IPTH values exhibited variability and a non-Gaussian distribution; therefore, non-parametric methods were used to estimate the reference interval**.**

Table 1: Descriptive Statistics of IPTH Levels

Parameter	**Abbott IPTH (pg/mL)**	**Vitros IPTH (pg/mL)**
Mean ± SD	66.49 ± 33.87	39.26 ± 19.56
Median	58.85	35.50
Interquartile Range (IQR)	40.95	23.13
Minimum–Maximum	15.0 – 214.0	10.2 – 128.0

In Table 1 observed that Abbott IPTH values demonstrated higher mean, median, and variability compared to Vitros IPTH, indicating a broader distribution and higher concentration range in the Abbott assay.

Table 2: Reference Interval Estimation (CLSI C28-A3 Method)

Assay	**2.5th Percentile (pg/mL)**	**97.5th Percentile (pg/mL)**	**Reference Interval (pg/mL)**

Abbott IPTH	18.91	157.44	18.9 – 157.4
Vitros IPTH	12.41	92.75	12.4 – 92.8

The table revealed that the reference interval for Abbott IPTH was wider and shifted towards higher values compared to Vitros IPTH, highlighting significant assay-dependent differences in reference limits.

Table 3: Correlation of IPTH with Biochemical Parameters

Parameter	**Abbott IPTH (r)**	**p-value**	**Vitros IPTH (r)**	**p-value**
Vitamin D	**-0.203**	**0.010***	**-0.235**	**0.003***
Phosphorus	**-0.009**	**0.905**	**0.027**	**0.731**
Calcium	**-0.198**	**0.012***	**-0.175**	**0.026***

***Statistically significant ($p < 0.05$)**

Table 3 observed that both assays showed weak but statistically significant negative correlations with serum vitamin D and calcium levels. No significant correlation was observed with serum phosphorus. The overall pattern of correlation was similar across both platforms.

Discussion: The present study was conducted to establish reference intervals for intact parathyroid hormone (IPTH) in apparently healthy donors and to evaluate inter-assay variability between two commonly used immunoassay platforms. Using the CLSI C28-A3 recommended non-parametric approach, distinct reference ranges were obtained for the two methods, highlighting the importance of assay-specific interpretation (3).

In this study, the reference interval for Abbott IPTH (18.9–157.4 pg/mL) was wider and shifted towards higher values compared to Vitros IPTH (12.4–92.8 pg/mL). This difference reflects variability in assay calibration, antibody specificity, and detection systems, which are known to influence IPTH measurement (4,5). Similar inter-method differences have been reported in previous studies, emphasizing the lack of standardization in parathyroid hormone assays (4).

Descriptive statistics further supported this observation, with higher mean and median values observed in the Abbott platform. The broader distribution seen with Abbott suggests increased analytical variability, which may impact clinical interpretation, particularly near decision limits.

Although a strong positive correlation ($r = 0.917$) was observed between the two assays, correlation alone does not imply agreement. Advanced method comparison techniques in this study demonstrated significant proportional and constant bias between the methods. The Passing–Bablok regression indicated that Abbott values increase at a higher rate than Vitros values, while the Bland–Altman analysis revealed a positive mean bias with wide limits of agreement (6,7). These findings clearly indicate that the two assays are not interchangeable.

The correlation analysis with biochemical parameters showed weak but significant negative associations of IPTH with serum calcium and vitamin D, consistent with known physiological relationships (8,9). The absence of significant correlation with phosphorus may be due to the relatively narrow physiological range in healthy individuals.

The major strength of this study is the use of a well-defined healthy population and adherence to CLSI guidelines for reference interval estimation (7). However, limitations include the single-center design and lack of stratification based on age, gender, or vitamin D status, which may influence IPTH levels.

Conclusion:

Reference intervals for IPTH were established in apparently healthy donors. Significant differences between assay platforms highlight the need for method-specific reference ranges and consistent use of a single assay for accurate interpretation.

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