

Biochemical analysis of cerebrospinal fluid in a tertiary hospital in South South Nigeria: a one-year perspective.

Abstract

Aim: Cerebrospinal fluid analysis is an investigation routinely carried out in patients to make a diagnosis, exclude a diagnosis or treat infectious and non-infectious diseases of the nervous system. Analysis of cerebrospinal fluid could be biochemical, microbiological or hematological.

The aim of the study was to review the biochemical characteristics of cerebrospinal fluid over a one year period in a tertiary health facility.

Study Design; This was a retrospective descriptive study of the biochemical analysis of 106 cerebrospinal fluid (CSF) samples over a one year period in a tertiary health facility.

Methodology: Data on the age, sex, diagnosis of the patients and the results of the biochemical analysis of the CSF were analysed using the SPSS 24 and results presented as descriptive data.

Results: A total of 106 CSF specimen were analysed with only two specimen being from adults. Most of the specimen were from males while the most common diagnoses for requesting for CSF analysis were meningitis, sepsis and febrile convulsion. Most specimen were sent between the months of October, December and January to March with March receiving the highest number. The total number of CSF glucose results that were

low when compared to the plasma glucose was 45 which is 42.3%. A little higher than a fifth (19.8%) had increased protein levels.

Conclusion: The CSF biochemistry request pattern showed that most of the specimen were from the paediatrics department, with a higher male preponderance, the three main diagnoses were, meningitis, sepsis and febrile convulsions. 42.3% of the specimen had reduced glucose levels, while 21.2% had increased protein levels which are in keeping with the biochemical findings for bacterial meningitis.

Keywords Meningitis, Sepsis, Febrile convulsions, Cerebrospinal Fluid Analysis, Port Harcourt

Introduction.

The first mention of Cerebrospinal Fluid (CSF) occurred in the 16th century BC and was found in the Edwin Smith Papyrus.¹ However it was named in 1842 by Francois Magendie.¹ By 1891, the process of Lumbar puncture was described by Heinrich Quincke.¹ The CSF is found in the spaces around the brain and spinal cord. It is formed from blood by a special filtration process. It supplies nutrients to the central nervous system (CNS) and also provides a cushioning effect.^{1,2,3}

CSF analysis is done routinely on almost all paediatric patients that come into the hospital unconscious or with altered state of consciousness. General indications for CSF analysis include to make diagnosis, to exclude a diagnosis, for treatment and to monitor response to treatment especially in conditions such as infectious disease of the brain and spinal cord (meningitis, encephalitis), subarachnoid haemorrhage, neurosyphilis, Guillaine Barre syndrome, Alzheimer' s disease, and other autoimmune

disorders, meningeal carcinomatosis and secondary tumours affecting the CNS.⁴ CSF analysis is useful in differentiating between bacterial meningitis and non-bacterial meningitis² and should be instituted immediately any of the above is suspected.² It is also indicated in parasitic infections of the CNS, including but not limited to cysticercosis as well as malaria paragonimiasis, toxocariasis and onchocerciasis.^{3,5}

Analysis of CSF includes biochemistry, microscopy, culture and sensitivity, polymerase chain reaction (PCR), lactate dehydrogenase. More advanced analysis includes CSF treponema test, (which can be very crucial to the diagnosis of asymptomatic neurosyphilis) and Human Prion Disease, (which checks for unique proteins in the CSF).³

Biochemical analysis include analysis of CSF glucose, protein(total and specific), electrolytes (Na^+ , K^+ , Mg^{2+} and Cl^-), lactate and lactate dehydrogenase, glutamine and acid-base parameters and white blood cell count (total, and neutrophil count) The CSF glucose level is compared to the serum glucose level and a normal CSF glucose should be 60% of the serum glucose level.

Three laboratory indices used to make a diagnosis of bacterial meningitis with 99% accuracy includes a glucose value less than 1.89mmol/L (34mg per dL), protein of more than 220mg/dl (2.2g/L) and the presence of White Blood Cell (WBC) of more than 200U1 (2000 μL), neutrophils of more than 1.180 μL .⁶ The absence of these 3 criteria however does not exclude the presence of bacterial meningitis.

The statistics for meningitis from a six and a half month report by WHO from October 2022 to mid April 2023 noted that the case fatality ratio of meningitis was 7%. This

is the ratio of the number of people who died of meningitis out of the number of people who were confirmed to have meningitis in the entire Nigeria. ⁷ From this report Rivers State falls within the zone of States that had the least incidence of meningitis. Some states had no record at all. ⁷

The gold standard for obtaining CSF is by a lumbar puncture which is a sterile procedure. Other methods include during an intra operative procedure and a cisternal tap. ⁸ And should only be performed by experienced and trained personnel.

Most reports on CSF analysis have been on the microbiological and culture ^{9,10,11} and few on biochemical pattern of CSF analysis.¹¹ The biochemical pattern of CSF analysis from our hospital has not been reported. The Aim of this study is to evaluate the biochemical presentation of patients who require CSF analysis and establish if the biochemical presentation corresponds with any other pattern previously published in Nigeria.

Methodology

Study Design

This is a descriptive retrospective study design. The record for one year of all CSF analysis done in the hospital was extracted. A total of 106 CSF specimen were sent to the Laboratory for analysis. The protein and glucose levels were assayed in each specimen as well as a concomitant plasma glucose assay.

Study area; this Study was carried out in the University of Port Harcourt teaching hospital, one of the two tertiary hospitals in Rivers State, Nigeria. It has over 500

beds and caters for over 400, 000 outpatients per annum. These patients come from within and outside the state.

Sample size; All 106 specimen that came into the laboratory for the duration of one year.

Data collection. The data extracted from the records were the age, sex, clinical diagnosis, month of request, plasma glucose and CSF protein and glucose values. The results obtained were compared with the standard range and described as normal or abnormal. The above data was imputed into Microsoft excel and analyzed using the IBM SPSS version 24. The results are presented as descriptive data - simple percentages, frequencies, tables and charts.

Results

A total of 106 CSF specimen were sent to the laboratory over a period of one year. Out of these only 2 were from adults and the remaining children.

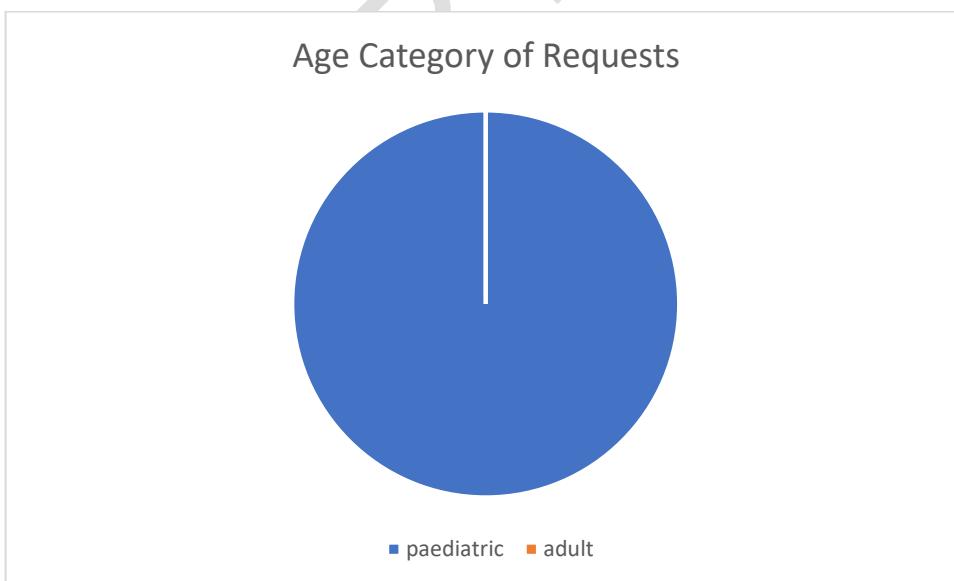


Fig 1-Pie chart showing Age Category of Requests

We had 72 males and 32 females and 2 unaccounted for as the sex column on the forms were not filled.

The most common diagnoses were meningitis, sepsis, febrile convulsions, and hydrocephalus. Others include retinoblastoma, neonatal jaundice, urinary tract infection, severe malaria, and asphyxia.

The most prominent age group was the 7–12months age group which accounted for 30.2% (32). Others were neonates 23.6% (25), the 5 weeks to 6 months age group 16% (17) , the 2–4 years group 12.2% (13) and then other groups.

Months and CSF analysis requests

The frequency by month showed that March, February, January, October and December, had the highest request for CSF analysis

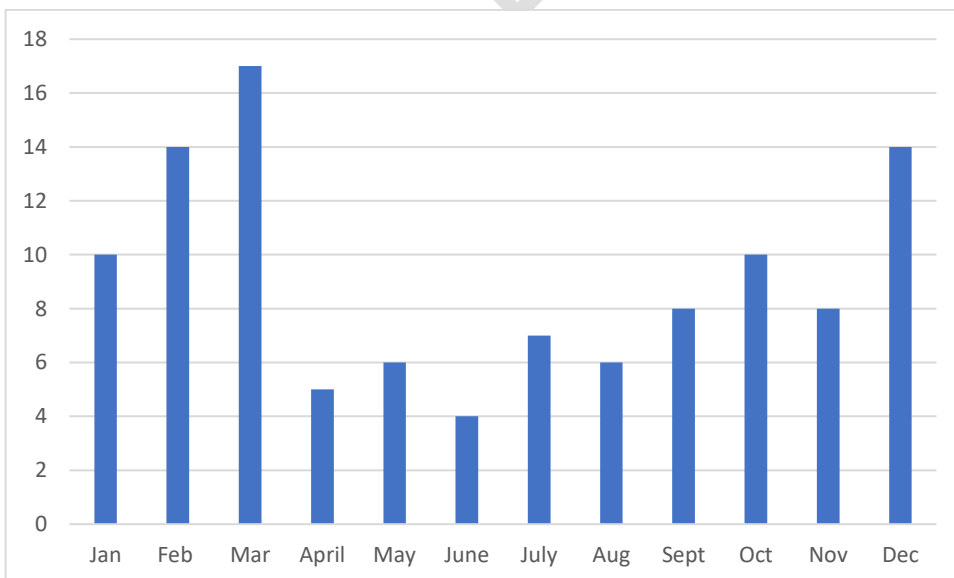


Fig 2- Bar graph showing Frequency of requests per month

The CSF specimen were all sent with a concomitant random blood glucose specimen except one. Twelve of the results were above the reference range for CSF glucose. Out of these, one of them did not have a corresponding plasma glucose value. Five of the CSF were lower than expected when correlated with plasma glucose, three had values that were higher than expected and three had correlated values.

Twenty six of the CSF glucose values were low when compared to the plasma glucose values even though they were within the expected reference range. Twenty of the CSF protein values were higher than the reference range for age. Nine had the typical biochemical result of low glucose and high protein and signified bacterial meningitis. All the rest of the results were within the reference ranges.

DISCUSSION.

Most (98%) of the request for CSF analysis came from the paediatric department. This is not unusual as children are more affected with meningitis than adults.

A study done in China among children less than five years reported that children less than six months represented more than half of those with confirmed meningitis.¹² In our study, most of the requests came from the less than six months age group. The total frequency for neonates (23.6%) and the five weeks to six months age group (16%) is 39.6%.

A global estimate on paediatric under five deaths reported that meningitis/encephalitis and neonatal sepsis accounted for two out of the top three causes of death.¹³ This is almost the same as in this study, meningitis had the highest frequency followed by all cause sepsis and then febrile convulsions.

Rivers State is in southern Nigeria and below the meningitis belt of Nigeria.¹⁴

Therefore, the incidence of meningitis is far lower than in the northern countries.

Peak season of meningitis is between December and June yearly in Nigeria.¹⁴ In general, using the requests for CSF biochemistry as a whole, the months with the highest frequencies in our study, overlapped slightly. The highest were October to March. These are the dryer months in the south when compared to the dry months in the north with the determining frequencies for the nation.

Among Children it has been found that there was a slightly higher preponderance of meningitis in males than females.^{15,16} In our study we had far more requests from males than females, however, this request covered all diagnosis and not just meningitis.

The next most common diagnosis was sepsis, including neonatal and post neonatal sepsis. Sepsis is the most important cause of death in paediatric age group all over the world.¹⁷ Males are more at risk as well.¹⁸ The type of specimen required to be sent to the laboratory for culture and also chemistry are blood, CSF (as soon as a lumbar puncture is feasible) and urine.¹⁸ Neisseria Meningitis, group B streptococcal and H influenza have been implicated in Paediatric sepsis.¹⁷ The need for full immunization coverage will be discussed below.

The third most common diagnosis in this study was febrile convulsions. Febrile convulsion is an umbrella term for convulsions that occur within a certain age group in children (6 to 60 months).^{19,20} with a temperature above 38 degrees Celsius.¹⁹ It is very common with 2-4% of children experiencing febrile convulsions.¹⁹ Febrile

convulsions are divided into two, simple and complex.¹⁹ A thorough investigation is necessary to exclude any serious underlying condition.¹⁹ The presence of bacterial meningitis should be excluded as a quarter of children with bacterial meningitis will present with convulsions.²⁰ Children with complex febrile convulsions should have a CSF analysis done.²⁰ Ideally the likelihood of some causes of meningitis in young children is low among those who have been vaccinated against H. Influenza and Strep Pneumonia.^{20,21} Febrile convulsions occur slightly more frequently in males than in females.¹⁹

Hepatitis B vaccine was added to the national programme of immunization (NPI) in Nigeria in 2004²² while H influenza and Pneumococcal vaccines were introduced in 2012. Studies have shown that less than 50% of children in Nigeria are fully immunized.²² Hence the likelihood of these infections is higher in the affected population.

This buttresses the fact that children with febrile convulsions in Nigeria would require CSF analysis.

Over all males are more at risk for the three most common diagnosis and this agrees with the overall male/ female distribution of the request that we had.

A total of 11.3% (which is equivalent to 12 specimen) of the results had CSF glucose values above the reference range. (CSF glucose values are ideally 60% that of plasma). Various factors can account for this and include, stress induced hyperglycaemia that sometimes occur in meningitis, post prandial hyperglycaemia, the effect of glucose based infusion and if the plasma glucose specimen is collected at a

different time from the CSF). Out of these five were lower when compared with plasma glucose levels. Three were as expected, three were slightly higher and one did not have a plasma glucose value.

Thirteen of the results had CSF glucose values that were lower than the reference range. Out of these when compared to plasma glucose, 10 were lower still.

The total number of CSF glucose results that were low when compared to the plasma glucose was 45 which is 42.3% and out of this the diagnosis with the highest frequency²³ was meningitis. Bacterial meningitis typically presents with reduced CSF glucose levels, so this is in keeping.

A little higher than a fifth (21.2%) had increased protein levels. Out of this, meningitis accounted for a fifth, and hydrocephalus related issues accounted for one seventh. Other miscellaneous causes were retinoblastoma, sepsis and febrile convulsions. A whopping 38% had no diagnosis attached to them. Just one specimen met the biochemical criteria for the diagnosis of bacteria meningitis with a CSF glucose level of 1.9mmol/L (which is borderline) and a CSF protein level of above 220mg/dl. However, that specific specimen did not have a diagnosis.

Limitation of the study

Effective interpretation of the biochemical results was not completely possible on account of improperly filled request forms. The importance of filling a form completely and perfectly cannot be over emphasized. It also aids in epidemiological studies such as this.

Conclusion

The CSF biochemistry request pattern showed that most of the specimen were from the paediatrics department, with a higher male preponderance, the three main diagnosis were, meningitis, sepsis and febrile convulsions. 42.3% of the specimen had reduced glucose levels, while 19.8% had increased protein levels which are in keeping with the biochemical findings for bacterial meningitis.

Recommendations

All laboratory request forms sent out should be properly filled. If there are no forms and one has to adapt, all details need to be written down. Constant campaign for full grass root immunization coverage is necessary.

References.

1. Czarniak N, Kamińska J, Karna JM, Koper-Lenkiewicz OM. Cerebrospinal fluid - basic concepts review. *Biomedicines* 2023;1(5):1461-1484
2. Young N, Thomas M. Meningitis in adults: diagnosis and management. *Intern Med J.* 2018;48(11):1294 - 1307
3. Gonzalez H, Koralnik IJ, Marra CM. Neurosyphilis. *Semin Neurol* 2019;39(4):448 - 455
4. Hrishi AP, Sethuraman M. Cerebrospinal Fluid (CSF) Analysis and Interpretation in Neurocritical Care for Acute Neurological Conditions. *Indian J Crit Care Med.* 2019 Jun;23(Suppl 2):S115-S119
5. Carpio A, Romo ML. Parasitic diseases of the central nervous system: lessons for clinicians and policy makers. *Expert review of neurotherapeutics.* 2016;16(4):401-414
6. Shahan B, Choi EY, Nieves G. Cerebrospinal fluid analysis. *Am Fam Physicians.* 2021;103(7):421-428

7. WHO. Disease Outbreak News. Meningitis Nigeria. April 27, 2023. <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON454>
8. Jane LA, Wray AA. Lumbar puncture. StatPearls[Internet] 2023;07(24):1-10 https://www.ncbi.nlm.nih.gov/books/NBK557553/#__NBK557553_dtls__
9. Eberechukwu Y, Awopeju A (2016). Neonatal CSF analysis as seen at the University of Port Harcourt Teaching hospital; a five year review. *Advances in Microbiology*. 2016;06:247-250. 10.4236/aim.2016.64024.
10. Awulachew E, Diriba K, Awoke N. Bacterial Isolates from CSF Samples and Their Antimicrobial Resistance Patterns Among Children Under Five Suspected to Have Meningitis in Dilla University Referral Hospital. *Infect Drug Resist*. 2020;13:4193-4202. doi:10.2147/IDR.S264692
11. Akinjinmi AA, Olasunkanmi OI, Akingbade OA, Onajobi IB, Okerentugba PO, Okonko IO. Biochemical and Bacteriological Profiles of Cerebrospinal Fluids of Children with Presumed Sepsis in a Tertiary Hospital in Abeokuta, Ogun
12. Kim SA, Kim DW, Dong BQ, Kim JS. An expanded age range for meningococcal meningitis: Molecular diagnostic evidence from population-based surveillance in Asia. *BMC Infectious Diseases* 2012;12(1):310
13. Wright C, Blake N, Glennie L, Smith V, Bender R, Kyu H, et al. The Global burden of Meningitis in Children: Challenges with Interpreting global health estimates. *Microorganisms*. 2021;9(2): 377
14. Omoleke SA, Kanmodi KK. Seasonal Meningococcal Meningitis Outbreaks in Nigeria: A Need for an Accelerated Introduction of a Conjugated Meningococcal Vaccine into the National Routine Immunization Schedule. *International Journal of Medical Research & Health Sciences*. 2020;9(6):31-37
15. Green MS, Schwartz N, Peer V. A meta-analytic evaluation of sex differences in meningococcal disease incidence rates in 10 countries. *Epidemiol Infect*. 2020;148:e246
16. NORD. Meningococcal Meningitis. Rare Diseases. 2015 <https://rarediseases.org/rare-diseases/meningococcal-meningitis/>
17. Randolph AG, McCulloh RJ. Pediatric sepsis, Important considerations for diagnosing and managing severe infections in infants, children, and adolescents. *Virulence* 2014;5(1):179 - 189
18. Tesini BL. Neonatal Sepsis (Sepsis Neonatorum). MSD Manual Professional Version. 2022 [Infections in Neonates in Paediatrics] <https://www.msmanuals.com/professional/pediatrics/infections-in-neonates/neonatal-sepsis>

19. Al-Ajlouni SF, Kodah IH. Febrile convulsions in children. *Neurosciences* 2000;5(3):151-155
20. Eilbert W, Chan C. Febrile seizures: A review. 2022;3(4):e12769
21. Carroll L, Odendal L. Febrile Seizure Clinical Pathway in Johns Hopkins All Children's Hospital (pub) 2022:1-12
22. Sadoh AE, Eregie CO. Timeliness and Completion Rate of Immunization among Nigerian Children Attending a Clinic-based Immunization Service. *J Health Popul Nutr.* 2009 Jun; 27(3): 391 - 395
23. Nte AR, Yarhere IE. A study of childhood malaria trends at the University of Port Harcourt Teaching Hospital: 2006 - 2018. *Niger Med J* 2023;64(2): 272-280

UNDER PEER REVIEW