

Evaluation of Procalcitonin as a Diagnostic Biomarker in Pediatric Infections: Implications for Antibiotic Stewardship

Mohammed Qasim Salih Mahdi^{1,*}, Fatima Abdul Hussein Mejbel², and Nabil Salim Saaid Tuwajj³

¹Department of Pathological Analysis, Faculty of Science, University of Kufa, Najaf, Iraq

^{2,3}Department of Biology, Faculty of Science, University of Kufa, Najaf, Iraq

Abstract. This study explores the utility of Procalcitonin (PCT) as a biomarker for distinguishing between bacterial and viral infections in pediatric patients less than six years. The study was constructed of 160 clinical specimens taken from pediatric patients (72 female and 88 male) who presented with bloodstream and respiratory tract infections, their CRP result was positive, and on that basis, the doctors prescribed antibiotics for them. The study was performed on those specimens using PCT levels as infection biomarker to evaluate their need to treatment with antibiotic. The PCT levels were divided into 5 ranges: <0.25, 0.25-0.5, 0.5-2, 2-10, and >10. In the female group, the numbers and percentages of patients in each PCT category were as follows: 34 patients (43.59%) had PCT < 0.25, 10 patients (12.82%) had PCT 0.25 - 0.5, 13 patients (16.67%) had PCT 0.5 - 2, 7 patients (8.97%) had PCT 2 - 10, and 14 patients (17.95%) had PCT > 10. In the male group, the distribution was slightly different: 36 patients (43.90%) had PCT < 0.25, 6 patients (7.32%) had PCT 0.25 - 0.5, 17 patients (20.73%) had PCT 0.5 - 2, 4 patients (4.88%) had PCT 2 - 10, and 19 patients (23.17%) had PCT > 10. Regarding PCT < 0.25 ng/mL this category includes 42.94% of the patients, reflecting those with PCT levels below the threshold where antibiotics are typically discontinued and this step was very important because this mean that 42.94% were using antibiotics inappropriately.

1 Introduction

In order to effectively treat pediatric patients and avoid the development of antibiotic resistance, it is essential to accurately differentiate between bacterial illnesses and viral infections. Clinical evaluations and fundamental laboratory tests, such as CRP, have traditionally been relied upon by doctors. However, these assays often fail to offer significant difference [1, 2]. The infection biomarker known as procalcitonin (PCT), which is elevated to a large degree in cases of bacterial infections, has emerged as a helpful technique for diagnostic purposes. The purpose of this research is to determine whether or not PCT is successful in providing pediatric patients with bloodstream and respiratory tract

* Corresponding author: nabeel.tuwajj@uokufa.edu.iq

infections with the information necessary to make choices about antibiotic treatment [3, 4].

This research attempts to elucidate the function that PCT plays in clinical decision-making processes by finding particular PCT thresholds that correspond with bacterial or viral etiologies at the baseline level. Contributing to more accurate antibiotic stewardship is the broad goal or expectation, with the intention of ensuring that antibiotics are only provided when they are absolutely required and in a manner that is suitable for the kind of illness [5,6].

The need for enhanced diagnostic accuracy in illness type identification is becoming more essential as antibiotic resistance becomes an increasingly serious problem in the context of global health [7, 8].

This research not only investigates the utility of PCT in reducing unnecessary antibiotic use but also examines its potential in enhancing patient care by preventing the adverse effects associated with antibiotic overuse. Unnecessarily long treatment durations often also result from the use of fixed antibiotic regimens advocated by practice guidelines [9, 10].

Today, a growing body of evidence-based literature supports the use of PCT to improve the clinical management of patients with suspicion of bacterial infection and to contribute to antibiotic stewardship initiatives. Importantly, PCT-guided antibiotic therapy strategies have been demonstrated to be safe and effective for patients, without increasing the risk for mortality, adverse effects, complications, length of stay, or treatment failure [11, 12].

2 Materials and Methods

2.1 Ethical Consideration

It was approved by the Institutional Ethics Committees of the College of Science at the University of Kufa and the Scientific Committee for Research in the Health Department of Najaf [13].

2.2. Patients

To evaluate PCT as a diagnostic tool, the study analyzed 160 clinical specimens from pediatric patients who were suspected with bloodstream and respiratory tract infections due to bacterial and viral infections at Al-Zahraa Hospital. The measurements of PCT levels were performed by using the VIDAS PCT quantitative test. The patients were divided into five predefined PCT groups: <0.25, 0.25-0.5, 0.5-2, 2-10, and >10 ng/ml. The PCT group's differentiation served as the measure of the likelihood of the predominantly bacterial versus viral infection as well as the guidelines for antibiotic therapy choice. The study and the collected data were subjected to statistical analysis to evaluate the correlation between PCT measurement and clinical diagnosis and outcomes across the five predefined groups.

2.3 Methods

The examination was carried out using a VIDAS device, and the work steps were carried out according to the recommendations of the manufacturer (BioMerieux, France). It was necessary to reconstitute vials of standards and controls with distilled water; the reagents were required to be stable for 8 hours at 2-8°C or until the kit's expiry at $-25 \pm 6^\circ\text{C}$, with allowance of five freeze/thaw cycles. Master lot data entry was done by scanning the kit's barcode. Calibrations were carried out using calibrators provided with the kit while opening a new reagent's lot and every 28 days after the first one. The procedure implied running samples, controls, and calibrators and pipetting 200 μL and initiating an assay

automatically and completing it within approximately 20 minutes.

3 Results

In the comprehensive analysis of 160 clinical specimens obtained from pediatric patients afflicted with bloodstream and respiratory tract infections, the investigation delved into the intricate nuances of Procalcitonin (PCT) levels across genders. Among the female participants, a notable 43.59% exhibited PCT levels falling below the critical threshold of 0.25 ng/mL, suggesting a propensity towards viral infections. Further disaggregation of the data revealed that 12.82% of female patients fell within the range of 0.25-0.5 ng/mL, while 16.67% displayed PCT levels ranging from 0.5 to 2 ng/mL. Moreover, 8.97% of the cohort demonstrated PCT levels between 2 and 10 ng/mL, signifying a moderate to severe bacterial infection, with an additional 17.95% presenting PCT levels exceeding the 10 ng/mL mark, indicative of a particularly acute bacterial infection (Fig.1).

Conversely, within the male subset, 43.90% showcased PCT levels below 0.25 ng/mL, aligning closely with the distribution observed in the female cohort. However, slight deviations were discernible in the subsequent categories, with 7.32% displaying PCT levels ranging from 0.25 to 0.5 ng/mL, 20.73% exhibiting levels between 0.5 and 2 ng/mL, 4.88% registering levels between 2 and 10 ng/mL, and 23.17% surpassing the critical threshold of 10 ng/mL (Fig.1).

This study helps doctors understand when antibiotics are really needed for kids with infections. It shows that many kids with low PCT levels might not benefit from antibiotics, which could help reduce unnecessary antibiotic use and prevent antibiotic resistance (Fig.2, 3), (Table 1, 2).

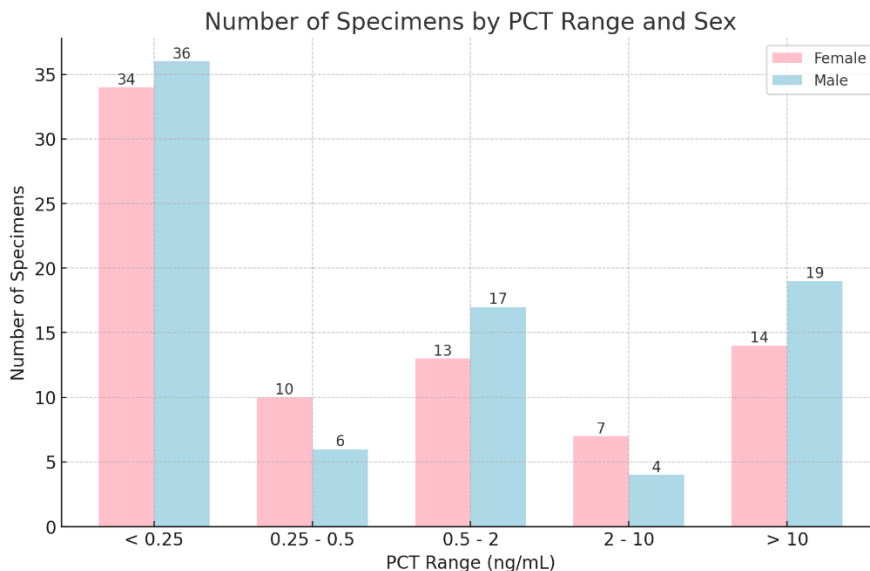


Fig. 1. Distribution of procalcitonin levels.

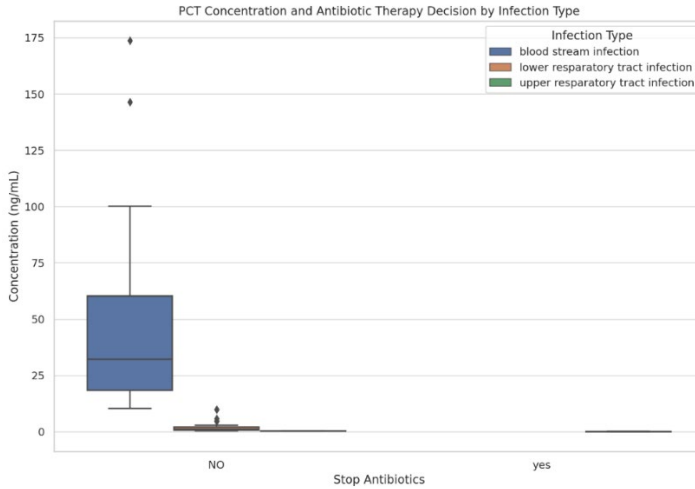


Fig. 2. How PCT concentrations influence antibiotic therapy decisions across different types of infections.

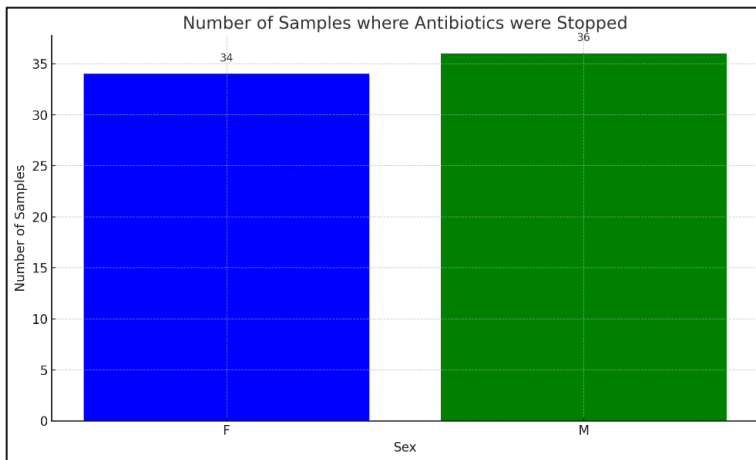


Fig. 3. Number of specimens where antibiotics stooped.

Table 1. VIDAS PCT results

	Sex	NO.	PCT range	CRP	NO.	Stop antibiotics
160	F	78	(< 0.25)	Positive	34	Yes
			(0.25 - 0.5)	Positive	10	No
			(0.5. - 2)	Positive	13	No
			(2 - 10)	Positive	7	No
			(>10)	Positive	14	No

M	82	(< 0.25)	Positive	36	Yes
		(0.25 - 0.5)	Positive	6	No
		(0.5 - 2)	Positive	17	No
		(2 - 10)	Positive	4	No
		(>10)	Positive	19	No

Table 2. Provides detailed statistics for PCT concentrations within each category of infection and antibiotic decision

Infection Type	Antibiotics Stopped	Mean Concentration	Median	Minimum	Maximum	Count
Blood Stream Infection	No	47.19 ng/mL	32.17 ng/mL	10.34 ng/mL	173.80 ng/mL	33
Lower Respiratory Tract Infection	No	2.01 ng/mL	1.19 ng/mL	0.50 ng/mL	9.89 ng/mL	42
Upper Respiratory Tract Infection	No	0.37 ng/mL	0.38 ng/mL	0.26 ng/mL	0.47 ng/mL	15
Upper Respiratory Tract Infection	Yes	0.10 ng/mL	0.05 ng/mL	0.05 ng/mL	0.25 ng/mL	70

4 Discussion

The study's findings highlight Procalcitonin (PCT) as a robust biomarker for distinguishing bacterial from viral infections, aligning with and expanding upon previous research. The significant variation in PCT levels between suspected bacterial and viral infections confirms its diagnostic reliability and clinical utility [14, 15]. By establishing clear PCT thresholds for antibiotic initiation and discontinuation, this research contributes to more targeted and judicious use of antibiotics in pediatric settings [16, 17].

Importantly, the results underscore the potential of PCT-guided therapy to not only improve patient outcomes by ensuring appropriate treatment but also mitigate the broader issue of antibiotic resistance. This is particularly relevant in pediatric care, where overuse of antibiotics has long-term consequences on health and antibiotic efficacy [18, 19].

Future research should focus on longitudinal studies to further refine PCT cutoff values and assess the long-term benefits of PCT-guided treatment protocols. Additionally, the integration of PCT measurements into existing clinical workflows could be explored to enhance the accessibility and impact of this diagnostic tool [20, 21].

Overall, the findings advocate for a shift towards more evidence-based approaches in the management of pediatric infections, emphasizing the critical role of biomarkers like PCT in contemporary healthcare practices [22, 23].

5 Conclusion

In conclusion, this study validates the effectiveness of Procalcitonin (PCT) as a diagnostic

tool in pediatric infections, demonstrating its capacity to accurately differentiate between bacterial and viral etiologies. By implementing PCT-based guidelines, clinicians can optimize antibiotic usage, enhancing treatment efficacy and patient safety while combating antibiotic resistance. The results advocate for the routine use of PCT in pediatric clinical settings, emphasizing its significant role in improving diagnostic accuracy and supporting antibiotic stewardship. Ultimately, PCT offers a pragmatic approach to reducing unnecessary antibiotic use, underscoring its value in modern medical practice.

References

1. M. Christ-Crain, D. Jaccard-Stolz, R. Bingisser, M. M. Gencay, P. R. Huber, M. Tamm, B. Müller, *Lancet*, **365**, 1059-1066 (2005)
2. E. T. Covington, M. Z. Roberts, P. Dong, *Crit. Care Med.*, **46**, 691-696 (2018)
3. U. Garay, N. Tran, P. Garcia, *J. Clin. Med.*, **10**, 1126 (2021)
4. J. Geraerds, E. de Jong, R. K. van den Tooren-de Groot, *Diagn. Microbiol. Infect. Dis.*, **99**, 115056 (2021)
5. D. T. Hamade, Huang, *Clin. Chem.*, **66**, 280-289 (2020)
6. E. Heilmann, J. Gregson, L. Peto, *J. Antimicrob. Chemother.*, **75**, 3336-3344 (2020)
7. P. Lenihan, G. Kelen, *BMC Infect. Dis.*, **22**, 209 (2022)
8. M.A. Ali and A.A.J. Aljanaby, *E3S Web of Conferences*, **381**, 01102, 1-6 (2023)
9. G. Lippi, M. Plebani, *J. Emerg. Med.*, **58**, 254-261 (2020)
10. R. C. Maves, J. Downar, J. R. Dichter, D. Hickman, M. Hyer, C. L. Sprung, A. Isakov, *Crit. Care*, **27**, 1-10 (2023)
11. K. Razazi, V. Deiler, S. Katsahian, *Intensive Care Med.*, **46**, 2043-2057 (2020)
12. M.H Kamooona and A.A.J Aljanaby, *E3S Web of Conferences*, **389**, 03108, 1-8 (2023)
13. M. A. F. Al-Salami, & N. S. S. Tuwajj, *BIO Web of Conferences* **84**, 03015 (2024)
14. F. Quadir, P. Britton, *J. Paediatr. Child Health*, **54** (2018)
15. T. Waterfield, J. Maney, M. Hanna, D. Fairley, M. Shields, *BMC Pediatrics*, **18** (2018)
16. R. Sahulee, J. McKinstry, S. B. Chakravarti, *Curr. Pediatrics Rep.* (2019)
17. J. Damman, P. Arias, J. Kerner, Ke-You Zhang, M. Dehghan, G. Krishnan, C. Nespor, R. Bensen, K. Park, *Hosp. Pediatrics*, **9**, 434-439 (2019)
18. S. Bobillo-Pérez, J. Rodríguez-Fanjul, I. Jordan Garcia, *Biomarker Insights*, **13** (2018)
19. V. Tan, W. S. Moore, A. Chopra, J. Cies, *Perfusion*, **33**, 278-282 (2018)
20. J. J. Choi, M. McCarthy, *Expert Rev. Mol. Diagn.*, **18**, 27-34 (2018)
21. H.M.Y. Al-labban, A.I. Al-luhaiby, N.S. Salih, W.I. Yahya and A.A.J. Aljanaby, *Journal of Experimental Biology and Agricultural Sciences*, **9(3)**, 401-406 (2021)
22. R. Erixon, K. Cunningham, A. N. Schlicher, M. V. Dajud, A. Ferguson, A. Fondell, J. Hess, H. L. Smith, *JPPT*, **25**, 445-450 (2020)
23. H. Xiao, P. Zhang, Y. Xiao, H. Xiao, M. Ma, C. Lin, J. Luo, H. Quan, K. Tao, G. Huang, *Int. J. Surg.* (2020)