VALIDATION OF POINT OF CARE C-REACTIVE PROTEIN (CRP) TESTING IN AN ADULT CRITICAL CARE UNIT IN A JOHANNESBURG ACADEMIC HOSPITAL

Final submission for Master of Medicine in Emergency Medicine

Dr Anzanne du Preez (MBChB)

Student no: 2500975

Supervisors:

Dr Radha Gihwala

Dr Ming-Tung Wu

Professor Mervyn Mer

Title:

Validation of Point-of-Care C-reactive protein (CRP) Testing in an Adult Critical Care Unit at a Johannesburg Academic Hospital.

Abstract:

Introduction: CRP is a widely used biomarker for detecting infection and inflammation, and it may aid in antimicrobial stewardship. Rapid point-of-care (POC) CRP testing can support timely decisions in resource-constrained, high-acuity environments, such as critical care.

Methods: This prospective, single-centre study was conducted in the ICU of Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) from September 2023 to April 2024. A total of 110 adult patients were enrolled through convenience sampling. Paired central or arterial blood samples were tested using both the Afinion™ 2 POC device and standard laboratory methods (Roche Cobas™). Data collected included CRP levels and relevant clinical variables. Ethics approval was obtained.

Results: Sixty-two valid POC CRP results were analysed. The median CRP was 90 mg/l (POC) vs. to 120 mg/l (laboratory). The POC test demonstrated 100% sensitivity for CRP >10 mg/l, and 100% sensitivity with 92.5% specificity for CRP >100 mg/l. A strong correlation was observed between POC and laboratory results ($r = 0.97$; 95% CI: 0.96–0.97; $p < 0.0001$). Bland-Altman analysis showed acceptable mean differences (–25.4 to 33.9 mg/l). The median time to result was significantly shorter for POC (4 minutes) compared to laboratory testing (5.5 hours; $p < 0.001$).

Conclusion: The Afinion 2 POC CRP test provides reliable and rapid results, supporting its integration into critical care workflows to improve clinical decision-making and promote responsible antimicrobial use.

Contribution: The study substantiates the clinical utility of the Afinion™ 2 POC CRP test as a dependable, swift, and pragmatic instrument for application in critical care. It emphasises the potential of POC CRP testing to improve patient outcomes, optimise workflows, and encourage judicious antibiotic utilisation, all of which are essential for the advancement of healthcare delivery.

Keywords: Point of care testing (POCT), C-reactive protein (CRP), Intensive care unit (ICU), antimicrobial stewardship

Introduction:

Accurate and timely measurement of C-reactive protein (CRP) is crucial for effective diagnosis, prognosis, and patient management (1,2). Recent studies have emphasised the potential use of point-of-care (POC) CRP testing as a quick and convenient alternative to standard laboratory-based measurements (3,4). However, the comparative accuracy of these methods remains an ongoing question (5).

CRP is a protein produced by the liver that plays a crucial role in the body's inflammatory and immune responses (1). Its levels rise within 6 hours of tissue injury or infection, peak at around 36 hours, and have a half-life of about 19 hours (1). Monitoring CRP levels can provide insight into disease severity and help track recovery, as levels tend to drop rapidly once the underlying disease process is addressed (2). Typically, CRP levels are below 10 mg/L; however, readings above 100 mg/L may indicate severe inflammation and suggest the need for antibiotics (3,4).

Since its discovery in 1930, CRP has become a cornerstone of clinical practice, serving multiple functions, including screening and monitoring disease activity and supporting diagnostic decisions (1). Its prevalent use in healthcare results from its accessibility, simplicity, ease of interpretation, and cost-effectiveness (5). In critical care settings, CRP serves as a valuable biomarker for detecting and monitoring inflammation in conditions such as acute respiratory distress syndrome and pancreatitis, as well as for detecting infections and evaluating the effectiveness of treatments, especially antibiotic therapy (6,7). It also plays a vital role in prognostication and risk stratification (8).

Antibiotics are administered to approximately 71% of patients in Intensive Care Units (ICU) worldwide; however, the overuse of these medications has led to antimicrobial resistance (AMR), posing a significant global health challenge (8–11). Although physicians often initiate antibiotics based on clinical judgment, their decisions must be guided in conjunction with imaging and laboratory test results (12). Research has shown that stopping antibiotics based on CRP or Procalcitonin (PCT) levels can shorten treatment durations without raising the risk of death or recurrence (6,13). Unfortunately, access to PCT testing is often limited and expensive in many low- and middle-income regions (13).

At Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), continuous monitoring of ICU patients is the standard practice. Clinical assessments, imaging, and biomarkers guide treatment decisions, but daily blood tests sent to the laboratory may take several hours to return results. These delays can impede timely clinical decision-making and negatively impact patient care.

Effective patient management relies heavily on laboratory data, with about 70% of clinical decisions based on test outcomes (14). POC CRP testing can deliver rapid, actionable results, which help clinicians make quicker, more informed decisions that can improve patient care (15). Unlike conventional laboratory tests, POC CRP tests can be performed by healthcare providers or nurses without specialised equipment (16), and recent advancements allow for results in minutes that are as accurate as traditional laboratory methods (4,5). POC CRP testing is becoming more common in emergency and primary care settings, enhancing diagnosis and treatment (4).

The Afinion™ AS100, the predecessor to the Afinion™ 2, has been evaluated in various contexts, including primary care and paediatric populations, demonstrating its user-friendly nature. It requires minimal handling and generally provides better accuracy than other POC testing devices (10,17–19).

Despite the increased use of POC CRP devices in primary and emergency care, validation of these devices for the ICU patient population has been limited. This study aims to assess the performance of the Afinion™ 2 against the standard Roche Cobas™ method used by the National Health Laboratory Service (NHLS) for adult ICU patients at CMJAH.

Methods:

Study design and setting: This was a single-centre, prospective, comparative diagnostic study conducted in the multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a tertiary academic hospital in Parktown, Johannesburg.

Ethics: The study received ethical approval from the Human Research Ethics Committee of the University of the Witwatersrand (M230387) and adhered to the Declaration of Helsinki and relevant institutional guidelines. Permission to use laboratory data was granted by the NHLS. Written informed consent was obtained from all participants or their legal representatives.

Confidentiality was strictly maintained by using only hospital numbers for identification, and all data were stored on a password-protected computer to ensure data security.

Study Population and Sampling Strategy: This study involved a convenience sample of 110 adult ICU patients enrolled between September 18, 2023, and April 15, 2024. Participants were selected based on the availability of the principal investigator and the POC cartridges. The study extended beyond its initial timeline to achieve the designated sample size, which was calculated using Cochran's formula based on the average ICU admission rates over a three-month interval. This extension was undertaken to ensure sufficient statistical power and adequate representation of the population.

Inclusion and Exclusion Criteria: All adult patients (aged 18 years or older) admitted to the ICU during the study period were eligible for inclusion. Exclusion criteria included patients under the age of 18, those who did not provide adequate consent for blood sampling, and instances when either the principal investigator or POC testing cartridges were unavailable.

Data collection: Data regarding ICU admission, patient demographics, and CRP measurements from POCT and laboratory sources were collected. Additional information potentially affecting CRP values, which included steroid and antimicrobial use, recent surgery, and Renal replacement therapy (RRT) requirements. Information was collected on a pre-designed structured data collection sheet. The principal investigator, a qualified medical doctor working in the unit, collected all data.

Sample collection: Paired samples were obtained from indwelling arterial lines or central venous catheters. The initial 5 mL of blood was discarded to eliminate any contamination or tissue fluid that may affect test results. After that, 4 ml was collected into a lithium-heparin tube (green top) and an additional 4 ml into a gel clot-activated tube (yellow top), per ISO 15189 laboratory specifications at the NHLS central laboratory.

- **Laboratory CRP testing:**

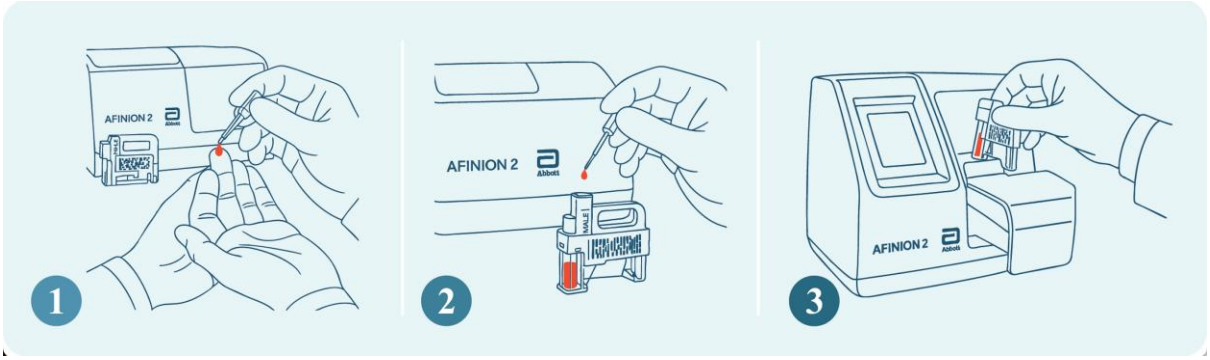
A laboratory messenger gathered samples from the ICU and submitted specimens to the laboratory reception, where the samples were duly recorded and appropriately allocated to the chemical pathology department for analysis. The laboratory conducted CRP measurements using serum, performed by trained technologists at the NHLS employing the Roche Cobas™ analyser, which utilizes particle-enhanced immunological agglutination to achieve a quantitative outcome. Dilutions were executed per laboratory protocol. The analytical laboratory's CRP reference range is <1 to 350 mg/l. The results were made accessible on the national health database, Trackcare. These laboratory CRP results were utilised for therapeutic decision-making within the ICU.

- **POC CRP testing:**

The Afinion™ 2 analyser was positioned in the ICU POC room and was secured with a password to maintain patient confidentiality and restrict access exclusively to the principal investigator. Hospital-assigned identification numbers were entered into the analyser to facilitate results tracking. Testing kits were stored in a temperature-controlled environment and allowed to acclimate to room temperature before each test, as specified by the product. Whole blood specimens utilized during testing were collected from the heparinised sample. The Afinion™ 2 employs a solid-phase immunochemical assay for its analysis, producing a quantitative result within the analytical reference range of <5 to 200 mg/l. Dilutions were not executed for results exceeding this range. All samples were tested within 15 minutes of collection by the principal investigator, who possesses the required training for operating the analyser. The controlled testing was executed in alignment with the manufacturer's recommendations. The treating clinician did not have access to the CRP POCT results. The analyser was

calibrated, and Obsidian representatives performed quality control tests throughout the study period to ensure measurement accuracy.

The Afinion™ 2 POC testing procedure consists of three simple steps (see Figure 1). It requires 2.5 µL of blood and provides CRP results in four minutes.



1. Blood sample collection (capillary or whole blood);
2. Using the self-contained capillary tube within the test cartridge to collect the blood;
3. The test cartridge is inserted into the analyser and is awaiting the result.

Figure 1: The POC testing process

Study objectives: To test the agreement between the POC CRP and the laboratory CRP. To test the accuracy of the POCT CRP. To evaluate the sensitivity and specificity of predicting a laboratory CRP value at three different thresholds (> 10 mg/l, > 100 mg/l, and > 150 mg/l) using the POCT CRP values. To compare the theoretical turnaround time for CRP results between laboratory and POCT methods.

Data analysis:

Data was electronically captured and analysed using IBM SPSS version 30 (20). Descriptive statistics were calculated for all variables, including the mean, median and interquartile ranges. Statistical significance was determined with a p-value of < 0.05. The agreement between the two measurement methods was assessed using a Bland-Altman plot and Cohen's Kappa. The Pearson correlation coefficient was calculated to evaluate the relationship between the variables. Sensitivity, specificity, and predictive values were calculated and presented as percentages, along with a 95% Confidence Interval (95% CI). Diagnostic categories are expressed through means, medians, and percentages. A Wilcoxon signed-rank test was employed to compare CRP results across various diagnostic categories. Time comparison analyses were performed using the paired t-test.

Results:

During the study, 62 POC CRP tests produced quantitative results (values within the range of 5– 200 mg/l) and met the criteria for analysis. Each laboratory CRP test generated an individual result. A CRP value exceeding 10 mg/L was considered a positive result for both assessments. Refer to the study flow diagram (Figure 2).

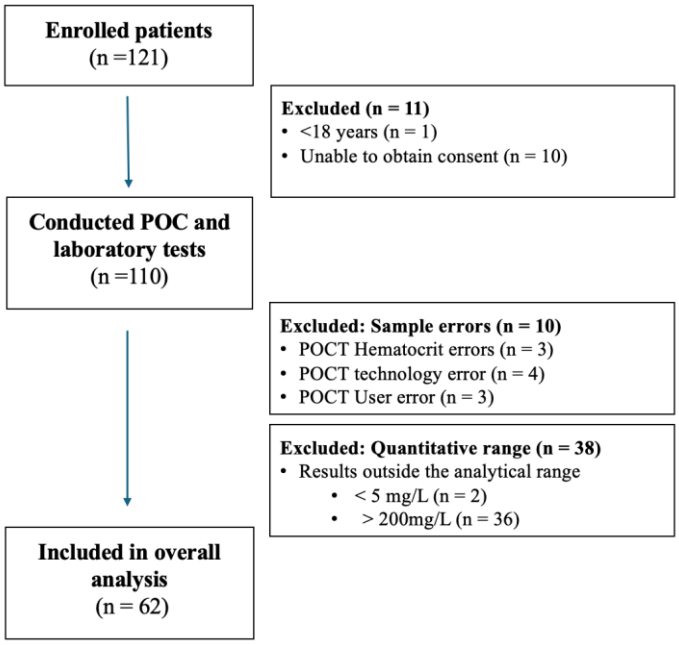


Figure 2: Study flow diagram

The baseline characteristics are provided in Table 1.

Table 1: Baseline characteristics

Variable	n (%)	Median	Interquartile range (IQR)
Age (years)	62	42.5	29 – 57
Gender – Females	31/62 (50)		
BMI > 25	17/62 (27.4)		
Days in ICU	62	4	2 – 10
WCC	62	13	8.9 – 15
PCT	61/62 (98)	2.5	45.5 – 92.5
POCT CRP	62	90	56 – 133
Laboratory CRP	62	120	54 - 124
Positive blood culture	18/62 (29)		
Antimicrobial therapy	29/62 (62.9)		

Antimicrobial therapy days	62	2	0 – 4

BMI – body mass index/ WCC – white cell count/ PCT - procalcitonin

Table 2 evaluates the diagnostic and clinical categories influencing CRP values. The Wilcoxon signed-rank test was employed to determine the p-values between POCT and Laboratory CRP values across the categorical findings.

Table 2: CRP by diagnostic and clinical categories

Diagnostic category	Status	n (%)	Median POCT CRP (mg/l)	Median Laboratory CRP (mg/l)	p-value
CRP		62 (100)	90	120	0.008
HIV	Yes (+)	11/62 (17.7)	129	120	0.042
	No (-)	51/62 (82.3)	85	98	0.050
Sepsis*	Yes	34/62 (54.9)	104	88	0.015
	No	28/62 (45.1)	80	98	0.262
RRT	Yes	7/62 (11.3)	122	108	0.176
	No	55/62 (99.7)	90	112	0.022
Steroids	Yes	26/62 (41.9)	91	95	0.053
	No	36/62 (58.1)	81	89	0.055
Recent surgery	Yes	26/62 (41.9)	98	95	0.105
	No	36/62 (58.1)	82	95	0.030

HIV – Human Immunodeficiency Virus/ RRT – Renal replacement therapy

*Criteria for sepsis: Documented infection in the file, positive blood culture at the time of sample collection, elevated PCT and CRP, septic shock

Table 3 presents CRP diagnostic accuracy and predictive values at various thresholds. The accuracy of CRP levels exceeding 100 mg/l has been evaluated at 97%.

Table 3: Predictive value of POC CRP concerning different laboratory CRP thresholds.

POCT CRP	>10 mg/l % (95%CI)	>100 mg/l % (95%CI)	>150 mg/l % (95%CI)
Sensitivity	100 (96.3 – 100)	100 (94 – 100)	95,8 (85.1 – 99.5)
Specificity	100 (15.8 – 100)	92.5 (79.6 – 98.4)	98.1 (98.7 – 99.9)
PPV*	100 (96.3 – 100)	95.2 (81.7 – 98.3)	97.9 (86.8 – 99.7)
NPV**	100 (15.8 – 100)	100 (90.5 – 100)	96.2 (86.8 – 992

**PPV (Positive predictive value)/ **NPV (Negative predictive value)*

Figure 3 presents the test agreement using a Bland–Altman plot, with a 95% confidence interval for the mean difference ranging from –25.4 to 33.9. Three outliers were observed, appearing to be randomly dispersed, which likely reflects random error. No shared characteristics were identified among these outlier samples. A negative bias of 46.2 mg/l (- 32%) was found between POCT CRP and laboratory CRP values.

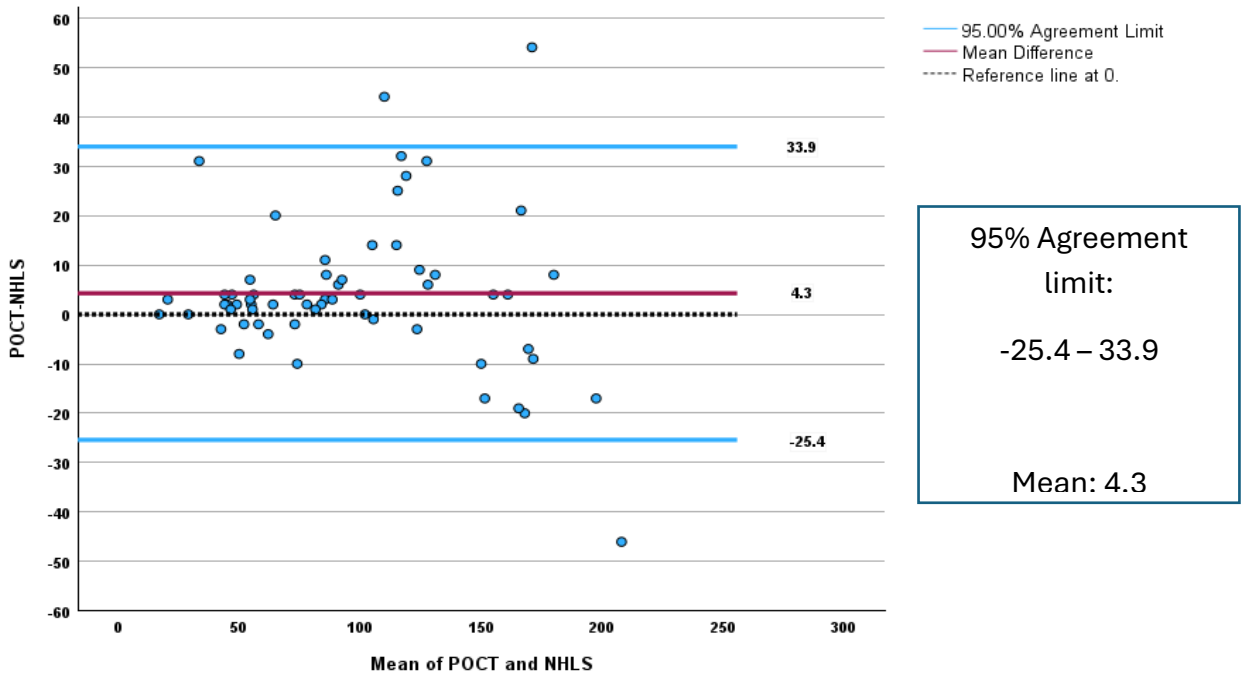


Figure 3: Bland-Altman plot

The linear regression plot is presented in Figure 4. The Spearman rank correlation coefficient (r) is 0.976 (95% CI 0.96 – 0.98) with a p < 0.0001, indicating that 97% of the variability in the POCT and laboratory test has been accounted for. A substantial agreement was observed between the POCT and laboratory CRP tests, as indicated by a Cohen's Kappa coefficient of 0.70 (95% CI: 0.60–0.81, $p < 0.001$)

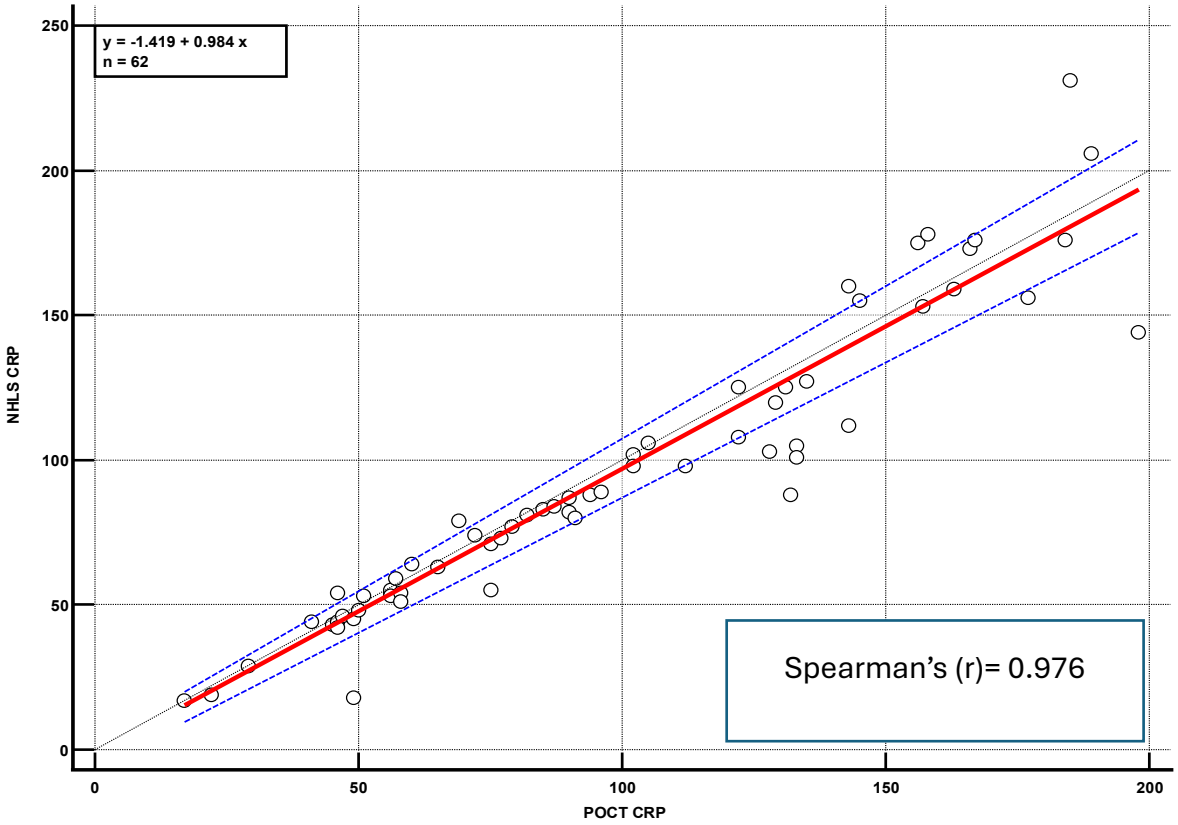


Figure 4: Linear Regression

Regarding turnaround time, the Afinion™ 2 CRP test provided results in just 4 minutes. In contrast, the median registration time at the laboratory was 1.9 hours (114 minutes), with a range of 13 minutes to 42.1 hours. The median time for laboratory results to become available was 5.5 hours (311 minutes), with a range of 0.6 to 42.1 hours (see Figure 4). A paired samples t-test demonstrated a statistically significant difference in time to results, yielding a t-value of –9.88 (p < 0.001).

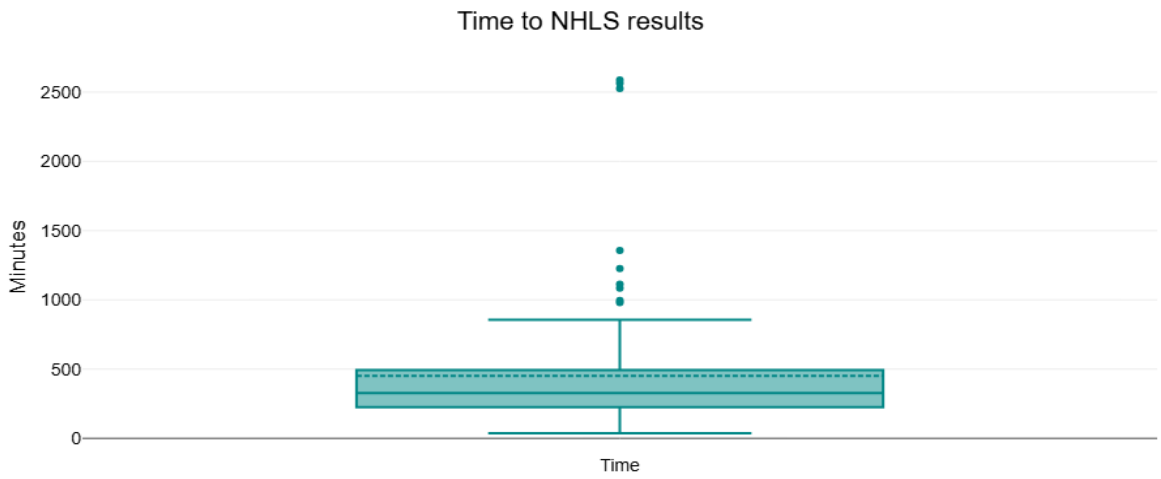


Figure 5: Box plot of time to Laboratory results (minutes)

Discussion:

This study evaluated the analytical performance of a commercially available POCT CRP device, the Afinion™ 2. It compared results from this platform with those obtained from a central laboratory CRP analyser.

The Afinion™ 2 demonstrated good overall performance in our setting, yielding valid results in over 90% of tests. The 9.1% failure rate we observed was mainly due to user errors, technical issues, and changes in haematocrit (HCT) levels. While the device can automatically adjust CRP values for HCT levels between 20% and 60%, it does not display results when whole blood samples fall outside this range. It is important to recognise that abnormal HCT levels can greatly influence CRP measurements – low HCT may cause results to be underestimated, whereas high HCT can lead to overestimation (21). This disparity can result in detrimental clinical choices, including unnecessary tests, inappropriate treatment increases, or overlooked diagnoses in high-risk patients. Other studies have found similar pre-analytical error rates. For instance, Fanshawe et al. evaluated three POC devices across various levels of healthcare, including the Afinion™2 CRP, and identified a 9% error rate (21). Moreover, Bouwer and Van Pelt observed that the small sample volume could influence error rates for the Afinion™ 2 compared to seven other commercially available POC devices (18). These findings highlight the impact of testing methods, sample characteristics, and the operator's expertise and performance. Consequently, conducting local on-site verification is essential to guarantee the accuracy and reliability of POCT devices in particular clinical environments.

Approximately 63% of our patient population received antibiotics. Although 54.9% of patients exhibited signs consistent with the clinical definition of presumed sepsis, only 29% of blood cultures yielded a positive result for an identifiable organism. This indicates that the overuse of antibiotics in our setting could range from 9% to 34%. A study by Sigakis et al. found that, although culture-positive and culture-negative patients had similar risk factors for mortality, identifying a pathogen in blood cultures was crucial for optimising antimicrobial use

and treatment duration (22). Randomised clinical trials evaluating CRP POCT consistently suggest avoiding antibiotics when CRP levels are below 20 mg/L and supporting their use when levels are at or above 100 mg/L. Additionally, these studies recommend withholding antibiotics when the CRP level is less than 50 mg/L, resulting in a 12–14% reduction in antibiotic use (23,24). The quick availability of CRP results in our clinical setting could enhance appropriate antibiotic prescribing.

Using the Afinion™ 2, we attained 100% sensitivity in identifying laboratory-confirmed CRP levels over 10 mg/L and 100 mg/L, with specificities of 100% and 92.5%, respectively. This highlights the test's outstanding performance within the crucial CRP range of 10 - 100 mg/L, confirming its reliability as a POC testing tool for infection management. Our findings are consistent with prior research; for instance, Matheeussen et al. reported a sensitivity of 75.5% and a specificity of 98% at CRP levels ≥10 mg/L and 92.6% sensitivity with 99.8% specificity at levels ≥100 mg/L (25). In a similar vein, a neonatal study in Cape Town discovered a sensitivity of 97% and a specificity of 99% for CRP levels above 10 mg/L (10), underscoring the effectiveness of CRP as a biomarker for the early detection of infectious or inflammatory conditions across varied populations and testing instruments. The implications of these diagnostic metrics are noteworthy. A CRP threshold of >10 mg/L shows 100% sensitivity and specificity, emphasising its potential for ruling out and confirming the necessity of antibiotic treatment. This empowers clinicians to confidently withhold antibiotics when CRP levels fall below this threshold, reducing unnecessary prescriptions. With a higher cutoff of >100 mg/L, the test retained 100% sensitivity but exhibited a slight decrease in specificity (92.5%), indicating a slight increase in false-positive results. This minor reduction in specificity could lead to some overtreatment if test results are considered in isolation, mainly since antibiotic decisions frequently rely on elevated CRP values.

The Afinion™ 2 demonstrated strong accuracy in detecting intermediate CRP levels (20 to 100 mg/L), consistent with findings by Minnaard et al., who evaluated various CRP POCT devices (19). However, when CRP levels surpass 100 mg/L, the consistency between POCT results and laboratory values becomes less reliable. This observation emphasises the need to carefully interpret elevated CRP results generated by the POCT, particularly when crucial treatment decisions, such as initiating antibiotic therapy, are based on these results. Therefore, validating these POC results with other relevant biomarkers and clinical and radiographic findings may be necessary to ensure an accurate diagnosis and, thus, an informed treatment plan.

The Afinion 2 analyser has demonstrated impressive analytical performance compared to standard laboratory CRP measurements, achieving a Spearman correlation coefficient of 0.97. This suggests a remarkable agreement between the two methods. With 62 paired observations and an alpha level of 0.05, this study was well-equipped to identify this robust correlation, reducing the likelihood of type II errors.

Bland–Altman analysis demonstrated a fixed mean difference of 4.3 mg/L, signifying that the test method consistently underestimated CRP levels. The 95% limits of agreement extended from –25.4 to 33.9 mg/L,

indicating that individual point-of-care CRP measurements could deviate from laboratory values by as much as ±30 mg/L. Furthermore, a proportional bias was observed, with the test method underestimating CRP concentrations by an average of 32%, approximately 46 mg/L at elevated levels. This phenomenon illustrates that the bias intensifies with increasing CRP levels, an aspect that warrants consideration when interpreting results in clinical practice. Although this level of variability may be acceptable for general clinical use within the range of 10–100 mg/L, it could be significant in high-stakes decisions, especially near critical thresholds. Notably, the Afinion™ 2 demonstrated only a slight average underestimation of 3%, which aligns with biases reported for other POCT devices like the Cobas b 101 (3%) and the QuikRead (6%) (25,26). Similarly, Verbakel et al. reported acceptable agreement using Bland–Altman analysis with 95% limits of agreement ranging from −15.4% to 12.8% and a negative bias of 28.2% (17). These findings support the reliability and clinical utility of the Afinion™ 2 CRP POCT system as a practical and efficient alternative to laboratory testing, particularly in primary or urgent care settings where rapid results are essential.

Regarding turnaround times, laboratory results were usually accessible 3.2 hours after registration, with a median of 5.5 hours. A comparable study conducted at Grootte Schuur Neonatal Unit indicated even longer turnaround times of 7 hours, even with NHLS present on-site (10). This delay in receiving laboratory results for CRP tests can greatly affect timely clinical decision-making. During this delay in result availability, crucial therapeutic decisions might not have been made effectively, such as adjusting treatment or discontinuing unnecessary therapy. Alternatively, access to POC CRP testing could enhance effective and efficient patient management.

Limitation:

This study was conducted at a single centre with a small sample size, focusing solely on an adult ICU population, which may limit its generalisability and reduce external validity. The extended duration of the study was due to the limited availability of test cartridges and scheduling constraints for administering the test. Convenience sampling, based on cartridge availability, may have introduced selection bias.

Haematocrit (Hct) values were not recorded, although three samples (2.7%) were rejected by the device due to Hct levels below the acceptable threshold (<20%). Additionally, 38% of the samples exceeded the device's CRP measurement range (5–200 mg/L) and were therefore excluded, as no dilutions were performed in keeping with typical bedside clinical practice. Consequently, only samples with moderate CRP elevations were analysed, limiting the generalizability of the findings to patients with CRP levels ≤200 mg/L. Diagnostics regarding precision testing and repeatability were outside the scope of this study.

Recommendations:

Future studies should incorporate dilution protocols for CRP levels >200 mg/L to capture high-risk patients. Broadening research to encompass larger and more diverse populations across multiple centres will enhance the

generalizability of findings. It is also crucial to investigate various CRP thresholds and to conduct outcome-based studies to optimise clinical application and promote effective antibiotic stewardship.

Conclusion:

Delays in CRP results can adversely affect patient outcomes in critical care by postponing targeted therapy. This study indicates that the Afinion™ 2 POCT CRP device demonstrates potential as a rapid alternative to conventional laboratory testing, thereby supporting clinical decision-making and antimicrobial stewardship. Although integrating CRP POCT into routine care alongside clinical algorithms could enhance patient management and resource utilisation, additional validation—particularly in patients with CRP levels exceeding 200 mg/L—is necessary prior to advocating for its widespread application in ICU settings. Local evaluation remains essential to verify the device's accuracy and suitability within specific clinical environments.

Dissemination of results:

The findings of this study will be communicated to the relevant departments, including the ICU, the NHLS, and Obsidian Health. Dissemination will occur through an internal report that highlights the results aimed at facilitating the potential implementation of the point-of-care device within this clinical environment.

Acknowledgements:

Declarations and funding:

Obsidian funded the testing cartridges used in this study and supplied the Afinion™ 2 analyser; no other funding sources were involved in the research. It is crucial to note that the results obtained from the POCT did not affect patient management within the ICU.

Competing interests:

The authors affirm that they possess no financial or personal relationships that could have unduly influenced their writing of this article.

Authors' contributions:

M.M. conceived the study concept. A.D.P. developed the study design, collected the data, conducted the analyses, and verified the statistical methods with support from a statistician. R.G., M.T.W., and M.M. provided critical input during manuscript preparation and supervised various aspects of the research process. All authors contributed to the interpretation of the findings, critically reviewed the manuscript, and approved the final version for publication.

Data availability statement:

The data supporting the findings of this study are available from the corresponding author, [A.D.P], upon reasonable request. These data are not publicly available due to restrictions related to the confidentiality and privacy of research participants.

Disclaimer:

The opinions stated in this article are solely those of the authors, stemming from their independent professional research. They do not necessarily represent the official policies or stances of affiliated institutions, funding agencies, or the publisher. The authors hold complete accountability for the content, findings, and conclusions shared in this work.

References:

1. Clyne B, Olshaker JS. The C-reactive protein. J Emerg Med. 1999 Nov;17(6):1019–25.
2. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. Journal of Clinical Investigation. 2003 Jun 15;111(12):1805–12.
3. Potempa LA, Rajab IM, Hart PC, Bordon J, Fernandez-Botran R. Insights into the use of C-Reactive Protein as a Diagnostic Index of Disease Severity in COVID-19 Infections. Am J Trop Med Hyg. 2020 Aug 5;103(2):561–3.
4. Cals JWL, Schot MJC, de Jong SAM, Dinant GJ, Hopstaken RM. Point-of-Care C-Reactive Protein Testing and Antibiotic Prescribing for Respiratory Tract Infections: A Randomised Controlled Trial. The Annals of Family Medicine. 2010 Mar 1;8(2):124–33.
5. Rabello LSCF, Póvoa P, Lapa e Silva JR, Azevedo LCP, da Silva Ramos FJ, Lisboa T, et al. Patterns of C-reactive protein ratio predicts outcomes in healthcare-associated pneumonia in critically ill patients with cancer. J Crit Care. 2017 Dec;42:231–7.
6. Kubo K, Sakuraya M, Sugimoto H, Takahashi N, Kano K ichi, Yoshimura J, et al. Benefits and Harms of Procalcitonin- or C-Reactive Protein-Guided Antimicrobial Discontinuation in Critically Ill Adults With Sepsis: A Systematic Review and Network Meta-Analysis*. Crit Care Med [Internet]. 2024 Oct 1;52(10):e522–34. Available from: https://journals.lww.com/10.1097/CCM.0000000000006366
7. Mahrous AA, Hassanien AA, Atta MS. Predictive value of C-reactive protein in Critically ill patients who develop acute lung injury. Egyptian Journal of Chest Diseases and Tuberculosis. 2015 Jan;64(1):225–36.
8. Vincent JL. International Study of the Prevalence and Outcomes of Infection in Intensive Care Units. JAMA. 2009 Dec 2;302(21):2323.

9. Carlet J, Jarlier V, Harbarth S, Voss A, Goossens H, Pittet D. Ready for a world without antibiotics? The Pensières Antibiotic Resistance Call to Action. Antimicrob Resist Infect Control. 2012;1(1):11.
10. Prince K. A comparison between standard C-reactive protein laboratory measurement to point of care C-reactive protein in a neonatal intensive care unit setting [MMed]. [Cape Town]: University of Cape Town; 2016.
11. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022 Feb;399(10325):629–55.
12. Thiab G, Workman A, Khawaja I. An Unrecognized Cause of Elevated Procalcitonin Level. Cureus. 2023 May 25;
13. Dias RF, de Paula ACRB, Hasparyk UG, de Oliveira Rabelo Bassalo Coutinho M, Alderete JRA, Kanjongo JC, et al. Use of C-reactive protein to guide the antibiotic therapy in hospitalized patients: a systematic review and meta-analysis. BMC Infect Dis. 2023 May 3;23(1):276.
14. Davids A, Zemlin AE, Kruger EC. Challenges with communication of critical laboratory results in a resource-limited setting in South Africa. Afr J Lab Med. 2024 Sep 23;13(1).
15. Nichols JH. Utilizing Point-of-Care Testing to Optimize Patient Care. EJIFCC. 2021 Jun;32(2):140–4.
16. Billetop A, Grant K, Beasmore J, Mills F, Odd D, Heep A. Clinical evaluation of point-of-care testing for wide-range C-reactive protein (wr-CRP) in neonates with suspected sepsis. Journal of Laboratory Medicine. 2019 Jun 26;43(3):135–40.
17. Verbakel JY, Aertgeerts B, Lemiengre M, Sutter A De, Bullens DMA, Buntinx F. Analytical accuracy and user-friendliness of the Afinion point-of-care CRP test. J Clin Pathol. 2014 Jan;67(1):83–6.
18. Brouwer N, van Pelt J. Validation and evaluation of eight commercially available Point of care CRP methods. Clinica Chimica Acta. 2015 Jan;439:195–201.
19. Minnaard MC, van de Pol AC, Broekhuizen BDL, Verheij TJM, Hopstaken RM, van Delft S, et al. Analytical performance, agreement and user-friendliness of five C-reactive protein point-of-care tests. Scand J Clin Lab Invest. 2013 Dec;73(8):627–34.
20. IBM Corp. IBM SPSS statistics for Windows. Armonk, New York; 2023.
21. Fanshawe TR, Glogowska M, Edwards G, Turner PJ, Smith I, Steele R, et al. Pre-analytical error for three point of care venous blood testing platforms in acute ambulatory settings: A mixed methods service evaluation. PLoS One. 2020 Feb 3;15(2):e0228687.
22. Sigakis MJG, Jewell E, Maile MD, Cinti SK, Bateman BT, Engoren M. Culture-Negative and Culture-Positive Sepsis: A Comparison of Characteristics and Outcomes. Anesth Analg. 2019 Nov;129(5):1300–9.
23. Cals JWL, Butler CC, Hopstaken RM, Hood K, Dinant GJ. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. BMJ. 2009 May 5;338(may05 1):b1374–b1374.
24. Do NTT, Ta NTD, Tran NTH, Than HM, Vu BTN, Hoang LB, et al. Point-of-care C-reactive protein testing to reduce inappropriate use of antibiotics for non-severe acute respiratory infections in Vietnamese primary health care: a randomised controlled trial. Lancet Glob Health. 2016 Sep;4(9):e633–41.

25. Matheeussen V, Van Hoof V, Loens K, Lammens C, Vanderstraeten A, Coenen S, et al. Analytical performance of a platform for point-of-care CRP testing in adults consulting for lower respiratory tract infection in primary care. European Journal of Clinical Microbiology & Infectious Diseases. 2018 Jul 10;37(7):1319–23.
26. Scharnhorst V, Noordzij PG, Lutz A, Graser U, Püntener D, Alquézar-Arbé A. A multicenter evaluation of a point of care CRP Test. Clin Biochem. 2019 Sep;71:38–45.