Journal of Health and Rehabilitation Research 2791-156X JHRR

For contributions to JHRR, contact at email: editor@jhrlmc.com

Original Article

Comparison of CSF Lactate and Serum Procalcitonin in Diagnosing Pyogenic Meningitis

Muhammad Ibrar Saleem[1], Imran Ahmed[1], Jalil Khan[1], Shehar Bano jadoon[1], Salman Khan[1], Fawad Ahmed[1], Muhammad Farrukh Habib[2]*

[1]Pak Emirates Military Hospital (PEMH) Rawalpindi

[2]National University of Medical Sciences (NUMS) Rawalpindi

Corresponding Author: Muhammad Farrukh Habib; Email: muhammadfarrukhhabib@gmail.com

Conflict of Interest: None.

Saleem MI., et al. (2023). 3(2): DOI: https://doi.org/10.61919/jhrr.v3i2.191

ABSTRACT

Background: Meningitis, a potentially life-threatening inflammation of the meninges, poses diagnostic challenges, particularly in differentiating bacterial meningitis (BM) from other forms. The identification of effective biomarkers is crucial for accurate diagnosis and treatment.

Objective: This study aimed to evaluate the diagnostic utility of cerebrospinal fluid (CSF) lactate levels and serum procalcitonin (PCT) in distinguishing BM from tuberculous and viral meningitis.

Methods: Conducted at the Neurology Department of Pak Emirates Military Hospital from February to May 2023, this observational study included 55 patients, with a mean age of 44.03 years. Patients were selected based on clinical signs and symptoms of meningitis, with those having received prior antibiotic treatment excluded. CSF and serum PCT levels were measured, and statistical analyses were performed to compare these biomarkers across different meningitis etiologies.

Results: Of the 55 patients, 30 (54.50%) were diagnosed with BM, 15 (27.30%) with viral meningitis, and 10 (18.20%) with tuberculous meningitis. The mean CSF lactate level in BM patients was 9.36 ± 7.95 mmol/L, significantly higher than in non-bacterial cases. Similarly, serum PCT levels were markedly elevated in BM patients (24.05 ng/ml ± 39.82 ng/ml). The study found a strong correlation between elevated CSF lactate and serum PCT levels with the diagnosis of BM ($P < 0.05$).

Conclusion: CSF lactate levels and serum PCT are reliable biomarkers for diagnosing BM. Their elevated levels in BM patients compared to those with tuberculous or viral meningitis can assist in accurate and timely diagnosis, contributing to improved patient outcomes and effective antibiotic stewardship.

Keywords: Meningitis, Bacterial Meningitis, Cerebrospinal Fluid, CSF Lactate, Serum Procalcitonin, Biomarkers, Diagnosis.

INTRODUCTION

The intricate relationship between the cerebrospinal fluid (CSF) and serum biomarkers in diagnosing pyogenic meningitis represents a crucial frontier in medical research (1). Meningitis, characterized by the inflammation of the meninges surrounding the brain and spinal cord, is a condition that can have devastating consequences if not promptly and accurately diagnosed (2, 3). The meninges, comprising the dura mater, arachnoid mater, and pia mater, serve as a protective barrier for the brain, and their inflammation can be indicative of meningitis caused by various pathogens, including bacteria, viruses, fungi, and tuberculosis, as well as non-pathogenic agents (4).

One of the primary diagnostic tools for meningitis is the analysis of cerebrospinal fluid (CSF), which bathes the brain and spinal cord within the subarachnoid space (5). The examination of CSF parameters such as cell counts, proteins, glucose, adenosine deaminase (ADA) levels, lactate levels, and culture & sensitivity plays a pivotal role in the diagnosis of meningitis (6). A lumber puncture, typically performed between the L3-L4 or L4-L5 vertebrae, is used to obtain CSF (7, 8). The immediate analysis of this fluid is essential for timely diagnosis and the initiation of empirical therapy, which significantly reduces morbidity, mortality, and long-term complications, especially in children.

Recent studies have shed light on the diagnostic and prognostic value of serum biomarkers in detecting bacterial infections, with particular focus on serum procalcitonin (PCT) levels. Wolf et al. (2019) explored the role of PCT as an early marker of sepsis, highlighting its potential utility in guiding antibiotic therapy (9). The study emphasized the need for sensitive and specific biomarkers

Journal of Health and Rehabilitation Research 2791-156X JHRR

for definitive diagnosis, considering the limitations of current indicators like C-reactive protein, lactate, presepsin, and cytokines such as IL-1 and IL-6 (10).

Goodrich et al. (2020) conducted a multisite retrospective review, finding that serum WBC count, CRP, procalcitonin, CSF WBC count, CSF neutrophil percentage, and CSF protein were significantly higher in patients with bacterial organisms compared to viral organisms (11). This underscores the importance of these biomarkers in distinguishing between bacterial and viral meningitis.

Araujo et al. (2020) utilized tandem mass spectrometry to measure concentrations of specific compounds in cell-free CSF samples from various patients (12). Their findings revealed that certain compounds equaled CSF cell count in distinguishing bacterial meningitis from viral meningitis/encephalitis and autoimmune CNS disorders, with higher sensitivity and negative predictive value.

Rajial et al. (2020) compared CSF and serum PCT levels in neonates to determine optimal cutoffs for diagnosing meningitis, highlighting the utility of these biomarkers in neonatal populations (13). Similarly, Kurdyumova et al. (2021) aimed to establish reference values for laboratory parameters in diagnosing neurosurgical meningitis, identifying specific thresholds for CSF cytosis, lactate, glucose, and CSF/blood glucose ratio as diagnostic indicators (14).

Huang et al. (2022) analyzed clinical characteristics and laboratory findings of cryptococcal meningitis patients, finding that increased CSF/serum albumin quotient was indicative of unfavorable outcomes in HIV-negative patients (15). Fisher et al. (2021) provided an evidence-based summary for the emergency medicine evaluation and management of cryptococcal meningitis, noting the high sensitivity and specificity of newer cryptococcal antigen tests both in serum and CSF (16).

Finally, Obreja et al. (2022) described the CSF analysis in meningitis cases, emphasizing neutrophilic pleocytosis, elevated protein level, decreased ratio of CSF glucose to serum glucose, and elevated lactate level as key diagnostic indicators (17). These studies collectively demonstrate the evolving landscape of meningitis diagnosis, where the integration of CSF and serum biomarkers is crucial for accurate and timely identification of the disease, ultimately improving patient outcomes.

The study's rationale centers on the urgent need to distinguish between bacterial and non-bacterial meningitis, a critical challenge in the accurate and prompt diagnosis of pyogenic meningitis, particularly in resource-limited settings and vulnerable populations (18). Focusing on the comparative efficacy of cerebrospinal fluid (CSF) lactate and serum procalcitonin (PCT) levels, the study aims to identify a more effective diagnostic marker for bacterial meningitis, thereby improving treatment strategies and antibiotic stewardship (19). This objective encompasses evaluating the sensitivity, specificity, and predictive values of these biomarkers across different age groups and healthcare settings, ultimately aiming to refine clinical guidelines and enhance patient outcomes in meningitis diagnosis.

MATERIAL AND METHODS

The observational study was meticulously conducted at the Neurology Department of Pak Emirates Military Hospital, following the receipt of approval from the institute's ethical committee, as per the letter numbered A/28/EC/525/23. The study spanned from February 23 to May 23, 2023, adhering to rigorous ethical standards. Informed consent was a cornerstone of the methodology; it was diligently obtained from all participants or their representatives in cases where patients were unconscious or drowsy. The purpose of the study was thoroughly explained to the participants, emphasizing its educational objectives.

Patient recruitment adhered to stringent inclusion and exclusion criteria. The study focused on patients who presented with clinical signs and symptoms of meningitis at the neurology department. A key inclusion criterion was that these patients had not received antibiotic treatment prior to their admission, either at home or at other medical centers. Moreover, the study was limited to adult patients, with an age threshold of 18 years and above. Importantly, only those patients without any known co-morbidities were considered eligible for inclusion, ensuring a more homogenous study group and reducing potential confounding variables.

Conversely, the exclusion criteria were comprehensive. Any patient who did not provide consent, or those below 18 years of age, were excluded. Additionally, patients presenting with co-morbidities or alternative diagnoses such as poisoning, hepatic, renal, septic, or metabolic encephalopathy were not considered for the study. This exclusion was pivotal in maintaining the study's focus on meningitis and avoiding diagnostic ambiguities.

Upon enrollment, comprehensive demographic data of all participants were collected. Diagnostic procedures began with a computed tomography (CT) scan of the brain, followed by a detailed analysis of cerebrospinal fluid (CSF), both conducted in the emergency department before any transfer to higher dependency units (HDU) or intensive therapy units (ITC). The CSF was subjected to a routine examination, including polymerase chain reaction (PCR) testing for Herpes Simplex Virus types 1 and 2, culture and sensitivity testing, and measurement of lactate levels. Concurrently, serum procalcitonin (PCT) levels were also obtained, prior to the initiation of any empirical therapy for meningitis. The analysis of CSF lactate levels was carried out using the SYNCHRON LX® 20 machine, while serum PCT was measured with the Lumitest® (Brahms, Germany). Reference values were adhered to, with CSF lactate levels considered normal between 1.1-2.4mmol/L and serum PCT levels deemed standard at <0.05ng/mL.

Journal of Health and Rehabilitation Research JHRR 2791-156X

The study's analytical focus was on comparing CSF parameters—specifically lactate, glucose, and protein levels—with serum PCT levels among patients diagnosed with bacterial meningitis versus those with other etiologies, such as tuberculous meningitis (TBM) and viral meningitis. A variety of descriptive and analytic tests were employed to assess these variables, maintaining rigorous statistical standards. A p-value of less than 0.05 was established as the threshold for statistical significance, ensuring that the study's findings were both robust and reliable. This comprehensive approach underscores the study's commitment to advancing the understanding of meningitis diagnostics through methodologically sound and ethically grounded research.

RESULTS

Total 55 patients were included in this study out of which 35 (63.60%) were males and 20 (36.40%) were females. The mean age of patients was 44.03 years (SD=15.11), the minimum age was 21, and the maximum was 76 years. The final diagnosis of Bacterial meningitis was confirmed in 30 (54.50%) patients, Viral meningitis in 15 (27.30%) and Tuberculous meningitis in 10 (18.20%), as shown in pie chart 1. 21 (70%) out of 30 patients with Bacterial meningitis, showed positive CSF culture. The mean value for CSF lactate level was 9.36 ± 7.95 mmol/L in patients with bacterial meningitis and 1.91 ± 1.41 mmol/L in patients with a diagnosis other than bacterial meningitis. The mean value for CSF glucose level in patients with bacterial meningitis was 1.41 ± 0.77 mmol/L as compared to 1.9 ± 0.55 mmol/L in patients with TBM and 3.74 ± 1.19 mmol/L in patients with viral meningitis. The CSF glucose level was lowest in patient with bacterial meningitis followed by TBM and Viral meningitis. The amount of proteins were also higher in patients with bacterial meningitis (mean 1235mg/ L ± 1131 mg/ L) as compared to 612mg/ L ± 189mg/ L in TBM and 405 mg/L ± 138mg/ L in viral meningitis. The higher levels of CSF lactate show direct relationship to diagnosis of Bacterial meningitis (P value 0.000) and inverse relationship to diagnosis of viral meningitis (P value 0.001) similar results for serum PCT were also seen. The serum PCT levels 24.05 ng/ml ± 39.82ng/ml in patients with bacterial meningitis were higher as compared to the other patients 1.66 ± 1.87. The different parameters of CSF and different etiologies of meningitis are given in table 1. Both CSF lactate and serum PCT levels were higher in patients with bacterial meningitis as shown in graph 1 and graph 2.

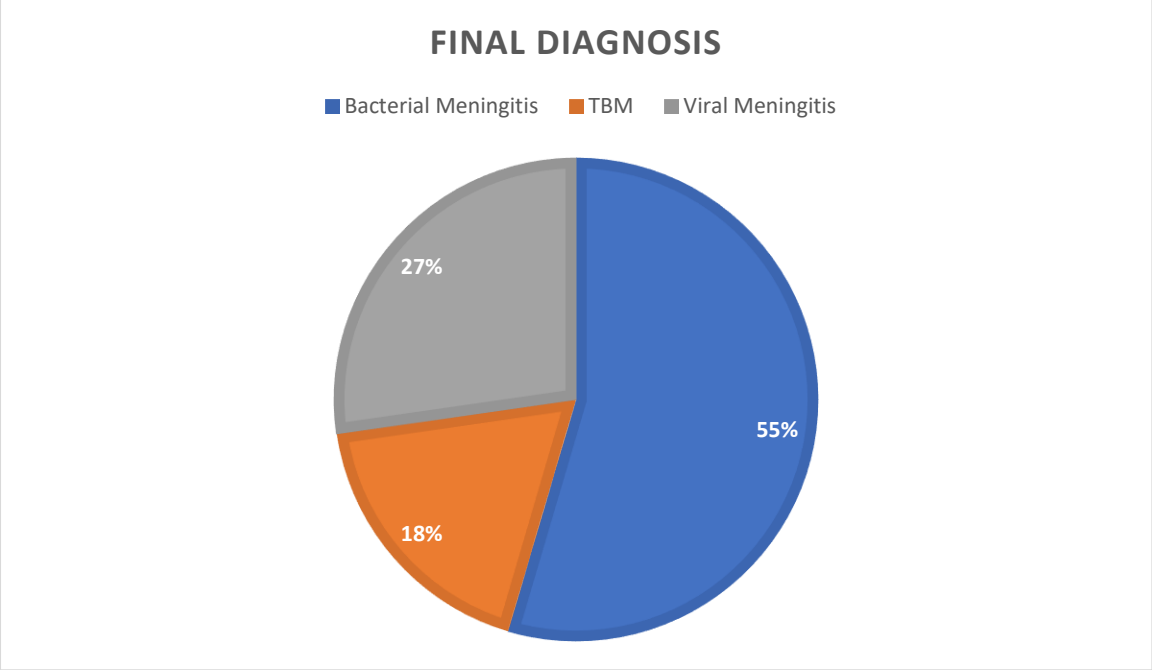

Figure 1 final diagnosis among patients with clinical sign and symptoms of meningitis.

Table 1 Different CSF parameters and etiology of meningitis

Parameters	Bacterial Meningitis	Viral meningitis	TBM	P value * < 0.05
CSF Cells	Predominantly Neutrophils	Predominantly lymphocytes	Predominantly lymphocytes	

Journal of Health and Rehabilitation Research 2791-156X JHRR

Parameters	Bacterial Meningitis	Viral meningitis	TBM	P value * < 0.05
CSF Glucose(mmol/L)	1.41 ± 0.77*	3.74 ± 1.19	1.9 ± 0.55	0.000
CSF Proteins (mg/ L)	1235 ± 1131*	405 ± 138	612 ± 189	0.002
CSF Lactate levels(mmol/L)	9.36 ± 7.95*	0.97 ± 0.13	3.33 ± 1.27	0.000
Serum PCT (ng/ml)	24.05 ± 39.82 *	0.77 ± 0.96	3.01 ± 2.14	0.007

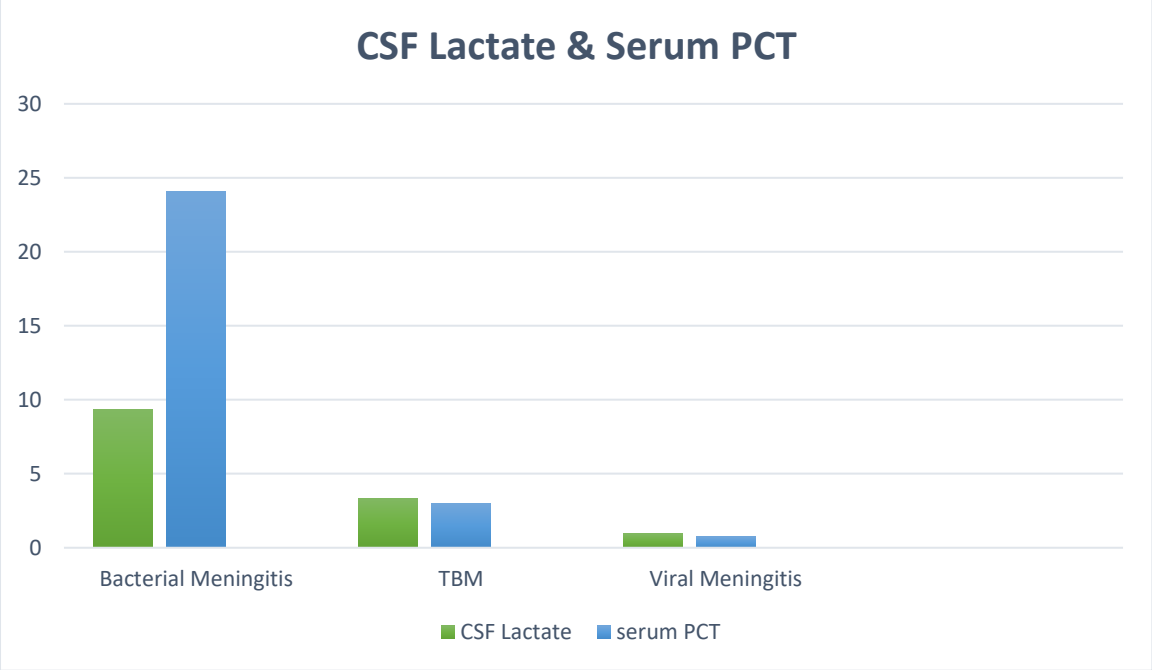

Figure 2 Higher levels of CSF lactate and serum PCT in patients with Bacterial meningitis

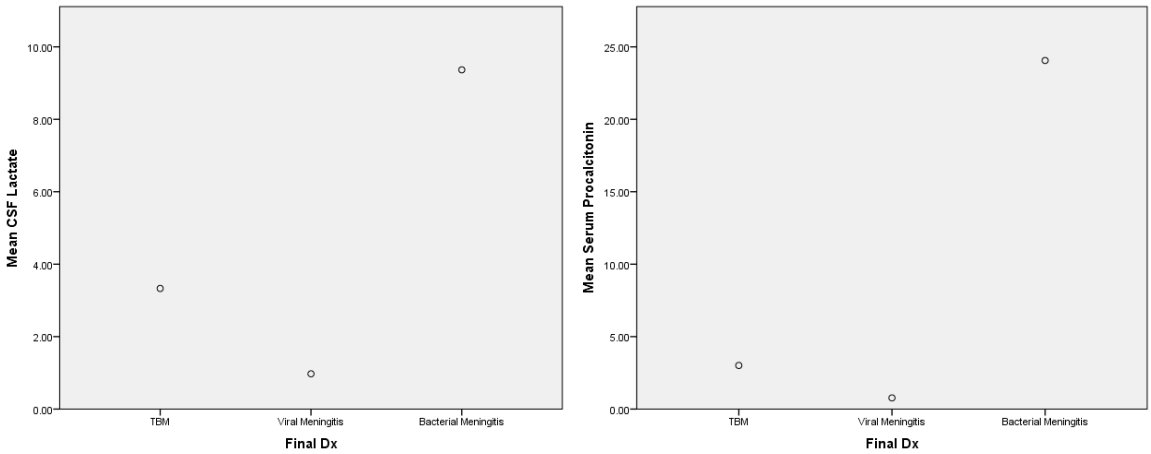

Figure 3 CSF lactate levels and Serum PCT levels in BM

DISCUSSION

The research conducted in our study provided valuable insights into the diagnostic utility of cerebrospinal fluid (CSF) lactate levels and serum procalcitonin (PCT) in identifying bacterial meningitis (BM). The study, undertaken with the dedicated collaboration of esteemed colleagues including Dr. Mubbasir and under the guidance of Prof. Muhammad Tariq Khan, yielded findings that contribute significantly to the existing body of knowledge on meningitis diagnostics.

Journal of Health and Rehabilitation Research 2791-156X JHRR

Our study's participant demographic showed a predominance of males over females, mirroring trends observed in similar studies. The elevated levels of CSF parameters, including glucose, proteins, and lactate, in patients with bacterial meningitis compared to those with tuberculous meningitis (TBM) and viral meningitis align with findings from other investigations. For instance, Huai et al.'s study highlighted the diagnostic value of CSF lactate in differentiating BM from non-bacterial meningitis, a result that resonates with our observations (20). Their study also provided insights into the pathophysiology behind elevated lactate concentrations in CSF, suggesting a potential link to decreased cerebral perfusion and anaerobic metabolism in BM, a hypothesis that aligns with our findings (21).

A study by Buch et al. explored the diagnostic implications of CSF lactate levels in early sepsis detection in BM patients (22). Although our study did not delve into the sepsis aspect, we observed parallel results regarding the association of lactate levels with BM. The similarity in lower CSF glucose and higher protein levels in BM patients between our study and Nitsch et al.'s work further strengthens the credibility of these biomarkers in diagnosing BM (23).

The importance of CSF lactate as a diagnostic biomarker in BM, particularly in children, was echoed in a study published in the Jornal de pediatria (24). Our study, which focused on an adult population, found similar elevated lactate levels in BM patients, suggesting a consistent diagnostic value across different age groups.

Our methodology included sending all CSF samples for lactate measurement using standard devices. This approach aligns with the study by Rousseau et al., which compared CSF lactate levels measured using arterial blood gas analyzers and conventional laboratory procedures, finding congruent results (25). This finding supports the viability of bedside CSF lactate measurement in diverse clinical settings, including emergency departments and intensive care units.

Bosworth et al. discussed the role of CSF lactate levels in guiding the treatment of meningitis, particularly in the context of empirical antibiotic use (26). Their findings underscore the importance of accurate diagnostic biomarkers in preventing unnecessary antibiotic administration and combating antibiotic resistance, an area of concern that our study also highlights.

The role of serum PCT in diagnosing BM was a focal point in our study, similar to the work of Zhang et al., who found elevated serum PCT levels in BM patients (27). Our results corroborate their findings, reinforcing the notion that serum PCT is a reliable biomarker in BM diagnosis, even in the absence of a corresponding study of C-reactive protein levels.

Furthermore, a systematic review and meta-analysis conducted by Velissaris et al. underscored the diagnostic value of serum PCT in distinguishing BM from viral meningitis, a conclusion that aligns with our own observations of marked elevation in serum PCT in BM patients (28).

Our study, alongside the Egyptian study by Wang et al., highlights the combined diagnostic utility of serum PCT and CSF lactate in differentiating BM from other meningitis etiologies (29). This combined approach enhances diagnostic accuracy, as evidenced by our findings and mirrored in the Iranian study conducted in Tehran, which examined various biomarkers in meningitis diagnosis.

In conclusion, our study affirms the significant role of CSF lactate levels and serum PCT as reliable biomarkers in differentiating BM from other forms of meningitis. Our findings contribute to the growing body of evidence supporting the use of these biomarkers in the diagnostic process.

The study, however, was limited by the small sample size and the exclusive focus on adult patients without co-morbidities. Future research, ideally encompassing a larger, more diverse population and including multi-center collaborations, would provide more comprehensive insights.

CONCLUSION

The conclusion of the study emphasizes the crucial role of cerebrospinal fluid (CSF) lactate levels and serum procalcitonin (PCT) as vital biomarkers in distinguishing bacterial meningitis (BM) from other forms of meningitis. The researchers observed a significant elevation in these markers in BM patients, in contrast to those with tuberculous and viral meningitis, underscoring their diagnostic value. These findings carry significant clinical implications, indicating that the concurrent assessment of CSF lactate and serum PCT could improve diagnostic precision, leading to more effective treatment approaches. This is particularly important in the realm of antibiotic stewardship, where accurate diagnosis is key to preventing unnecessary antibiotic use and addressing the growing issue of antibiotic resistance. The researchers advocate for integrating these biomarkers into standard clinical protocols, especially in emergency and intensive care units, to enable swift and accurate diagnosis, thereby enhancing patient outcomes in the management of meningitis.

Acknowledgment: Dr. Mubbasir and Prof. Muhammad Tariq Khan for their invaluable contributions and mentorship throughout this study.

Journal of Health and Rehabilitation Research JHRR 2791-156X

REFERENCES

1. Dittrich T, Marsch S, Egli A, Rüegg S, De Marchis GM, Tschudin-Sutter S, et al. Predictors of infectious meningitis or encephalitis: the yield of cerebrospinal fluid in a cross-sectional study. BMC infectious diseases. 2020;20(1):1-12.
2. Manyelo CM, Solomons RS, Walzl G, Chegou NN. Tuberculous meningitis: pathogenesis, immune responses, diagnostic challenges, and the potential of biomarker-based approaches. Journal of clinical microbiology. 2021;59(3):10.1128/jcm. 01771-20.
3. Shokrollahi MR, Shabanzadeh K, Noorbakhsh S, Tabatabaei A, Movahedi Z, Shamshiri AR. Diagnostic value of CRP, procalcitonin, and ferritin levels in cerebrospinal fluid of children with meningitis. Central Nervous System Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Central Nervous System Agents). 2018;18(1):58-62.
4. Nissen MS, Nilsson AC, Forsberg J, Milthers J, Wirenfeldt M, Bonde C, et al. Use of cerebrospinal fluid biomarkers in diagnosis and monitoring of rheumatoid meningitis. Frontiers in Neurology. 2019;10:666.
5. Singh L, Javali M, Mehta A, Pradeep R, Srinivasa R, Acharya P. Study of cerebrospinal fluid levels of lactate, lactate dehydrogenase and adenosine deaminase in the diagnosis and outcome of acute meningitis. Neurological Research. 2022;44(5):463-7.
6. Anil AA, Singh M, Ramakrishnan S, Roy NR. Cerebrospinal Fluid Adenosine De Aminase and Lactate Levels as a Rapid Diagnostic Marker for Tuberculous Meningitis among Adults. Annals of the Romanian Society for Cell Biology. 2021:4445-51.
7. Mondal SS, Sen I, Chandra A, Das M. The use of cerebrospinal fluid C reactive protein and adenosine deaminase as diagnostic markers in differential diagnosis of meningitis. J Med Sci Clin Res. 2018;6:10.18535.
8. Biswas B, Ghosh B, Mandal A, Saha D. Cerebrospinal fluid adenosine deaminase level as a diagnostic marker in adult tuberculous meningitis: a study conducted in a tertiary care hospital of Eastern India. International Journal of Basic & Clinical Pharmacology. 2020;9(6):849.
9. Wolf TA, Wimalawansa SJ, Razzaque MS. Procalcitonin as a biomarker for critically ill patients with sepsis: Effects of vitamin D supplementation. The Journal of steroid biochemistry and molecular biology. 2019;193:105428.
10. Sohrabi H, kholafazad Kordasht H, Pashazadeh-Panahi P, Nezhad-Mokhtari P, Hashemzaei M, Majidi MR, et al. Recent advances of electrochemical and optical biosensors for detection of C-reactive protein as a major inflammatory biomarker. Microchemical Journal. 2020;158:105287.
11. Goodrich N, Nabower AM, Rajbhandari P, Martin KC, Ekambaram M, Eisenberg J, et al., editors. 341. Clinical and Laboratory Data in Patients with Viral and Bacterial Meningitis in Conjunction with FilmArray Meningitis/Encephalitis Panel Use: A Multi-Site Retrospective Cohort Study. Open Forum Infectious Diseases; 2020: Oxford University Press US.
12. de Araujo LS, Pessler K, Sühs K-W, Novoselova N, Klawonn F, Kuhn M, et al. Phosphatidylcholine PC ae C44: 6 in cerebrospinal fluid is a sensitive biomarker for bacterial meningitis. Journal of Translational Medicine. 2020;18:1-8.
13. Rajial T, Batra P, Harit D, Singh NP. Utility of cerebrospinal fluid and serum procalcitonin for the diagnosis of neonatal meningitis. American Journal of Perinatology. 2020;39(04):373-8.
14. Kurdyumova N, Usachev DY, Savin I, Ershova O, Gadzhieva O, Shifrin M, et al. Nosocomial meningitis laboratory criteria in ICU patients: 5-year surveillance. Messenger of ANESTHESIOLOGY AND RESUSCITATION. 2021;18(5):47-56.
15. Lu Y, Ding M, Huang J, Fu C, Wan Y, Jiang J, et al. Clinical characteristics and image features of pulmonary cryptococcosis: a retrospective analysis of 50 cases in a Chinese hospital. BMC Pulmonary Medicine. 2022;22(1):1-8.
16. Fisher KM, Montrief T, Ramzy M, Koyfman A, Long B. Cryptococcal meningitis: a review for emergency clinicians. Internal and Emergency Medicine. 2021;16:1031-42.
17. Obreja M, Miftode EG, Stoleriu I, Constantinescu D, Vâță A, Leca D, et al. Heparin-Binding Protein (HBP), Neutrophil Gelatinase-Associated Lipocalin (NGAL) and S100 Calcium-Binding Protein B (S100B) Can Confirm Bacterial Meningitis and Inform Adequate Antibiotic Treatment. Antibiotics. 2022;11(6):824.
18. Younes HEB, Abdelsattar SA, Midan DAER, Abd Allah AA. Serum Procalcitonin as a Diagnostic and Prognostic Marker for Septic and Aseptic Meningitis. Egyptian Journal of Medical Microbiology. 2018;27(2):127-34.
19. Yekani M, Memar MY. Immunologic biomarkers for bacterial meningitis. Clinica Chimica Acta. 2023:117470.
20. Mwenda LA. An Examination of Lumbar and Ventricular Cerebrospinal Fluid Findings in Children with Tuberculous Meningitis and Hydrocephalus: Faculty of Health Sciences; 2019.
21. Faried A, Arief G, Arifin MZ, Nataprawira HM. Correlation of lactate concentration in peripheral plasma and cerebrospinal fluid with Glasgow outcome scale for patients with tuberculous meningitis complicated by acute hydrocephalus treated with fluid diversions. World Neurosurgery. 2018;111:e178-e82.

Journal of Health and Rehabilitation Research 2791-156X JHRR

22. Buch K, Bodilsen J, Knudsen A, Larsen L, Helweg-Larsen J, Storgaard M, et al. Cerebrospinal fluid lactate as a marker to differentiate between community-acquired acute bacterial meningitis and aseptic meningitis/encephalitis in adults: a Danish prospective observational cohort study. Infectious Diseases. 2018;50(7):514-21.

23. Goto R, Horiuchi Y, Kawakami H, Chikada A, Yasuda T, Takeuchi S, et al. Cerebrospinal fluid analysis is associated with enhancement on MRI in bacterial and tuberculous meningitis: A retrospective observational study. Clinical neurology and neurosurgery. 2022;212:107036.

24. Nazir M, Wani WA, Malik MA, Mir MR, Ashraf Y, Kawoosa K, et al. Cerebrospinal fluid lactate: a differential biomarker for bacterial and viral meningitis in children. Jornal de pediatria. 2018;94:88-92.

25. Rousseau G, Asmolov R, Auvet A, Grammatico-Guillon L, Guillon A. Can we use a point-of-care blood gas analyzer to measure the lactate concentration in cerebrospinal fluid of patients with suspected meningitis? Clinical Chemistry and Laboratory Medicine (CCLM). 2018;56(9):e247-e8.

26. Bosworth A, Bhatt K, Nance A, Winzor G, Atabani SF. Elevated lactate levels in the cerebrospinal fluid associated with bacterial meningitis. Journal of Infection. 2019;79(4):389-99.

27. Zhang L, Ma L, Zhou X, Meng J, Wen J, Huang R, et al. Diagnostic value of Procalcitonin for bacterial meningitis in children: a comparison analysis between serum and cerebrospinal fluid Procalcitonin levels. Clinical pediatrics. 2019;58(2):159-65.

28. Velissaris D, Pintea M, Pantzaris N, Spatha E, Karamouzos V, Pierrakos C, et al. The role of procalcitonin in the diagnosis of meningitis: a literature review. Journal of clinical medicine. 2018;7(6):148.

29. Wang Y, Li J, Yao M, Wang L, Ouyang B. Predictive value of cerebrospinal fluid lactate for the diagnosis and treatment efficacy of post-neurosurgery bacterial meningitis. 2019.