Vol 7 No 1 February 2026

E-ISSN :2722-0877

NARRATIVE REVIEW

Analysis of the Predictive Value of Procalcitonin and C-Reactive Protein for Coalescent Mastoiditis in Pediatric Patients: A Narrative Review

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Abstract: Coalescent mastoiditis (CM) is a severe complication of acute otitis media in children for which definitive diagnosis requires a CT scan, creating a clinical need for non-invasive biomarkers. This narrative review aims to evaluate the roles of C-reactive protein (CRP) and procalcitonin (PCT) as predictors of CM. The methodology involved a structured literature search of databases including PubMed and Scopus for publications within the last five years (2020-2025). The results indicate that CRP is a reliable biomarker, with a level of ≥98.7 mg/L predicting the need for surgical intervention with 100% sensitivity and 74.6% specificity. Conversely, evidence for PCT is significantly lacking; indirect data suggest its levels do not consistently increase in localized infections such as CM. In conclusion, CRP is a validated and clinically useful biomarker for the risk stratification of CM in children, whereas the role of PCT remains unproven and appears to be limited.

Keywords: C-Reactive Protein (CRP), Coalescent Mastoiditis, Pediatric, Procalcitonin (PCT)

INTRODUCTION

Acute otitis media (AOM) is one of the most common diagnoses in children, with peak prevalence occurring at 6 to 12 months of age.[3] Several risk factors, including young age and the shorter, more horizontal anatomy of the Eustachian tube in children, contribute to this high incidence.[4] Although most cases of acute otitis media (AOM) resolve without complications, a small proportion may progress to severe suppurative complications, namely acute mastoiditis (AM).[1,2,5] Acute mastoiditis which is an inflammation of the mastoid air cells in the temporal bone, occurs in approximately 0.24% of patients with acute otitis media.[1,2,5] The more severe and destructive form of acute mastoiditis is known as coalescent mastoiditis (CM), characterized by osteitic destruction of the bony septa separating the mastoid air cells.[6] This condition can be considered a localized empyema within the temporal bone.[7] The pathophysiology of coalescent mastoiditis begins with the spread of infection from the middle ear to the mastoid air cells, which represents an early phase in almost all cases of acute otitis media.[1,8] Progression to coalescent mastoiditis occurs when drainage from the mastoid becomes obstructed, typically due to severe mucosal swelling.[1,6] This obstruction causes the accumulation of pus under high pressure, which then disrupts the blood supply to the bony septa, resulting in necrosis, bone

E-ISSN :2722-0877

resorption, and ultimately coalescence or fusion of the air cells.[1,8] The coalescence process significantly increases the risk of potentially life-threatening complications. Pus can penetrate the bone and spread to surrounding structures, with the most common complication being a subperiosteal abscess (found in about 50% of cases).[1,6] In addition, medial spread can trigger serious intracranial complications such as meningitis, brain abscess, or venous sinus thrombosis.[9] The definitive diagnosis of CT depends on radiological evidence of bone destruction, for which contrast-enhanced CT scan is considered the gold standard.[7] However, there are significant concerns regarding radiation exposure in the pediatric population, prompting an urgent clinical need for reliable non-invasive biomarkers.[7,8] Such biomarkers could help with risk stratification, identify cases with the highest likelihood of coalescence, and guide clinical decisions for earlier imaging or surgical intervention.[8,9] Two key inflammatory biomarkers under scrutiny are C-reactive protein (CRP) and procalcitonin (PCT). CRP is an acute-phase reactant that is highly sensitive to inflammation, although not specific.[10] Meanwhile, PCT, a prohormone of calcitonin, has been recognized as a more specific marker for systemic bacterial infection. Its production is strongly stimulated by bacterial endotoxins and tends to be inhibited by cytokines predominant in viral infections.[10,11] Given this background, this narrative review aims to critically examine the scientific literature from the past five years to evaluate the role and usefulness of CRP and PCT in predicting the occurrence of coalescent mastoiditis in children.

METHODS

This narrative review was conducted through a structured literature search across five databases: PubMed, Scopus, ScienceDirect, Cochrane Library, and Google Scholar. The search was limited to publications in English or Indonesian within the past five years (January 2020 – September 2025). The process employed a combination of specific keywords and Boolean operators (AND/OR), such as: (“pediatric” OR “childhood”) AND (“acute mastoiditis”) AND (“inflammatory biomarkers” OR “C-reactive protein” OR “procalcitonin”) AND (“severity” OR “complications” OR “surgical intervention”).

Articles retrieved were screened according to the following criteria: (1) Inclusion criteria: studies focusing on pediatric populations (0–18 years) with acute mastoiditis; observational studies, systematic reviews, or meta-analyses; and studies specifically evaluating the relationship between CRP or PCT levels and disease severity (such as surgical indication or complications). (2) Exclusion criteria: editorials, single case reports, abstracts without full text, and studies focusing on adult or animal populations.

Data from eligible articles were systematically extracted, including biomarker types, predictive values (e.g., cut-off values, sensitivity, and specificity), and authors’ conclusions. The collected data were not statistically analyzed but

E-ISSN :2722-0877

were synthesized narratively. Findings from the various studies were grouped by major themes and critically analyzed to identify trends, inconsistencies, and existing research gaps.

The study selection process began with a literature search that identified 27 articles. After a systematic screening process based on inclusion and exclusion criteria, 27 articles were deemed eligible and relevant for narrative review synthesis. From this cohort of studies, six articles that directly compared the predictive value of biomarkers and represented key findings were extracted in depth and are presented in Table 2.

RESULTS

A comprehensive review of 27 literature studies revealed a clear pattern regarding the varying functions of PCT and CRP in relation to mastoiditis in children. Although CRP has been shown to be a reliable and measurable marker of disease severity, the significance of PCT remains largely speculative and lacks substantial direct evidence. A comparison of key aspects of these two biomarkers is initially offered to establish a baseline understanding.

Table 1. Comparison of Characteristics of Inflammatory Biomarkers CRP and PCT.

CHARACTERISTICS	C-REACTIVE PROTEIN (CRP)	PROCALCITONIN (PCT)
BIOMARKER TYPES	Acute Phase Reactants	Calcitonin Prohormone
MAIN STIMULUS	Pro-inflammatory cytokines, especially Interleukin-6 (IL-6).[12]	Bacterial endotoxins (LPS) and specific cytokines (e.g., TNF-α, IL-1β).[12,13]
SOURCES OF PRODUCTION	Especially hepatocytes (liver cells).[12]	Various parenchymal cells throughout the body (e.g., liver, lungs, intestines).[13,14]
KINETICS OF ENHANCEMENT	Begins to increase within 6–8 hours after the stimulus.[15]	Starts to increase more rapidly, within 3–6 hours after the stimulus.[11,16]
PEAK TIME	Reach the peak in about 48 hours.[17]	Reach the summit early, around 6–12 hours.[11,13]
HALF LIFE	Around 19 hours.[18]	Longer, around 24–30 hours.[11,13]
MAIN ADVANTAGES	Highly sensitive to inflammation, wide availability, relatively low cost. [12]	High specificity for systemic bacterial infection, strong negative predictive value for ruling out sepsis.[11,13]
LIMITATIONS	Non-specific; may increase in non-infectious conditions (trauma, autoimmune).[15]	Less sensitive for localized bacterial infections, higher cost, availability may be limited. [19,20]

Gold Standard Diagnosis and Clinical Challenges of Coalescent Mastoiditis

The diagnosis of acute mastoiditis in children is largely based on clinical findings, such as redness and pain behind the ear.[2] However, clinical examination cannot consistently differentiate between simple mastoid inflammation and coalescent mastoiditis (CM) which is characterized by bone destruction.[4,5] To confirm the diagnosis of MK, radiological evidence is required, where a computed tomography (CT) scan with contrast is considered the diagnostic gold

standard.[5,7,21,22] CT scans are able to provide detailed images of erosion of the bony septa and mastoid cortex which are characteristic of the coalescent process.[5,7] The main clinical challenge lies in making the decision to perform a CT scan, given the significant concerns regarding ionizing radiation exposure in the pediatric population.[7,8] This situation creates an urgent need for reliable, non-invasive biomarkers to assist clinicians in risk stratification, identifying patients with the highest likelihood of developing coalescence, and guiding decisions to perform more selective imaging.[8,9]

C-Reactive Protein (CRP): A Key Biomarker for Risk Stratification

In the search for non-radiological predictors, C-Reactive Protein (CRP) has emerged as the most studied and most useful serum biomarker in the context of MA.[4,23,24] Several studies have consistently shown that very high CRP levels correlate with a more severe disease course and the need for definitive surgical intervention (mastoidectomy), which can serve as a clinical proxy for the presence of MK or abscess formation. A key study by Israeli et al. (2023) provides quantitative data on this. They found that pediatric patients who ultimately required mastoidectomy had a mean CRP level on admission of 227.6 mg/L, which was significantly higher than the mean CRP level in the conservatively managed group, which was 74.6 mg/L ($p<0.001$).[25] Furthermore, a Receiver Operating Characteristic (ROC) analysis from the same study successfully identified the optimal CRP cutoff value for predicting the need for surgery. It was found that a CRP value ≥98.7 mg/L had 100% sensitivity and 74.6% specificity, with an Area Under Curve (AUC) of 0.927, indicating excellent discriminatory ability.[25] These findings have important clinical implications. A sensitivity of 100% indicates that if a child has a CRP level below the threshold of ~98 mg/L, they likely do not have significant coalescence and will respond well to intravenous antibiotic therapy.[25] This may support the decision to delay or avoid a CT scan. Conversely, CRP levels significantly above this threshold should be considered a strong warning sign, prompting immediate radiological evaluation and surgical consultation without delay.[25]

Procalcitonin (PCT): Theoretical Potential and Evidence Gaps

In contrast to CRP, Procalcitonin (PCT) theoretically has advantages because it is more specific for systemic bacterial infections and has faster increase kinetics.[10,11,12] However, an extensive literature search over the past five years failed to identify a single study specifically designed to evaluate the role of PCT in predicting MK in children.

The available indirect evidence suggests potential limitations of PCT in this context. A study by Park et al. (2022) categorized mastoiditis into the subgroup of "localized bacterial infection" (LBI).[14] Analysis of this subgroup showed that although the mean CRP level was quite high (69.0 mg/L), the mean PCT level was reported to be very low, at only 0.6 ng/mL.[14] This finding is supported by a case report by Fujita et al. (2021) of a child with severe intracranial complications of otitis media;

E-ISSN :2722-0877

the patient showed very high CRP levels (165.4 mg/L), but simultaneously, his PCT levels were barely detectable (0.00032 ng/mL).[27] This phenomenon can be explained by the pathophysiology of MK, which is essentially an abscess or "empyema" contained within the temporal bone structure.[6,7] The intense infection process within this confined space is sufficient to trigger a massive systemic acute phase response from the liver, resulting in the production of large amounts of CRP.[13] However, this process does not always result in bacteremia or the release of significant amounts of endotoxin into the systemic circulation.[11,12] Because PCT production is highly dependent on this systemic stimulus, if the infection remains anatomically confined, the primary stimulus for a large PCT surge may be absent. This suggests that PCT may potentially produce false-negative (low) results in patients with localized disease who are actually very severe.

Synthesis and Future Research Directions

Based on the synthesis of currently available evidence, CRP is clearly the most useful and quantitatively validated serum biomarker for assessing MK risk in children with MA. High CRP levels, particularly above the threshold of approximately 98 mg/L, should significantly raise clinical suspicion of a coalescent process and prompt consideration of diagnostic imaging and more aggressive management.[25] The role of PCT in this specific clinical scenario remains unproven and likely limited, given the often anatomically localized nature of mastoiditis infection. To address this evidence gap, future prospective studies are needed that simultaneously measure CRP and PCT levels in a cohort of children with MA and correlate the results with CT scan findings (the gold standard) and clinical outcomes such as the need for mastoidectomy.

E-ISSN :2722-0877

Table 2. Literature Comparison

Author and Year	Article Title	Research purposes	Study Type/Design	Intervention	Key Findings Relevant to the Review
Cassano et al. (2020)	Acute mastoiditis in children	Provides an overview of acute mastoiditis (MA) in children, with reference to the author's clinical experience.	Review article with retrospective case series report.	Tinjauan terapi antibiotik (terutama sefalosporin IV) dan pendekatan bedah (misalnya, miringotomi, masteidektomi) berdasarkan tingkat keparahan dan komplikasi penyakit.	Explains in detail the progression from AOM to CM, the role of *aditus ad antrum* obstruction, and the importance of CT scan.
Israeli et al. (2023)	Analysis of Prognostic Factors Impacting Pediatric Acute Mastoiditis Outcomes	To review the outcomes of pediatric patients with MA and examine the role of intravenous (IV) steroid therapy, demographics, and serum inflammatory values as prognostic factors.	Retrospective Cohort Study	Analisis data pasien yang menerima terapi antibiotik IV, dengan beberapa pasien menerima kortikosteroid IV tambahan. Pembedahan dilakukan jika kondisi tidak membaik	Provides key quantitative data: mean CRP in the surgical group (227.6 mg/L) vs. conservative (74.6 mg/L) and a cutoff of ≥98.7 mg/L with 100% sensitivity.
Park et al. (2022)	Usefulness of Procalcitonin in the Diagnosis of Bacterial Infection in Immunocompetent Children	To evaluate the usefulness of procalcitonin (PCT) in diagnosing bacterial infections (BI), especially invasive bacterial infections (IBI), in children.	Retrospective Study	Membandingkan kadar PCT dengan penanda inflamasi lain (CRP, WBC, ESR) antara kelompok infeksi bakteri (IB) dan non-bakteri (NBI)	Categorized mastoiditis as a “localized bacterial infection” and reported a low mean PCT (0.6 ng/mL) despite a high CRP (69.0 mg/L).
Lucidi et al. (2025)	Pediatric Acute Mastoiditis: Which Factors Influence CT Scan Prescription and Surgical Intervention? A Multivariate Analysis	To investigate factors associated with the prescription of CT scan and surgical intervention in pediatric patients with acute mastoiditis (AM).	Retrospective Cohort Study	Analisis multivariat untuk membandingkan variabel klinis dan laboratorium di antara 3 kelompok pasien (Grup A: tanpa CT/bedah; Grup B: CT, tanpa bedah; Grup C: CT dan bedah)	Found that higher WBC and CRP levels were independent predictors of the need for CT scan and surgical intervention.
Abakay et al. (2022)	Management of Acute Mastoiditis and Accompanying Complications in Pediatric Patients: Single Center Experience	To identify clinical characteristics, management, outcomes, and the relationship between complications, laboratory findings, and recurrence with AM treatment protocols..	Retrospective Study	Pendekatan manajemen bertahap: antibiotik IV, miringotomi ± tabung ventilasi (VT), drainase abses, dan masteidektomi kortikal, tergantung pada ada atau tidaknya komplikasi.	Found that CRP levels were significantly higher in patients with intracranial complications (p=0.028).
Fujita et al. (2021)	Cerebral haemorrhagic infarction associated with acute otitis media in a 4-year-old boy	Reporting a rare case of cerebral hemorrhagic infarction as a complication of acute otitis media (AOM) in a child..	Case Report	Pemberian antibiotik (cefotaxime, ampicillin) dan kortikosteroid	Reporting a case with very high CRP (165.4 mg/L) but very low PCT (0.00032 ng/mL).

E-ISSN :2722-0877

CONCLUSION

Based on the synthesis of the 27 referenced literatures, C-Reactive Protein (CRP) is a strong predictive biomarker and has been shown to be very valuable for identifying coalescent mastoiditis in children. Significantly elevated CRP levels, with a cutoff value of approximately 98 mg/L, demonstrate very high sensitivity for identifying patients requiring surgical intervention, making them a reliable tool for clinical risk stratification. In contrast, there is a significant lack of scientific evidence regarding the usefulness of procalcitonin (PCT) in this context. Indirect evidence indicates that coalescent mastoiditis, as an often anatomically confined infection, does not consistently induce a robust systemic PCT response. Consequently, the predictive role of PCT remains unproven and its potential appears limited. Overall, the most effective clinical strategy currently is to combine careful clinical evaluation with CRP measurement to guide critical decisions regarding the need for follow-up imaging and timely surgical intervention.

REFERENCES

1. Danishyar A, Ashurst J V. *Acute Otitis Media*. StatPearls Publishing; 2025.

2. Jamal A, Alsabea A, Tarakmeh M, Safar A. Etiology, Diagnosis, Complications, and Management of Acute Otitis Media in Children. *Cureus*. Published online August 15, 2022. doi:10.7759/cureus.28019

3. The Royal Children's Hospital Melbourne. Acute otitis media: Clinical Practice Guidelines. https://www.rch.org.au/clinicalguide/guideline_index/acute_otitis_media/.

4. Cassano P, Ciprandi G, Passali D. Acute mastoiditis in children. *Acta Biomedica*. 2020;91:54-59. doi:10.23750/abm.v91i1-S.9259

5. Kucur C, Özbay İ, Topuz MF, et al. Acute Otitis Media Complications. *Journal of Clinical and Experimental Investigations*. 2018;8(4). doi:10.5799/jcei.382431

6. Mansour S, Magnan J, Nicolas K, Haidar H. Acute Otitis Media and Acute Coalescent Mastoiditis. In: *Middle Ear Diseases*. Springer International Publishing; 2018:85-113. doi:10.1007/978-3-319-72962-6_2

7. Öztepe MF, Gökharman FD. Diagnostic Importance of Computed Tomography and Magnetic Resonance Imaging in Coalescent Mastoiditis, a Severe Complication of Acute Otitis Media. *Current Research in MRI*. 2025;3(3):95-97. doi:10.5152/CurrResMRI.2024.24099

8. Lucidi D, Reale M, Cantaffa C, et al. Pediatric Acute Mastoiditis: Which Factors Influence CT Scan Prescription and Surgical Intervention? A Multivariate Analysis. *Journal of International Advanced Otology*. 2025;21(4). doi:10.5152/iao.2025.251899

9. Sapir A, Eshel Y, Heilig Y, et al. Sinus Vein Thrombosis in Pediatric Patients After Acute Mastoiditis. *Journal of International Advanced Otology*. 2025;21(2):1-5. doi:10.5152/iao.2025.241721

10. Friedman ND. Antimicrobial stewardship: The need to cover all bases. *Antibiotics.MDPI AG*. 2013;2(3):400-418. doi:10.3390/antibiotics2030400

11. Bhat A, Alsadhan N, Alsadhan N, et al. Procalcitonin and C-reactive protein as early diagnostic markers of sepsis or septic shock in children who presented with fever to the pediatric emergency department at a tertiary hospital, in Riyadh, Saudi Arabia. *Int J Emerg Med*. 2025;18(1). doi:10.1186/s12245-025-00888-2

12. Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis. *Clinical Infectious Diseases*. 2004;39(2):206-217. doi:10.1086/421997

13. Downes KJ. Procalcitonin in Pediatric Sepsis: What Is It Good for? *J Pediatric Infect Dis Soc*. 2021;10(12):1108-1110. doi:10.1093/jpids/piab066

14. Park HN, Kim SY, Lee NM, et al. Usefulness of Procalcitonin in the Diagnosis of Bacterial Infection in Immunocompetent Children. *Children*. 2022;9(8). doi:10.3390/children9081263

15. Llor C. C-reactive protein point-of-care testing to guide antibiotic prescribing for respiratory tract infections. *Expert Rev Respir Med.Taylor and Francis Ltd.* Preprint posted online August 3, 2025. doi:10.1080/17476348.2025.2510378

16. Katz SE, Crook J, McHenry R, Szeles A, Halasa N, Banerjee R. Prospective Observational Study to Determine Kinetics of Procalcitonin in Hospitalized Children Receiving Antibiotic Therapy for Non-Critical Acute Bacterial Infections. *Infect Dis Ther*. 2021;10(1):595-603. doi:10.1007/s40121-020-00358-7

17. Staiano A, Bjerrum L, Llor C, et al. C-reactive protein point-of-care testing and complementary strategies to improve antibiotic stewardship in children with acute respiratory infections in primary care. *Front Pediatr*. 2023;11. doi:10.3389/fped.2023.1221007

18. Malluvalasa S, Arigela V, Lanka S, Padala S. Comparative study of procalcitonin versus c-reactive protein in the diagnosis of sepsis in children below 16 years-a single centre observational study. *J PediatrRes*. Published online January 28, 2017.

19. Fang C, Hong A, Ying D. *Diagnostic Value of Procalcitomin on Pediatric Severe Infection*. www.biomedres.info

20. Tissières P, Esteban Torné E, Hübner J, Randolph AG, Rey Galán C, Weiss SL. Use of procalcitonin in therapeutic decisions in the pediatric intensive care unit. *Ann Intensive Care.Springer Science and Business Media Deutschland GmbH*. 2025;15(1). doi:10.1186/s13613-025-01470-y

21. Shiran SI, Pratt LT, DeRowe A, Matot S, Neiderman NC, Wasserzug O. The Clinical Value of Cranial CT Venography for Predicting Fusobacterium necrophorum as the Causative Agent in Children with Complicated Acute Mastoiditis. *American Journal of Neuroradiology*.

2024;45(6):761-768. doi:10.3174/ajnr.A8217

22. Alshehri S, Alahmari KA. Pediatric Acute Mastoiditis in Saudi Arabia: Demographic Insights, Clinical Profiles, and Prognostic Factors. *Children*. 2024;11(4). doi:10.3390/children11040402

23. Lin HW, Shargorodsky J, Gopen Q. Clinical Strategies for the Management of Acute Mastoiditis in the Pediatric Population. *Clin Pediatr (Phila)*. 2010;49(2):110-115. doi:10.1177/0009922809344349

24. Israeli A, Kosec A, Shochat I, et al. Analysis of Prognostic Factors Impacting Pediatric Acute Mastoiditis Outcomes. *Journal of International Advanced Otology*. 2023;19(1):50-54. doi:10.5152/iao.2023.22794

25. García-Sánchez P, Parra Rodríguez B, López López R, Molina Gutiérrez MÁ, Bueno Barriocanal M, de Ceano-Vivas la Calle M. Retrospective study of acute mastoiditis in children in Spain attended in a Pediatric Emergency department. *Enferm Infecc Microbiol Clin*. 2024;42(5):263-266. doi:10.1016/j.eimc.2024.02.011

26. Fujita Y, Imataka G, Ohkusu M, Yoshihara S. Cerebral haemorrhagic infarction associated with acute otitis media in a 4-year-old boy. *BMJ Case Rep.BMJ Publishing Group*. 2021;14(5). doi:10.1136/bcr-2021-242098

27. Abakay MA, et al. Management of Acute Mastoiditis and Accompanying Complications in Pediatric Patients: Single Center Experience. *Medical Journal of Bakirkoy*. 2022;18(2):230-237. doi:10.4274/BMJ.galenos.2022.2022.3-22