Academic Journal of Medical Sciences
ISSN: 2708-2725
ORIGINAL ARTICLE

Estimation of Serum Osmolarity and CRP in Pediatric Patients with Central Nervous System Infections

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Funding information
Self-funded

Conflict of interest
None declared by author

ABSTRACT

Background: *Central nervous system infections are an important cause of morbidity and mortality in children.*

Objective: *Estimation level of osmolality in serum of pediatric patients with central nervous system infections.*

Method: *This Cross-sectional prospective study included all infants and children who were admitted in Pediatric Neurological ward at CWTH, Baghdad, Iraq from November 1, 2020, to November 1, 2021. Patient were Diagnosed and treated as cases of CNS infection according to clinical symptoms, general workup and CSF finding all together with the assistance of CSF Culture (if positive). children's age: between 1 month and 13 years of both sexes, c-reactive protein (CRP), renal function test and electrolyte to calculate osmolality.*

Result: *There was significant difference between groups regarding age, admission duration, cerebrospinal fluid cells, cerebrospinal fluid glucose, and CRP, group C also managed by multiple courses of antibiotics and multiple antiseizure drugs during admission, in compared to other groups.*

Conclusion: *CSF's Protein was insignificant in pediatric patients with CNS infection, CSF's Sugar was significantly different in between groups A and C (P<0.001), also between group B and C (p=0.0106) while there were no significant difference between group A and B . CRP significantly different among the groups, however, a significance difference between group A and C, while no significant differences between groups A vs. B and B vs. C. No significant differences in osmolality were found between groups.*

Keywords: serum osmolality; pediatric patients; central nervous system infections.

1. INTRODUCTION

Infections of the central nervous system (CNS) are an important cause of morbidity and mortality in children, according to literatures and published reports, CNS infections are more incident among pediatric population, particularly the infants. In newborns, the incidence range was estimated at 400 per 100,000 newborns while in older childern at or under the age of two years, the rates was much lower and it was estimated at 20/100,000 of this pediatric population (1). The entry of glucose into the brain ISF is governed by the capillary endothelial cell membrane through the transporters (2). The normal concentration levels of plasma glucose ranged between 70-120 mg/dL while in CSF the concentration id usually lower, however, CSF glucose levels ranged between 45-80 mg/dL, in other words, the CSF concentration of glucose is about two-third of that in plasam. Nonetheless, the glucose often balanced between ISF and CSF. It has been thought that higher metabolic rate for glucose attributted to the decline in its plasma level and this is considered as a sign of the higher metabolic rate. From other point of view, hypoglycorrhachia (glucose concentration of (<40) mg/dL in the CSF or CSF to plasma glucose ratio (less than two-third) are denoted as abnoormal (3). Moreover, in certain circumstances, the CSF glucose concentration may reachs very low levels which may be undetectable on laboratory testing. These very low levels linked to ABM as the most often characteristic. In fungal On the other hand, in some infections that caused by tubberculous, fungi, protozoa, parasites and spirocheats are frequently associated with mild to moderately low concentrations. However, in viral infections low concentration of glucose in the CSF is not common despite it can also be observed in some cases. Moreover, lower levels of CSF glucose can be seen in some non-infectious states such as subarachnoid hemorrhages, meningeal carcinomatosis, plasma hypoglycemia, chemicl meningitis and sarcoidoisis (4).

In a variety of causes of meningeal inflammation there is an increase in the utilization of glucose by the brain and the spinal cord adjacent to the CSF which lead to lowering in the glucose concentration in the CSF. Also, leucocytes, particularly, polymorhoneuclear cells play a role in the lower CSF glucose concentration through utilization of glucose. Other cause of lower CSF concentration attributted to the inhibition of glucose transport to the CSF. Studies have shown that decreased CSF glucose concentration below 20 mg/dL at the time of admission could be associated with hearing loss (5).

The endothelial glucose transporters' saturability only permits a partial parallel increase in the CSF glucose concentration in the presence of plasma hyperglycemia. Acute changes in plasma glucose concentration are maximum reflected in the CSF concentration after 2 hours, and equilibration following a transient change can take up to 4 hours. Diabetic patients without meningitis symptoms can have CSF to plasma glucose ratios of less than one third (6). Therefore, after the patient fasts for four hours, a concomitant plasma glucose measurement is necessary for the best interpretation of the CSF glucose level (3). The blood–CSF barrier keeps the majority of plasma proteins out of the CSF, hence the protein content of CSF is very low in comparison to plasma concentrations (7). Neonates have a higher total protein content than older infants and children (8,9). The anatomical region from which the CSF is sampled can also affect the protein levels. The CSF protein concentration in healthy infants and adults is 6–15 mg/dL in the ventricles, 15–25 mg/dL in the cisterna magna, and 20–50 mg/dL in the lumbar sac (10). This concentration gradient is caused by regional variations in the permeability of the blood–CSF barrier (11). Osmolar changes correlate linearly with CNS state, and measurement of serum and urine osmolality can assist in prediction of morbidity and mortality in children with acute CNS disease. The purpose of our work is to highlight the value of serum osmolality measurement as a neurological morbidity indicator (12). Several neurologic conditions linked to the breakdown of the blood–brain barrier cause a slight increase in the lumbar CSF protein content, between 45 and 75 mg/dL in older infants and adults. This process can be seen on neuroimaging as vasogenic cerebral edema and contrast enhancement of the leptomeninges. Patients with meningitis and subarachnoid hemorrhage have higher CSF protein concentrations (>500 mg/dL), which may slow the rate at which proteins are absorbed from the CSF and raise protein levels even further (13).

Aim of study: To describe the results of brain MRI of infants and children with CNS infection, and how much these brain MRI findings can assist diagnosis and treatment of CNS infection,

2. METHODOLOGY

This Cross-sectional prospective study included all infants and children who were admitted in Pediatric Neurological ward at CWTH, Baghdad, Iraq from November 1, 2020, to November 1, 2021. Patient were Diagnosed and treated as cases of CNS infection according to clinical symptoms, general workup and CSF finding all together with the assistance of CSF Culture (if positive). children's age: between 1 month and 13 years of both sexes, c-reactive protein (CRP) , renal function test and electrolyte to calculate osmolality.

Statistical Analysis

After finishing the second entry, all data related to Age, Admission duration, CSF findings (Cells, Protein, Sugar), CRP Titer, and Osmolality were recorded in a statistical program called GraphPad Prism 8 version 8.0.2 (263), January- 2019. The data entry was as groups, plotting the Y-value for each point, using main column effect, the 2way ANOVA multiple comparisons was carried on using Tukey's multiple comparisons test. Tukey's multiple comparisons test used to test the significance of associations between discrete variables. The level of significance was set at P value equal to 0.05 (14)

3. RESULTS

The total numbers of participants were 101 patients, The differences between all groups whether A, B and C for CSF's Neutrophils, CSF's Lymphocytes and CSF's Protein was insignificant as seen in (**Figure 1**). The difference in the CSF's sugar concentration in between group A and C was significant($P<0.001$), also between group B and C ($p=0.0106$) while there were no significance difference between group A and B, (**Figure 2**). All low CSF glucose samples were compared to Blood glucose; they were less than 2/3 of blood glucose which indicates low CSF glucose. The CRP was significantly different within the groups in general, however,a significant difference between group A and C was found but no significant differences between groups A vs. B and B vs. C, , (**Figure 3**)..

Regarding Osmolality, there was no significance differences between groups A, B and C as illustrated in (**Table 1**).

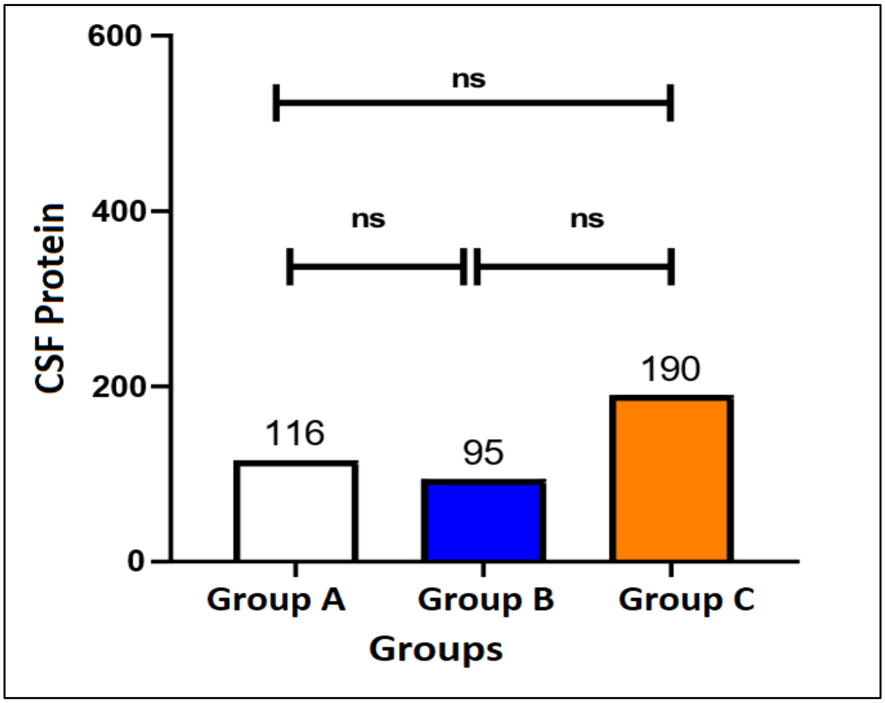

Figure 1. CSF's Protein distribution within the groups

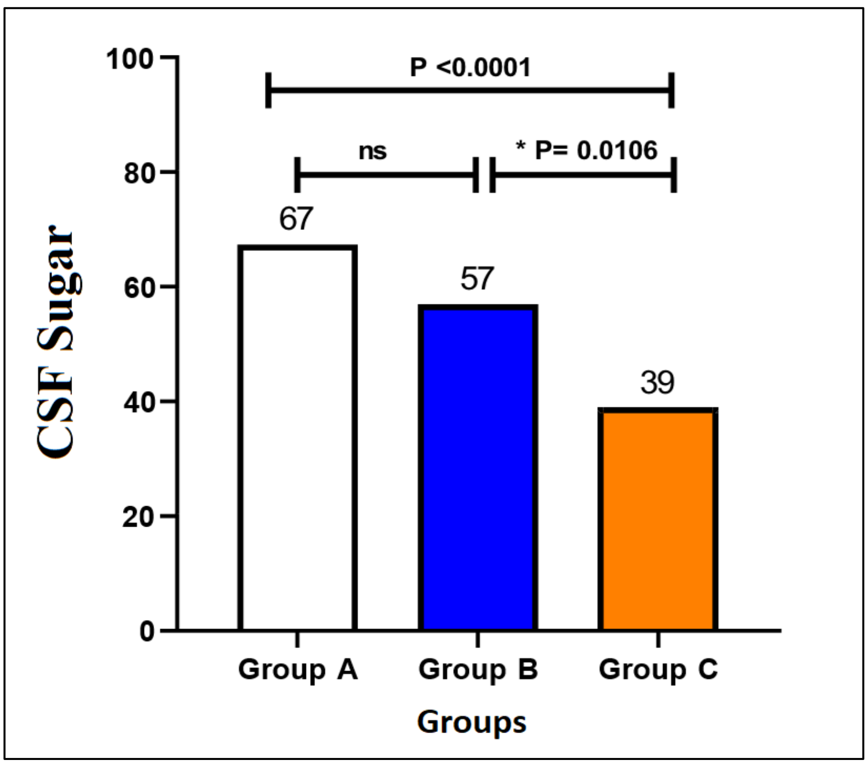

Figure 2. CSF's Sugar distribution within the groups

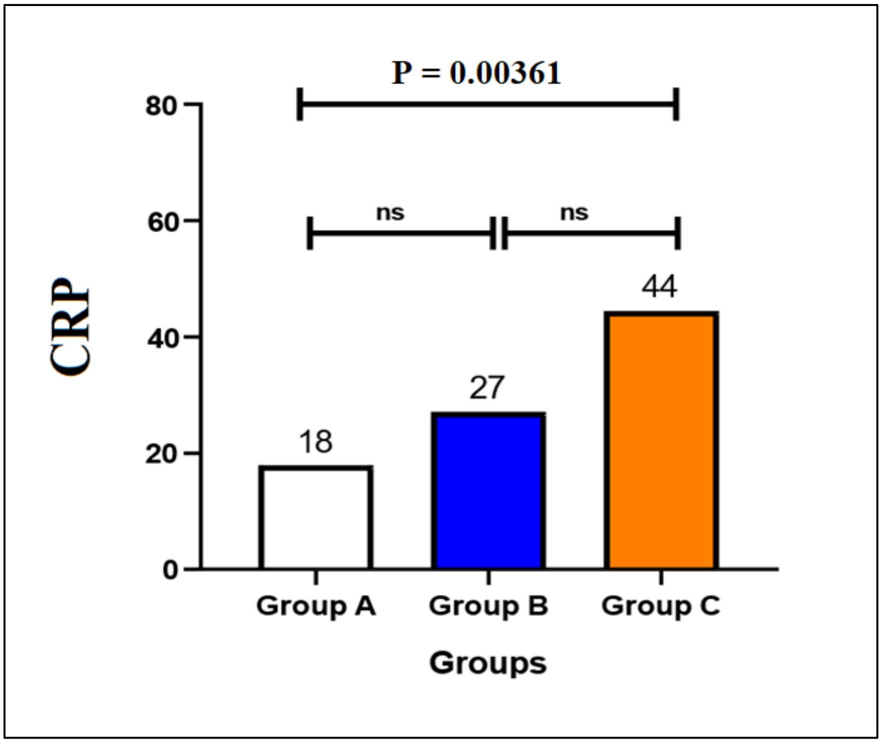

Figure 3. CRP distribution within the groups

Table 1. Mean serum osmolality among groups

Group	Osmolality (mOsm/kg)
Group A (n=12)	293.3
Group B (n=40)	293.7
Group C (n=49)	294.7

* Normal values range from 275 to 295 mOsm/kg

4. DISCUSSION

This study Goals do not aim to differentiate between different Types of CNS infections whether bacterial, viral, and fungal or other organisms but to find the aid and impact of neuroimaging finding on patients with CNS infection. The distribution of CSF findings among groups showed a significant difference regarding CSF's WBCs between group A and B, and Group B and C, while no significance association between group A and C, however There was no statistical significance between groups regarding CSF neutrophils, lymphocytes, and protein. CSF glucose was found to be significantly low in group C in compared to group A and B while there was no significant difference between group A and B, Baud et al. observed in their study concluded that 50.1% of cases with microbial infections had a CSF glucose concentration of less than 40 mg/dL (Hypoglycorrhachia), however, moderate to high specificity was reported for the performance of absolute CSF glucose concentration and CSF/Plasma glucose ratio as predictors and diagnostic for microbial meningitis (15). In a Japanies study published in 2014, Tamune et al. concluded that CSF to blood glucose ratio can serve as good predictor in detection of bacterial meningitis and also it can help to rule out bacterial meningitis when there is negative results of cultures (16). In current study group C had the lower CSF glucose, so we can assume it is caused by bacterial etiology, which cause low CSF glucose in lower aged patients with subsequently positive neuroimaging findings(complications). Earlier studies that had been concentrated on CRP showed the value of CRP in differentiate between BM and AM, an example is a study performed by Sormunen et al. in Finland-1999, which documented the usefulness of CRP, because it was capable of distinguishing Gram stain -ve BM from viral meningitis with high sensitivity (96%), high specificity (93%), in children over 3 months of age (17). Javadinia et al. who investigate CRP in Iran/2019 confirmed the statistically significant ($p<0.001$) difference between septic and AM and there was 95% sensitivity and 86% specificity to differentiate septic and AM (18). In the current study, CRP shows significance difference between group A and C, which can be interpreted as group C having more septic meningitis than other groups and also it carried the lowest aged patients who are vulnerable to complications and subsequently positive neuroimaging findings. Both CSF and blood's CRP have shown to be highly sensitive in screeining for BM, but CSF's CRP screening showed higher specificity compared to blood's CRP , therefore, it can be a supportive tool when combined to other tests like CSF microbiology, biochemistry and cytology for dtection of meningitis (19). Our findings revealed no significance differences in the osmolality between groups, this finding agreed that reported by Powell et al (20) and supported the hypothesis that hypovolemia causes high serum arginine vasopressin concentrations in meningitis patients, which return to normal when enough sodium is administered to allow the kidney's proximal tubule to reabsorb water. Meningitis patients can get maintenance and replacement fluids, but they should be closely watched for the emergence of the syndrome of inappropriate antidiuretic hormone secretion. Usually, our practice to give 2/3 of the maintenance fluid, that's may clarify our results in which although there is no significance differences between groups, but blood osmolality were in the upper normal level (293, 294 and 295 for group A, B and C respectively), so it is better to give full maintenance fluid with monitor the development of syndrome of inappropriate anti-diuretic hormone.

5. CONCLUSIONS

1. CSF's Protein was insignificant in pediatric patients infected NCS.
2. The CSF's Sugar in between group A and C was found Stunningly significant ($p \geq 0.0001$), also between group B and C ($p=0.0106$) while there were no significance association between group A and B, respectively.
3. CRP significant differences within the groups, so there a significance differences between group A and C, while no significant differences between groups A and B, B and C. no significance differences in osmolality between groups

Ethical clearance

Ethical issues were approved by the authors in accordance with WMA declaration of Helsinki 2013 of the ethical principles for researches involving humans. Oral and signed consent were obtained from all parents/guardians of the included pediatric patients.

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Citation:

Mohammed A.M, Farhaan S.H, Abd Al-Hameed S,M Estimation of Serum Osmolarity and CRP in Pediatric Patients with Central Nervous System Infections. AJMS 2024; 11 (3):132-41