

ORIGINAL RESEARCH

INTENSIVE CARE

Evaluation of agreement between point-of-care and laboratory automated immunoassay in procalcitonin measurement among critically ill patients

Muhamad Aizuddin Ismail¹, Mohd Zulfakar Mazlan², Shamsul Kamalrujan Hassan³, Wan Norlina Wan Azman⁴, Tan Say Koon⁵, Najib Majdi Yaacob⁶, Mahamarowi Omar⁷, Nik Abdullah Nik Mohamad⁸

Author affiliation:

1. Muhamad Aizuddin Ismail, Department of Anaesthesiology and Intensive Care, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: aizuddin157@student.usm.my
2. Mohd Zulfakar Mazlan, Department of Anaesthesiology and Intensive Care, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: zulfakar@usm.my; ORCID: {0000-0002-3452-1280}
3. Shamsul Kamalrujan Hassan, Department of Anaesthesiology and Intensive Care, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: wanishamsul@yahoo.com
4. Wan Norlina Wan Azman, Department of Chemical Pathology, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: dr_wannorlina@usm.my
5. Tan Say Koon, Department of Chemical Pathology, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: saykoon@usm.my
6. Najib Majdi Yaacob, Department of Biostatistics and Research Methodology, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: najibmy@usm.my
7. Mahamarowi Omar, Department of Anaesthesiology and Intensive Care, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: marowi@usm.my
8. Nik Abdullah Nik Mohamad, Department of Anaesthesiology and Intensive Care, School of Medical Sciences, 16150 Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia; E-mail: nikabdullah@usm.my

Correspondence: Mohd Zulfakar Mazlan; E-mail: zulfakar@usm.my; Phone: 097676104; Mobile: +60 01921124

ABSTRACT

Introduction: Procalcitonin (PCT) has attracted significant attention as a novel biomarker of sepsis. This study aimed to assess the agreement between blood results of PCT, obtained using the Fineware™ FIA Meter Plus (FS113), a point-of-care (POC) procalcitonin testing device, and the automated Elecsys® BRAHMS PCT assay on the Cobas e411, among critically ill septic patients.

Methodology: This observational study was conducted in the intensive care unit of Hospital Universiti Sains Malaysia, in 2021. Whole blood samples were collected and tested with the Fineware™ FIA Meter Plus (FS113) (Wondfo, China) for PCT measurement. Additionally, the same whole blood samples were centrifuged to produce plasma samples, which were then analyzed using the automated Elecsys® BRAHMS PCT assay on the Cobas e411 (Roche Diagnostics, Germany).

Results: A total of 40 samples were analyzed in this study. Both PCT measurement techniques demonstrated a significant correlation, with a correlation coefficient of 0.96. Regression analysis revealed the following results: an Ordinary Least Square (OLS) slope of 0.91 (95% CI 0.83, 1.00) with an intercept of 1.27 (95% CI -0.75, 3.29); a Deming slope of 0.95 (95% CI 0.80, 1.10) with an intercept of 0.77 (95% CI -0.44, 1.85); and a Passing-Bablok slope of 1.16 (95% CI 0.99, 1.36) with an intercept of 0.22 (95% CI 0.08, 0.58).

Conclusion: The point-of-care procalcitonin measurement provided by the Fineware™ FIA Meter Plus presents a viable alternative for assessing procalcitonin levels among septic patients in the intensive care unit (ICU).

Abbreviations: CLIA- chemiluminescence immunoassays; PCT- Procalcitonin; POC- Point-of-care

Key words: procalcitonin, point of care, sepsis, Intensive care unit

Citation: Ismail MA, Mazlan MZ, Hassan SK, Azman WNW, Koon TS, Yaacob NM, Omar M, Mohamad NAN. Evaluation of agreement between point-of-care and laboratory automated immunoassay in procalcitonin measurement among critically ill patients. *Anaesth. pain intensive care* 2023;27(4):470–477; DOI: [10.35975/apic.v27i4.2277](https://doi.org/10.35975/apic.v27i4.2277)

Received: November 27, 2022; **Reviewed:** July 11, 2023; **Accepted:** July 11, 2023

1. INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection.¹ It affects millions of people around the globe and has become one of the leading causes of death worldwide. Sepsis needs prompt recognition as it rapidly progresses into a shock state, multiorgan failure, and even death. Many biomarkers have been investigated to identify sepsis at an earlier stage. C-reactive protein (CRP) is commonly used as the biomarker of choice. However, it lacks specificity, limiting its usefulness in managing sepsis.²

Procalcitonin has attracted much clinician attention as a novel biomarker of sepsis. Le Moullec et al. first described procalcitonin (PCT) as a small protein and prohormone of calcitonin synthesized in the C cell of the thyroid that comprises 116 amino acid residues with a molecular weight of approximately 13 kDa.³ In 1993, it became popular after Assicot revealed a positive correlation with a bacterial infection.⁴ Following bacterial endotoxin invasion, the PCT begins to rise as early as 4 h, peaks at 6 h, and plateaus between 8–24 h before it declines.^{5,6} The average serum concentration is typically kept below 0.1 ng/ml.⁷ However, the level may be elevated as it is also produced by other tissues such as the lung and intestine in response to systemic inflammation, particularly bacterial infection. The cut-off PCT value commonly used worldwide to guide antibiotic duration in ICU is 0.5 ng/ml.⁸ However, the sensitivity and specificity of PCT vary at different cut-off values. The overall sensitivity is 76%, and specificity is 69% at the cut-off value of 0.5 ng/ml.⁹ The PCT level of less than 0.1 ng/ml demonstrates a 96% negative predictive value for bacterial infection.¹⁰

In 2009, the first PCT assay was developed based on manual immunochemistry methods (Brahms PCT LIA), which was later replaced with fully automated immunochemistry methods (Brahms Kryptor, Brahms LIAISON, Olympus SphereLighr 180).¹¹ Since then, PCT assay has become a routine method in most central laboratories.^{12–15} This assay is then further improved to be used on an integrated immunochemistry analyzer family such as Roche Elecsys®, Cobas, and the Roche Modular E170 systems. Nonetheless, there is a potential delay in measuring PCT when many processes need to be carried out before sending a sample to the laboratory. Furthermore, laboratory measurement needs to be

analyzed by batch for cost-effectiveness. Therefore, point-of-care (POC) testing carries a vital role in overcoming this delay issue.

The POC procalcitonin test kit is a good alternative. A single-arm clinical trial which included 253 subjects, reported a PCT-guided strategy with rapid POC testing that safely allowed selection of empirical narrow-spectrum antibiotics in outpatients with CAP.¹⁶ Many PCT detection kits have been designed for clinical application, such as kits that work on the principle of chemiluminescence immunoassays (CLIA), time-resolved immunofluoroassay (TRFIA), enzyme-linked fluorescent assays (ELISA) and immunochromatographic tests (ICT).¹⁷ Access to rapid diagnostic information is a core value of POC technology.

Analytical and diagnostic performance is variable among the various POC PCT test kits. In 2021, a study found that only the AQT90 FLEX (Radiometer Medical, Denmark) POC PCT immunoassay analyzer was comparable in terms of performance to the Cobas e411 platform (Roche Diagnostics, Germany).¹⁸ From the same study, the analytical and diagnostic performance of the Finecare™ (Wondfo, China) PCT test kit was unsatisfactory. However, the sample population of this study did not include septic patients admitted to the intensive care unit.

We compared the agreement between the Finecare™ (Wondfo, China) POC PCT and automated Elecsys® BRAHMS PCT assay on the Cobas e411 platform (Roche Diagnostics, Germany) in this study.

2. METHODOLOGY

This is a parallel comparative observational study conducted in the ICU of Hospital Universiti Sains Malaysia. The study received approval from the local ethics committee with the code USM/JEPeM/21030239. The objective of the study was to investigate whole blood samples using the Finecare™ PCT method. A total of 40 samples were included in the analysis, and all samples were processed within 30 min.

The sample size requirement for this study was calculated using the *blandPower* package in R software version 4.0.3. A previous study indicated that the mean difference between the two methods of PCT measurements was 0.38 (Liaison vs BRAHMS™ PCT

sensitive KRYPTOR™), and the standard deviation of the differences was calculated to be 2.30.²² Based on the calculation, this study would require 32 samples to achieve a power of 80% at 5% Type I error and a 7-unit maximum allowed difference between the methods (the clinical agreement limit). Anticipating 20% dropout due to pre-analytical errors, the corrected sample size was 40 samples.

The similar whole blood samples were centrifuged within 24–48 h to generate plasma for comparison with a laboratory reference immunoassay. The laboratory reference immunoassay used in this study was the automated Elecsys® BRAHMS PCT assay, which was performed on the Cobas e411 platform. All measurements were conducted over a period of 3 months, specifically from January to March 2022.

In this study, arterial blood samples were withdrawn from the arterial line of sepsis patients and immediately tested using the POC PCT located in the ICU. Any remaining blood from the sample was stored in a refrigerator at temperatures between 2–8 °C, while awaiting centrifuging and further testing on the Cobas e411 platform.

The samples were centrifuged in the laboratory at a speed of 3200 rpm for a duration of 10 min.

The POC PCT rapid quantitative test utilizes fluorescence immunoassay technology, employing a sandwich immunodetection method. When a blood, serum, or plasma sample is added to the sample well of the test cartridge, the fluorescence-labelled detector PCT antibodies on the sample pad bind to PCT antigens present in the specimen, forming immune complexes.

As the immune complexes migrate through the nitrocellulose matrix of the test strip via capillary action, they are captured by PCT antibodies that have been immobilized on the test strip. Consequently, the more PCT antigens present in the blood specimen, the greater the accumulation of complexes on the test strip. The fluorescence signal intensity of the detector antibodies is indicative of the amount of captured PCT. The Finecare™ FIA Meter machine processes the data and provides the PCT concentration in the blood specimen.

The default result unit of the Finecare™ PCT Rapid Test displayed on the Finecare™ FIA Meter is XXX ng/mL. The manufacturer has reported a working range of 0.1–100 ng/mL and a detection limit of 0.1 ng/mL. A value below 0.1 ng/mL is considered within the normal range.

Interpretation of the results is as follows:

- A value between 0.1–0.5 ng/mL suggests a partial bacterial infection or viral infection.

- A value of 0.5–2.0 ng/mL indicates a positive result for the diagnosis of a bacterial infection.
- Levels ranging from 2.0–10.0 ng/mL indicate a systemic infection and a high risk of severe systemic infection.
- A level > 10 ng/mL is considered indicative of severe systemic infection.

It's important to note that these interpretation ranges are provided based on the information given, but the actual clinical interpretation may vary and should be done by a qualified healthcare professional.

Statistical analysis

The descriptive statistics of the patients were analyzed based on various factors including age, gender, race, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, total white cell count (TWC), and CRP. PCT levels were measured using the Finecare™ assay, as well as using the BRAHMS assay. The paired t-test helps assess whether there is a meaningful difference between two related measurements taken on the same individuals.

A scatter plot was constructed to visualize the linear relationship between the two paired measurements. Pearson correlation analysis was implemented to determine the direction and strength of the linear relationship between the two measurements. The correlation coefficient can range from -1 to 1, where a value close to 1 indicates a strong positive correlation, close to -1 indicates a strong negative correlation, and close to 0 indicates no linear correlation. A correlation coefficient (r) was then calculated. Linear regression was plotted to define the degree to which the data fit into a linear regression model. The coefficient of determination (r^2) was then measured from the linear regression.

Regression analysis, Deming regression was performed as an alternate way of calculating regression statistics. Deming regression was the preferred tool as errors were allowed to occur in both methods in proportion to the variances of the methods. Passing & Bablok regression analysis was carried out to describe a linear regression of the data with no particular assumptions on the sample distribution and the measurement errors. The Bland-Altman method was used to plot the differences, ratios, or percentages between the two PCT measurement techniques. The data were analyzed using R software.

3. RESULTS

A total of 40 blood samples of critically ill sepsis patients were collected for this study. The mean age of the population was 46.83 y. Thirty-two subjects (80%) were male, and the remaining eight (20%) were female. The majority were Malay (92.5%), and the rest were Indians (7.5%). Kelantan is a state in Malaysia with the majority of the population consisting of Malay (96%) ethnic origin. The mean total white cell (TWC) was 14.12 mmol/L, and the mean CRP was 105.00 mmol/L. In addition, the mean APACHE score measured was 14.53; whereas the mean SOFA score was 7.55.

Paired sample t-test revealed that the mean difference between the two sets of data points was zero with a $P = 0.92$ (Table 2). It meant that there was statistically no significant difference between the data points observed from the two comparison methods.

A scatterplot constructed showed a linear relationship between the data points. The coefficient of determination calculated was high, 0.92. Pearson correlation coefficient was 0.96 (Figure 1). These measurements showed a positive correlation between Finecare™ point of care and automated Eleccys® BRAHMS PCT assay.

In regard to regression analysis, all simple, Deming and Passing-Bablok regression (Figures 2 and 3) illustrated a good correlation between the Roche laboratory automated immunoassay and the Finecare™ PCT rapid quantitative test kit (95% CI for the slope included value of 1). Out of these analyses, the Passing-Bablok regression line indicated a much better agreement as compared to the simple and Deming regression lines. Furthermore, the Passing-Bablok line was intercepted at an even lower value of 0.218 ng/mL (Table 3). This intercept indicated systematic bias (difference) between the two methods.

The intraclass correlation coefficient indicates that there was an excellent reliability between the two measurement methods ($ICC = 0.979$, 95% CI 0.962–0.989). Last but not least, the Bland-Altman analysis further confirmed this good agreement as the plot (Figure 3) showed that most data points lay within the 95% confidence interval limits for the average

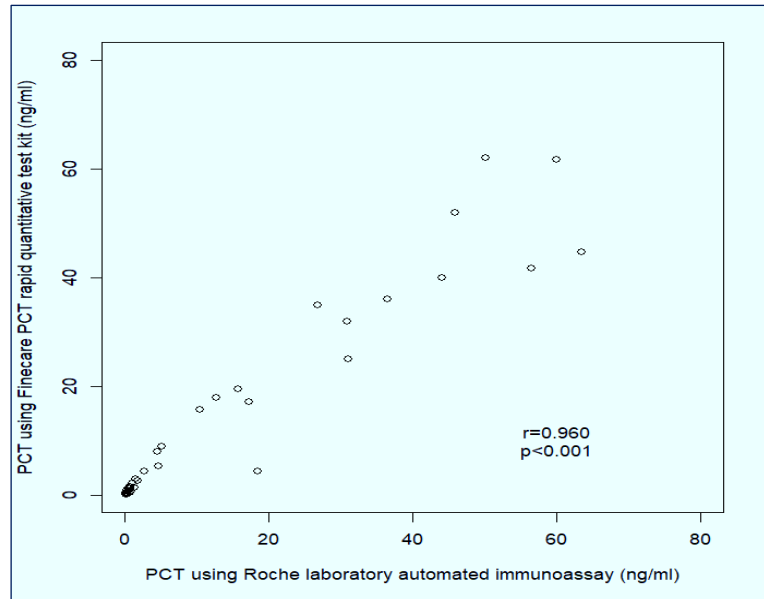


Figure 1: A scatter plot visualizes linear relationship between the two paired measurements.

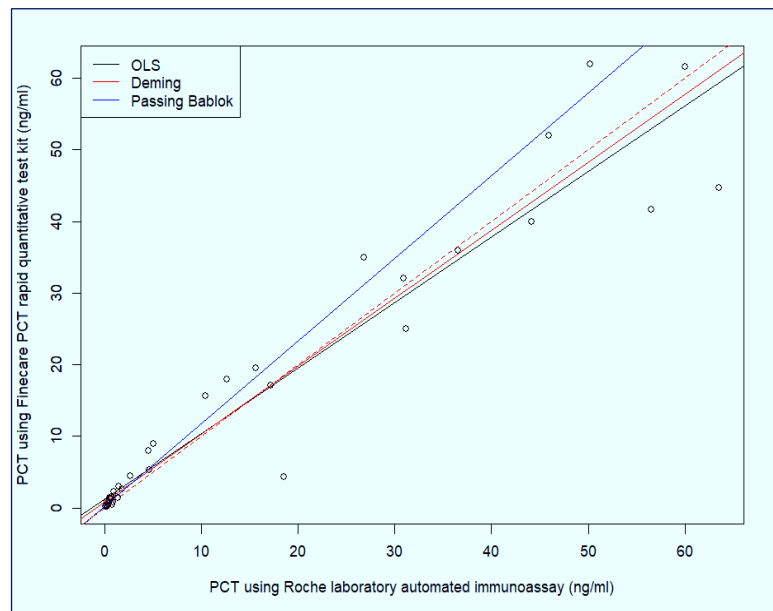


Figure 2: Ordinary Least Square, Deming & Passing-Bablok Regression lines of Finecare versus Cobas

difference. A good correlation and agreement were exhibited from these regression analyses.

4. DISCUSSION

There is a growing use of the PCT level as the key biomarker in managing sepsis. Many shreds of evidence have supported this practice. The combination of PCT, Systemic Inflammatory Response Syndrome (SIRS), or

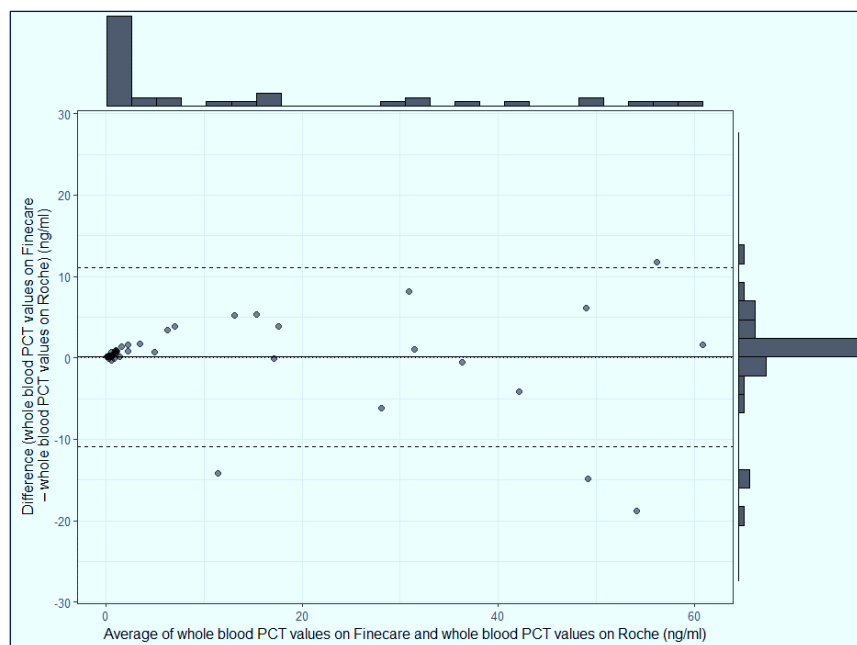


Figure 3: Bland-Altman analysis of PCT results in whole blood of Finecare versus Cobas

quick Sequential Organ Failure Assessment (qSOFA) score with Mid-regional proadrenomedullin (MR-proADM) results in a diagnostic and prognostic evaluation for 99.9% of patients. This evaluation can be performed with a turnaround time of approximately 45 min, compared to 90 min without PCT measurement.¹⁹

Table 1: Patient demographics (n = 40)

Variables	Mean (SD) / n (%)
Age (y) ^a	46.83 ± 19.16
Gender	
• Male	32 (80%)
• Female	8 (20%)
Race	
• Malay	37 (92.5%)
• India	3 (7.5%)
SOFA ^a	7.30 ± 4.47
APACHE 11 ^a	13.93 ± 7.03
TWC (x 10 ⁹ /L) ^a	14.12 ± 12.37
CRP (mg/L) ^a	102.68 ± 66.88
PCT Finecare (ng/ml) ^a	13.86 ± 18.72
PCT Brahms (ng/ml) ^a	13.77 ± 19.65

SOFA= Sequential Organ Failure Assessment, APACHE II = Acute Physiology and Chronic Health Evaluation II, TWC = Total White Cell, CRP = C-Reactive Protein, PCT = Procalcitonin, ^aMean ± SD

The pathophysiology of sepsis requires unambiguous diagnostic criteria for rapid patient identification and adequate therapeutic intervention to improve the outcome of sepsis. Therefore, the application of procalcitonin as part of our practice is paramount and needs full attention of all of the clinicians.

Many clinical trials have proved the utility of PCT values in establishing sepsis diagnosis and antibiotic choice. There is a rapid growth of the commercial models of different types of immunoassays to be implemented in the clinical setting. The novel POC PCT assay on the AFIAS-6 platform is as reliable to be used as compared to the standard PCT KRYPTOR™ Compact Plus assay.²⁰ The ABSOGEN POC

PCT kit manufactured in Suwon, Korea, and the standard Roche Modular E170 also revealed the POC test kit's high accuracy.²¹

Aside from linearity and precision which was not performed in this study, we assessed the relative diagnostic performance of the Finecare™ POC PCT rapid quantitative test kit by comparing it to a reference PCT assay in the clinical laboratory, i.e., the automated Roche Elec PCT assay on the Cobas e411 platform (Roche Diagnostics, Germany). We first assumed all results obtained with the reference method were valid and free from errors for this comparison. Consequently, any conclusion from these analyses is based on assumptions.

To date, we yet to have any single PCT measuring method to be regarded as the gold standard. Automated Roche Elec PCT assay on the Cobas e411 platform (Roche Diagnostics, Germany) was used as reference immunoassay since it is readily available in our central laboratory and its performance has been fully established.¹⁸ In addition, a multicenter study was done in Italy which compared results of BRAHMS™ PCT sensitive KRYPTOR™ with those obtained using four BRAHMS-partnered PCT automated immunoassays (Roche Cobas e601, DiaSorin Liaison, BioMerieux Vidas, and Siemens Advia Centaur) which can be used as reference immunoassay.²²

Table 2: Comparison of PCT measurement by Finecare PCT rapid quantitative test kit and Roche laboratory automated immunoassay using paired sample t-test (n=40).

Method	PCT measurement (Mean ± SD) (ng/ml)	Mean difference (95% CI)	t (df)	P-value
Finecare PCT rapid quantitative test kit	13.86 ± 18.72	0.090 (-1.67–1.85)	0.10 (39)	0.918
Roche laboratory automated immunoassay	13.77 ± 19.65			

Table 3: OLS, Deming, and Passing Bablok Regression with “Best Fit” expression between Finecare and Cobas.

Regression method	Intercept (95% CI)	Slope (95% CI)
OLS regression	1.27 (-0.75–3.29)	0.91 (0.83–1.00)
Deming Regression	0.77 (-0.44–1.85)	0.95 (0.80–1.10)
Passing Bablok regression	0.22 (0.08–0.58)	1.16 (0.99–1.36)

The Liaison BRAHMS PCT assay showed excellent concordance with the LUMitest PCT, with a mean bias and 95% confidence interval (CI) of 0.38 ng/mL (-0.08–0.83 ng/mL) in one study. Another comparison between the Liaison BRAHMS PCT assay and the Cobas C501 revealed a mean bias and 95% CI of -0.88 ng/mL (-1.35–-0.40 ng/mL). Additionally, a comparison between the KRYPTOR™ and VIDAS systems exhibited a mean bias of 0.108 ng/mL (-0.044–0.260 ng/mL) based on a Bland-Altman plot analysis.

In the comparison between the BRAHMS™ PCT sensitive KRYPTOR™ PCT assay performed on the Roche Cobas e411 and the Finecare™ FIA meter, the study reported a mean bias of -0.021 ng/mL (-0.053–0.015 ng/mL). These results provide information about the level of agreement or discrepancy between different PCT assay methods and platforms. The mean biases and 95% confidence intervals give insights into the average differences observed between the assays, allowing for an assessment of their comparative accuracy and reliability.

In this study, the comparison was conducted between the BRAHMS™ PCT sensitive KRYPTOR™ assay method performed on the Roche Cobas e411 platform and the Finecare™ FIA Meter Plus (FS113). The comparison involved testing whole blood samples using the Finecare™ FIA Meter Plus and plasma samples (obtained by centrifuging the previous whole blood samples) using the Cobas e411. The results of the comparison revealed a mean bias of 0.22 ng/mL, with a 95% confidence interval ranging from 0.08–0.58 ng/mL. The purpose of comparing whole blood and plasma samples was to assess the practicality of bedside POC testing for PCT. This option was considered for

clinicians who do not have access to centrifugal machines in their ICU. By demonstrating that the accuracy of the POC PCT testing performed on the Finecare™ FIA Meter Plus (FS113) was similar to that of previous studies, our study established the reliability of using this POC method for PCT measurements.^{18,22,23,25}

Regarding precision, the manufacturer claims that the Finecare™ PCT test kit has a coefficient of variation (CV) of less than 15%. This is found to be true, as proven by a study done in Shanghai, China.¹⁸ The study reported a coefficient of variation (CV) of 8.7% at a clinical value of 0.5 ng/mL PCT. The CV was even higher at 5.25% when the sample was obtained from whole blood.¹⁸ At a higher cutoff level of PCT value (2.0 ng/mL), the precision ranges between 811% in plasma samples and 510% for whole blood samples.¹⁸ This study supported that the Finecare™ PCT test has acceptable precision coefficient of variation. However, the trial failed to prove a good correlation between the Finecare™ PCT test kit and the standard laboratory method using the Cobas e411 platform. In our study the precision and linearity between the whole blood samples POC PCT and reference immunoassay was not performed in view of the Roche Cobas e411 machine inability to analyze the whole blood sample. The machine only can process sample from the plasma or serum. Therefore, the whole blood POC PCT comparison with reference immunoassay was not performed.

Overall, our study shows that the Finecare™ PCT rapid quantitative test kit has a good agreement or correlation with the standard laboratory automated immunoassay using the Cobas platform. This is contrary to the trial's finding conducted in Shanghai, as mentioned earlier.¹⁸ This may be affected by the study population where we included only septic patients, whereas the trial in Shanghai recruited random patients with variable levels of PCT. Our study initiates the first step in establishing the reliability of utilizing this kit in the clinical setting. In a nutshell, the observations above depict the Finecare™ PCT rapid test kit as an excellent tool to be

applied in our clinical setting as it has a perfect correlation or concordance with our current central laboratory method. As emphasized earlier, POC technology will ease the process of getting the PCT results as rapidly as possible. Apart from being more cost-effective, it is also portable and does not consume ample space to be placed in the critical care setting or hospital emergency unit.

5. LIMITATIONS

Our study was just an agreement or correlation study. More studies need to be performed soon to investigate further the precision, linearity, assay range, cross-reactivity and detection limit of the Finecare™ PCT rapid test kit. The other limitation is the comparison is between the whole and plasma sample. However, this comparison is practically useful since the bedside test usually will be performed in ICU using whole blood. Nevertheless, our study manages to explore the accuracy of this test kit by demonstrating a good correlation with commercially available laboratory automated immunoassay.

6. CONCLUSION

In comparison to the automated Roche Elec PCT assay on the Cobas e411 platform (Roche Diagnostics, Germany), the Finecare™ PCT performed on Finecare™ FIA Meter Plus (FS113) offers a good alternative for procalcitonin measurement among critically ill patients. On the basis of our data, the Finecare™ point of care PCT test kit reveal good agreement and concordance with the standard central laboratory method.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

We gratefully thank the hospital director, the Chemical Pathology Department, Biostatistics and Research Methodology Department, and all ward staff for their methodological and biostatistical support and scientific writing assistance in this study.

9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

MAI: Manuscript writing

MZM, SKH: Manuscript editing

WNA, TSK: Laboratory work

NMY: Statistical analysis

MO, NANM: Literature search

11. REFERENCES

- De Backer D, Dorman T. Surviving sepsis guidelines: a continuous move toward better care of patients with sepsis. *JAMA*. 2017;317(8):807-8. [PubMed] DOI: [10.1001/jama.2017.0059](https://doi.org/10.1001/jama.2017.0059)
- Ebihara Y, Kobayashi K, Ishida A, Maeda T, Takahashi N, Taji Y, et al. Diagnostic performance of procalcitonin, presepsin, and C-reactive protein in patients with hematological malignancies. *J Clin Lab Anal*. 2017;31(6):e22147. [PubMed] DOI: [10.1002/jcla.22147](https://doi.org/10.1002/jcla.22147)
- Le Moullec JM, Jullienne A, Chenais J, Lasmoles F, Guliana JM, Milhaud G, et al. The complete sequence of human preprocalcitonin. *FEBS Lett*. 1984;167(1):93-7. [PubMed] DOI: [10.1016/0014-5793\(84\)80839-x](https://doi.org/10.1016/0014-5793(84)80839-x)
- Assicot M, Bohuon C, Gendrel D, Raymond J, Carsin H, Guilbaud J. High serum procalcitonin concentrations in patients with sepsis and infection. *Lancet*. 1993;341(8844):515-8. [PubMed] DOI: [10.1016/0140-6736\(93\)90277-n](https://doi.org/10.1016/0140-6736(93)90277-n)
- Dandona P, Nix D, Wilson MF, Aljada A, Love J, Assicot M, et al. Procalcitonin increase after endotoxin injection in normal subjects. *J Clin Endocrinol Metab*. 1994;79(6):1605-8. [PubMed] DOI: [10.1210/jcem.79.6.7989463](https://doi.org/10.1210/jcem.79.6.7989463)
- Brunkhorst FM, Heinz U, Forycki ZF. Kinetics of procalcitonin in iatrogenic sepsis. *Intensive Care Med*. 1998; 24(8):888-9. [PubMed] DOI: [10.1007/s001340050683](https://doi.org/10.1007/s001340050683)
- Müller B, White JC, Nylén ES, Snider RH, Becker KL, Habener JF. Ubiquitous expression of the calcitonin-i gene in multiple tissues in response to sepsis. *J Clin Endocrinol Metab*. 2001;86(1):396-404. [PubMed] DOI: [10.1210/jcem.86.1.7089](https://doi.org/10.1210/jcem.86.1.7089)
- Bouadma L, Luyt CE, Tubach F, Cracco C, Alvarez A, Schwebel C, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomized control trial. *Lancet*. 2010;375(9713):463-74. [PubMed] DOI: [10.1016/S0140-6736\(09\)61879-1](https://doi.org/10.1016/S0140-6736(09)61879-1)
- Hoeboer SH, van der Geest PJ, Nieboer D, Groeneveld AJ. The diagnostic accuracy of procalcitonin for bacteraemia: a systematic review and meta-analysis. *Clin Microbiol Infect*. 2015;21(5):474-81. [PubMed] DOI: [10.1016/j.cmi.2014.12.026](https://doi.org/10.1016/j.cmi.2014.12.026)
- Lippi G, Sanchis-Gomar F. Procalcitonin in inflammatory bowel disease: Drawbacks and opportunities. *World J Gastroenterol*. 2017;23(47):8283-90. [PubMed] DOI: [10.3748/wjg.v23.i47.8283](https://doi.org/10.3748/wjg.v23.i47.8283)
- de Wolf HK, Gunnewiek JK, Berk Y, van den Ouweland J, de Metz M. Comparison of a new procalcitonin assay from roche with the established method on the brahms kryptor. *Clin Chem*. 2009;55(5):1043-4. [PubMed] DOI: [10.1373/clinchem.2008.117655](https://doi.org/10.1373/clinchem.2008.117655)
- Dupuy AM, Chevrier Q, Olejnik Y, Bargnoux AS, Badiou S, Cristol JP. Analytical evaluation of point-of-care procalcitonin (PCT) and clinical performances in an unselected population as compared with central lab PCT assay. *Clin Chem Lab Med*. 2017; 55(8): e167-71. [PubMed] DOI: [10.1515/cclm-2016-0887](https://doi.org/10.1515/cclm-2016-0887)
- Dupuy AM, Bargnoux AS, Andreeva A, Zins C, Kuster N, Badiou S, et al. Analytical performances of a novel point-of-care procalcitonin assay. *Pract Lab Med*. 2019;18:e00145. [PubMed] DOI: [10.1016/j.plabm.2019.e00145](https://doi.org/10.1016/j.plabm.2019.e00145)

2. Dupuy AM, Bargnoux AS, Larcher R, Merindol A, Masetto T, Badiou S, et al. Bioanalytical performance of a new particle-enhanced method for measuring procalcitonin. *Diagnostics (Basel)*. 2020;10(7):461. [PubMed] DOI: [10.3390/diagnostics10070461](https://doi.org/10.3390/diagnostics10070461)
12. Lippi G, Salvagno GL, Gelati M, Pucci M, Demonte D, Faggian D, et al. Analytical evaluation of the new Beckman Coulter access procalcitonin (PCT) chemiluminescent immunoassay. *Diagnostics*. 2020;10(3):128. [PubMed] DOI: [10.3390/diagnostics10030128](https://doi.org/10.3390/diagnostics10030128)
13. Masiá M, Padilla S, Ortiz de la Tabla V, González M, Bas C, Gutiérrez F. Procalcitonin for selecting the antibiotic regimen in outpatients with low-risk community-acquired pneumonia using a rapid point-of-care testing: A single-arm clinical trial. *PLoS One*. 2017;12(4):e0175634. [PubMed] DOI: [10.1371/journal.pone.0175634](https://doi.org/10.1371/journal.pone.0175634)
14. Shao XY, Wang CR, Xie CM, Wang XG, Liang RL, Xu WW. Rapid and sensitive lateral flow immunoassay method for procalcitonin (PCT) based on time-resolved immunochromatography. *Sensors*. 2017;17(3):480. [PubMed] DOI: [10.3390/s17030480](https://doi.org/10.3390/s17030480)
15. Li C, Huang Y, Xu Y. Determining procalcitonin at point-of-care; A method comparison study of four commercial PCT assays. *Pract Lab Med*. 2021;25:e00214. [PubMed] DOI: [10.1016/j.plabm.2021.e00214](https://doi.org/10.1016/j.plabm.2021.e00214)
16. Spoto S, Nobile E, Carnà EP, Fogolari M, Caputo D, De Florio L, et al. Best diagnostic accuracy of sepsis combining SIRS criteria or qSOFA score with Procalcitonin and Mid-Regional pro-Adrenomedullin outside ICU. *Sci Rep*. 2020;10(1):16605. [PubMed] DOI: [10.1038/s41598-020-73676-y](https://doi.org/10.1038/s41598-020-73676-y)
17. Dupuy AM, Bargnoux AS, Andreeva A, Zins C, Kuster N, Badiou S, et al. Analytical performances of a novel point-of-care procalcitonin assay. *Pract Lab Med*. 2019;18:e00145. [PubMed] DOI: [10.1016/j.plabm.2019.e00145](https://doi.org/10.1016/j.plabm.2019.e00145)
18. Kwon HJ, Lee J, Park HI, Han K. Evaluation of a novel point-of-care test kit, ABSOGEN™ PCT, in semi-quantitative measurement of procalcitonin in whole blood. *J Clin Lab Anal*. 2017;31(6):e22111. [PubMed] DOI: [10.1002/jcla.22111](https://doi.org/10.1002/jcla.22111)
19. Dipalo M, Guido L, Micca G, Pittalis S, Locatelli M, Motta A, et al. Multicenter comparison of automated procalcitonin immunoassays. *Pract Lab Med*. 2015;2:22–28. [PubMed] DOI: [10.1016/j.plabm.2015.07.001](https://doi.org/10.1016/j.plabm.2015.07.001)
20. Hubl W, Krassler J, Zingler C, Pertschy A, Hentschel J, Gerhards-Reich C, et al. Evaluation of a fully automated procalcitonin chemiluminescence immunoassay. *Clin Lab*. 2003;49(78):31927. [PubMed]
21. de Wolf HK, Gunnewiek JK, Berk Y, van den Ouweland J, de Metz M. Comparison of a new procalcitonin assay from roche with the established method on the brahms kryptor. *Clin Chem*. 2009;55(5):1043-4. [PubMed] DOI: [10.1373/clinchem.2008.117655](https://doi.org/10.1373/clinchem.2008.117655)
22. Hausfater P, Brochet C, Freund Y, Charles V, Bernard M. Procalcitonin measurement in routine emergency medicine practice: comparison between two immunoassays. *Clin Chem Lab Med*. 2010;48(4):501-4. [PubMed] DOI: [10.1515/CCLM.2010.091](https://doi.org/10.1515/CCLM.2010.091)