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ORIGINAL ARTICLE

Role of Transcranial Doppler Ultrasound in diagnosis of pediatric sepsis

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ABSTRACT

Background: Systemic inflammatory response syndrome (SIRS) is a systemic illness brought on by an infectious pathogen entering the body and causing production of inflammatory mediators. The purpose of this study was to investigate the use of transcranial Doppler ultrasound (TCD) in the detection of sepsis in children.

Methods: This case control study was carried out in the Department of Pediatrics in Zagazig University Hospital on 24 septic children and 24 non-septic while, TCD ultrasonography involved the use of a low-frequency (usually $\leq 3-5$ MHz) transducer. The probe is placed on the scalp, and the technique starts using the two-dimensional color-coded image. Once the appropriate blood vessel is isolated, pulsed wave Doppler is used to measure real-time blood flow velocity. TCD examination should be recorded bilaterally for at least 10 cardiac cycles after stabilization. In clinical practice, the most relevant scanning view is the temporal window, located on the line between the tragus and the external canthus. This window allows to identify the mesencephalon and the first segments of middle cerebral artery (MCA) at a depth of 30–60 mm according to the age, and to measure blood flow velocities, including peak systolic (VS) and end-diastolic (VD) velocities.

Results: Our study found no significant difference in Middle Cerebral Artery (MCA) peak systolic velocity (PSV) between septic patients and controls. However, we observed significantly lower pulsatility index (PI) and resistance index (RI) in the septic group. Similar to MCA findings, anterior Cerebral Artery (ACA) measurements showed significantly lower PI and RI in septic patients, with a slightly higher PSV. The lower PI and RI in our study might indicate decreased cerebrovascular resistance, possibly due to the inflammatory effects of sepsis on cerebral autoregulation. In our study, MCA_PI and MCA_RI showed strong negative correlations with heart rate, respiratory rate, and temperature, and strong positive correlations with blood pressure. This suggests that as sepsis severity increases (indicated by higher heart rate, respiratory rate, and temperature, and lower blood pressure), cerebral blood flow becomes less pulsatile and resistant.

Conclusion: Our study demonstrated that TCD can detect significant changes in cerebral hemodynamics in children with sepsis.

Key words: Transcranial Doppler Ultrasound; Applications; Septic Child

INTRODUCTION

Systemic vascular resistance (SVR) frequently falls as a result of a Gram-negative sepsis, which is an immune-mediated systemic illness. An infection is typically contained by the immune

system. We refer to this as a localized infection. White blood cells are produced by the body to accomplish this (1). To eradicate the infection-causing bacteria, white blood cells migrate to the infection site. This causes inflammation or swelling

of the tissue. This aids in combating the infection and stopping its spread. However, if the immune system is compromised or the infection is severe, it may spread to other areas of the body. Pervasive inflammation can disrupt blood flow and harm tissue (1).

Hyperdynamic systemic circulation with redistribution phenomena in many organ systems is the outcome. There is proof that if the SVR-index falls, the cerebral mean and end-diastolic blood flow velocities (BFV) in the middle cerebral arteries are markedly increased. In certain cases, a downstroke latent steal phenomena was seen in conjunction with a significantly decreased SVRI. The severity and prognosis of the disease were significantly correlated with TCD abnormalities (2). A moderate vasospasm of the basal cerebral arteries explains the elevated BFV. TCD seems to be a useful technique for keeping an eye on these individuals' cerebral hemodynamics. If patients have therapeutic or spontaneous hyperventilation, which TCD may be able to detect, they are especially vulnerable to ischemic brain damage (2).

The cardiac index is frequently elevated in septic shock patients. Regional hypoperfusion and blood flow maldistribution have been identified as major contributors to the pathophysiology of organ dysfunction in these patients. Cerebral blood flow and cardiac index in septic shock patients: Doppler ultrasonography techniques revealed a correlation between cerebral blood flow and cardiac index in septic patients. In septic shock patients, carotid flow was unaffected by mean arterial pressure, PaCO₂, and PaO₂ (3).

Outside of the neurocritical care setting, intracranial pressure (ICP), a signal that is crucial for directing treatment of patients with acute brain disorders, is frequently disregarded. This is mostly because of the inherent dangers of the intrusive methods that are currently available, which have made it impossible to monitor intracranial pressure in a variety of disorders that impact intracranial homeostasis, ranging from liver encephalopathy to mild traumatic brain injury (4).

In this situation, non-invasive ICP monitoring techniques (nICP) may enhance the clinical treatment of these disorders. The majority of the publications highlight one possible benefit of TCD, which is the ability to track variations in ICP over time. TCD-based techniques have an overall accuracy of about ± 12 mmHg and have a great deal of potential for tracking dynamic changes in ICP over time, especially those that are vasogenic (4).

The most common proximate causes of mortality for children admitted to pediatric intensive care units (PICUs) are neurological disorders, which are commonly encountered there. Since sedation sometimes prevents daily clinical examinations, managing neurological problems in critically sick children can be difficult (5).

These patients can be evaluated at the patient's bedside using transcranial Doppler (TCD) ultrasound, a non-invasive, easily accessible method for measuring and tracking cerebral blood flow in real time. The use of TCD to screen for sickle cell disease in children whose risk of a first stroke would be decreased by a blood transfusion is currently supported by strong evidence (4).

Because of TCD's ease of use and demonstrated diagnostic and prognostic utility in some adult populations, PICU intensivists have recently shown a growing interest in its wider applicability. Therefore, the international recommendations for pediatric neurocritical care do not yet advocate TCD (5).

TCD can, however, offer pertinent cerebrovascular hemodynamic data in children with a range of neurological illnesses, such as stroke and cerebrovascular disorders, CNS infections, and brain death, according to the findings of primarily observational studies and case reports. In addition to main neurological dysfunctions, TCD may also be useful for evaluating children with diabetic ketoacidosis and those receiving extracorporeal membrane oxygenation (ECMO) (5,6).

The purpose of this study was to assess how well transcranial Doppler ultrasounds diagnose sepsis in pediatric patients.

METHODS

Study type and population

A single center prospective case control study that was conducted at a tertiary hospital and included two groups the first group is the case group and included septic kids and some of them received sedated drugs and others were already sedated, the child between the ages of one month and fourteen who satisfied the sepsis criteria in our study. The control children are the second group: youngsters who were admitted to the PICU or pediatric department for reasons other than sepsis, during the period from October 2023 to October 2024, in addition to the TCD data, the variables collected from all patients and control group included the patients' demographics, medical history included complete history taking, which includes regular drug dosages, age, sex, domicile, socioeconomic situation, and complete nutritional

history, and clinical characteristics included weight, height, and vitals (heart rate, respiration rate, blood pressure, and blood sugar) are examples of anthropometric measurements. Systemic examination, which includes an examination of the heart, chest, and abdomen. Laboratory tests, such as CRP and complete blood counts. Cultures from body fluids such as feces, urine, and sputum, as well as blood. The kids with congenital infections ($n = 2$), epilepsy ($n = 5$), or trauma ($n = 9$) TCD measurement failure or missing clinical data ($n=7$) were excluded from our study. Finally, 48 patients were enrolled in the study, their age ranged from 1 month -14 years with a mean age of 20.13 ± 5.511 months in case group and 19.46 ± 4.139 months in control group. The study has been carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki). Ethical Principles for Medical Research Involving Human Subjects. Approval was obtained from our institutional review board (IRB) (Zu-IRB #10405-6-2024) and the informed consent was taken from parents of pediatric patients. All patients were subjected to TCD.

TCD study and image interpretation

1. The Toshiba Canon Aplio 500 ultrasound equipment (manufactured in Japan) with a low frequency 3.–5MHz linear probe was used to complete the imaging study, which included TCD and ultrasound. The TCD was performed by a radiologist with ten years of experience.

2. The individuals were in a supine position. The method begins by placing the probe on the scalp and using the color-coded, two-dimensional image. Real-time blood flow velocity is measured using pulsed wave Doppler after the relevant blood vessel has been isolated. After stabilization, a bilateral TCD test should be recorded for a minimum of ten cardiac cycles. The temporal window, which is situated on the boundary between the external canthus and the tragus, is the most pertinent scanning view. This window enables the measurement of blood flow velocities, including peak systolic (PVS) and end-diastolic (EDV) velocities, as well as the identification of the mesencephalon and the first segments of the middle cerebral artery (MCA) at a depth of 30 to 60 mm, depending on age.

3. In a similar manner, the resistivity index (RI), pulsatility index (PI), and mean flow velocity (MFV) were determined. The normative values for the following significant determinants of blood flow velocities are displayed in brackets: temperature (36°C – 37.5°C), oxygen saturation ($>92\%$), venous PCO₂ (40–50 mmHg), arterial PCO₂ (35–45

mmHg), and/or end-tidal PCO₂ (31–41 mmHg). The patient's age was taken into consideration when interpreting arterial blood pressure, heart rate, and hemoglobin levels. The patient's electronic medical records were searched for additional clinical information, such as the primary diagnosis, neurological diagnosis, and patient outcomes.

4. On the day of the TCD examination, the Pediatric Logistic Organ Dysfunction (PELOD) score was used to gauge the degree of severe illness. The most recent worldwide consensus conference on pediatric sepsis established the definition of organ failure. The 11th edition of the International Classification of Diseases (ICD-11) was used to define primary and neurological illnesses.

5. They reported the following therapeutic interventions: (i) hemodynamic optimization (administration of vasopressors/inotropes or fluid resuscitation); (ii) de-escalation (discontinuation or reduction of dosage) of neurological drug treatments, including osmotherapeutic agents, sedatives, and neuromuscular blocking agents; and (iii) escalation (initiation, addition, or intensification) of the aforementioned neurological drug treatments.

Statistical Analysis

Software called SPSS version 24 was used to tabulate and analyze the gathered data (SPSS Inc, Chicago, ILL Company). Numbers and percentages were used to display categorical data. To examine categorical variables, the chi square test (χ^2) was employed. The mean \pm standard deviation, median, and range were used to express the quantitative data. Two independent groups' normally distributed variables were analyzed using the student "t" test. The correlation between non-parametric variables was evaluated using Spearman's correlation coefficient (ρ). The risk of association was examined using regression analysis. To find cutoff values with the best sensitivity and specificity, a ROC curve was employed (Figure 1). In this study, 0.05 was the declared level of significance ($P < 0.05$ was deemed significant).

RESULTS

The study consisted of 24 case group and 24 control group who were referred for trans cranial ultrasound and doppler. The mean age was 20.13 ± 5.5 months in septic patients and 19.46 ± 4.13 months most of septic patients (45.8%) were low socio-economic status (Supplementary Table 1).

There is no significant difference in the mean middle cerebral artery peak systolic velocity (MCA_PSV) between the sepsis and control groups. In contrast to the control group, the sepsis group's middle cerebral

artery pulsatility index (MCA_PI) is noticeably lower. In a similar vein, the sepsis group has a lower middle cerebral artery resistance index (MCA_RI) than the control group. The sepsis group has a higher peak systolic velocity (ACA_PSV) for the anterior cerebral artery (ACA) than the control group. Additionally, the sepsis group's ACA pulsatility index (ACA_PI) and resistance index (ACA_RI) are noticeably lower than those of the control group (Table 1).

Age, sepsis grades, heart rate, respiratory rate, systolic and diastolic blood pressure, temperature, white blood cell count (WBCs), C-reactive protein (CRP), PRISM score, Glasgow Coma Scale (GCS), MCA_PI, MCA_RI, ACA_PSV, ACA_PI, and ACA_RI did not differ statistically significantly from MCA_PSV (Table 2).

For a number of parameters, strong and statistically significant associations are found. In particular, there are highly significant relationships between MCA_PI and heart rate, respiration rate, temperature, systolic and diastolic blood pressure, white blood cell count, and C-reactive protein. There are no discernible relationships between MCA_PI and the PRISM score or Glasgow Coma Scale (GCS). Furthermore, Table 3 shows that MCA_PI has a substantial connection with various cerebral hemodynamic indices, including MCA_RI, ACA_PI, and ACA_RI.

Heart rate, respiration rate, temperature, white blood cell count, and C-reactive protein all show significant negative relationships with MCA_RI. On the other hand, there are significant positive associations between MCA_RI and both diastolic and systolic blood pressures. Additionally, MCA_RI has robust positive associations with ACA_PI and ACA_RI, two major cerebral hemodynamic indices. There are modest and non-significant relationships between MCA_RI and age and sepsis grades. There are

Table 1: Correlation between Sepsis group and Control group regarding Transcranial Doppler Ultrasound parameters.

		Sepsis group	Control group	T-test	P-value
MCA_PSV (cm/sec)	Mean ± SD	.689± .054	.687± .043	.117	.908
MCA_PI	Mean ± SD	.911± .063	1.77± .047	-53.117-	.000
MCA_RI	Mean ± SD	.544± .022	.779± .042	-24.081-	.000
ACA_PSV (cm/sec)	Mean ± SD	66.88± 2.36	64.83± 1.63	3.480	.001
ACA_PI	Mean ± SD	.885± .069	1.75± .093	-36.455-	.000
ACA_RI	Mean ± SD	.550± .030	.847± .050	-24.748-	.000

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, CRP: C-reactive protein, RI: resistivity index

Table 2: Correlation between MCA_PSV and other variables.

additional non-significant connections between MCA_RI and the PRISM score and Glasgow Coma Scale (GCS). Furthermore, Table 4 shows a slight inverse relationship between MCA_RI and ACA_PSV.

Heart rate, respiration rate, temperature, white blood cell count, and C-reactive protein all show significant positive relationships with ACA_PSV. On the other hand, there are notable negative connections between ACA_PSV and ACA_PI, ACA_RI, systolic blood pressure, and diastolic blood pressure. Table 5 shows weak and non-significant relationships between ACA_PSV and age, grades of sepsis, PRISM score, and Glasgow Coma Scale (GCS).

Heart rate, respiration rate, temperature, white blood cell count, and C-reactive protein all show significant negative relationships with ACA_PI. On the other hand, there are significant positive associations between ACA_PI and both diastolic and systolic blood pressure, indicating that higher ACA_PI is associated with higher blood pressure readings. There is a very strong link between ACA_PI and ACA_RI. There are modest and non-significant relationships between ACA_PI and age and sepsis grades. Likewise, there are no discernible relationships between the PRISM score and the Glasgow Coma Scale (GCS) and ACA_PI (Table 6). Heart rate, respiratory rate, temperature, white blood cell count, and C-reactive protein all show significant negative relationships with ACA_RI. On the other hand, ACA_RI has robust positive associations with both diastolic and systolic blood pressure, indicating a relationship between elevated ACA_RI and elevated blood pressure. Age, sepsis grades, PRISM score, and Glasgow Coma Scale Table all show weak and non-significant associations with ACA_RI (Table 7).

Correlation	Pearson's correlation	
	R	P-value
Age (months) * MCA_PSV (cm/sec)	.043	.769
Grades of sepsis (days) * MCA_PSV (cm/sec)	.271	.201
Heart rate (beat/min) * MCA_PSV (cm/sec)	-.130-	.380
Respiratory rate (/min) * MCA_PSV (cm/sec)	-.020-	.891
SBP (mmHg) * MCA_PSV (cm/sec)	.036	.809
DBP (mmHg) * MCA_PSV (cm/sec)	.044	.766
Temperature (0C) * MCA_PSV (cm/sec)	.125	.399
WBCs (x103/mm3) * MCA_PSV (cm/sec)	.074	.616
CRP (mg/ml) * MCA_PSV (cm/sec)	.011	.939
PRISM score * MCA_PSV (cm/sec)	.316	.133
Glasgow Coma Scale * MCA_PSV (cm/sec)	-.293-	.165
MCA_PI * MCA_PSV (cm/sec)	.019	.899
MCA_RI * MCA_PSV (cm/sec)	-.006-	.967
ACA_PSV (cm/sec) * MCA_PSV (cm/sec)	.140	.342
ACA_PI * MCA_PSV (cm/sec)	-.003-	.984
ACA_RI * MCA_PSV (cm/sec)	-.004-	.978

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, CRP: C-reactive protein, RI: resistivity index

Comments

There was no statistically significant difference between MCA_PSV and age, grades of sepsis, heart rate, respiratory rate, systolic and diastolic blood pressure, temperature, white blood cell count (WBCs), C-reactive protein (CRP), PRISM score, Glasgow Coma Scale (GCS), MCA_PI, MCA_RI, ACA_PSV, ACA_PI, and ACA_RI

Table 3: Correlation between MCA_PI and other variables.

Correlation	Pearson's correlation	
	R	P-value
Age (months) * MCA_PI	-.062-	.673
Grades of sepsis (days) * MCA_PI	.252	.236
Heart rate (beat/min) * MCA_PI	-.739-	.000
Respiratory rate (/min) * MCA_PI	-.857-	.000
SBP (mmHg) * MCA_PI	.894	.000
DBP (mmHg) * MCA_PI	.805	.000
Temperature (0C) * MCA_PI	-.898-	.000
WBCs (x103/mm3) * MCA_PI	-.645-	.000
CRP (mg/ml) * MCA_PI	-.775-	.000
PRISM score * MCA_PI	.031	.887
Glasgow Coma Scale * MCA_PI	-.067-	.755
MCA_RI * MCA_PI	.961	.000
ACA_PSV (cm/sec) * MCA_PI	-.437-	.002
ACA_PI * MCA_PI	.977	.000
ACA_RI * MCA_PI	.965	.000

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, PSV: peak systolic volume, SBP: systolic blood pressure

CRP: C-reactive protein, RI: resistivity index

Comments

Strong and statistically significant correlations are observed for several parameters. Specifically, heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, temperature, white blood cell count, and C-reactive protein all show highly significant correlations with MCA_PI. The PRISM score and Glasgow Coma Scale (GCS) do not exhibit significant correlations with MCA_PI. Additionally, strong correlations are found between MCA_PI and other cerebral hemodynamic indices, such as MCA_RI, ACA_PI, and ACA_RI

Table 4: Correlation between MCA_RI and other variables.

Correlation	Pearson's correlation	
	R	P-value
Age (months) * MCA_RI	-.028-	.852
Grades of sepsis (days) * MCA_RI	-.157-	.463
Heart rate (beat/min) * MCA_RI	-.705-	.000
Respiratory rate (/min) * MCA_RI	-.823-	.000
SBP (mmHg) * MCA_RI	.866	.000
DBP (mmHg) * MCA_RI	.784	.000
Temperature (0C) * MCA_RI	-.851-	.000
WBCs (x103/mm3) * MCA_RI	-.633-	.000
CRP (mg/ml) * MCA_RI	-.770-	.000
PRISM score * MCA_RI	.095	.660
Glasgow Coma Scale * MCA_RI	-.102-	.636
ACA_PSV (cm/sec) * MCA_RI	-.357-	.013
ACA_PI * MCA_RI	.945	.000
ACA_RI * MCA_RI	.934	.000

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, PSV: peak systolic volume, SBP: systolic blood pressure, CRP: C-reactive protein, RI: resistivity index

Comments

Significant negative correlations are observed between MCA_RI and heart rate, respiratory rate, temperature, white blood cell count, and C-reactive protein. Conversely, strong positive correlations exist between MCA_RI and systolic blood pressure and diastolic blood pressure. MCA_RI also shows strong positive correlations with other cerebral hemodynamic indices, including ACA_PI and ACA_RI. Age and grades of sepsis show weak and non-significant correlations with MCA_RI. The PRISM score and Glasgow Coma Scale (GCS) also exhibit non-significant correlations with MCA_RI. Additionally, a modest negative correlation is observed between MCA_RI and ACA_PSV

Table 5: Correlation between ACA_PSV and other variables.

Correlation	Pearson's correlation	
	R	P-value
Age (months) * ACA_PSV (cm/sec)	-.038-	.798
Grades of sepsis (days) * ACA_PSV (cm/sec)	.220	.302
Heart rate (beat/min) * ACA_PSV (cm/sec)	.435	.002
Respiratory rate (/min) * ACA_PSV (cm/sec)	.307	.034
SBP (mmHg) * ACA_PSV (cm/sec)	-.415-	.003
DBP (mmHg) * ACA_PSV (cm/sec)	-.338-	.019
Temperature (0C) * ACA_PSV (cm/sec)	.587	.000
WBCs (x103/mm3) * ACA_PSV (cm/sec)	.321	.026
CRP (mg/ml) * ACA_PSV (cm/sec)	.390	.006

Correlation	Pearson's correlation	
	R	P-value
PRISM score * ACA_PSV (cm/sec)	.172	.423
Glasgow Coma Scale * ACA_PSV (cm/sec)	-.205-	.335
ACA_PI * ACA_PSV (cm/sec)	-.440-	.002
ACA_RI * ACA_PSV (cm/sec)	-.393-	.006

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, PSV: peak systolic volume, SBP: systolic blood pressure CRP= C-reactive protein, RI: resistivity index

Comments

Significant positive correlations are observed between ACA_PSV and heart rate, respiratory rate, temperature, white blood cell count, and C-reactive protein. Conversely, significant negative correlations are noted between ACA_PSV and systolic blood pressure, diastolic blood pressure, ACA_PI, and ACA_RI. The correlations between ACA_PSV and age, grades of sepsis, PRISM score, and Glasgow Coma Scale (GCS) are weak and non-significant

Table (6): Correlation between ACA_PI and other variables.

Correlation	Pearson's correlation	
	r	P-value
Age (months) * ACA_PI	-.060-	.687
Grades of sepsis (days) * ACA_PI	-.085-	.694
Heart rate (beat/min) * ACA_PI	-.713-	.000
Respiratory rate (/min) * ACA_PI	-.841-	.000
SBP (mmHg) * ACA_PI	.888	.000
DBP (mmHg) * ACA_PI	.785	.000
Temperature (0C) * ACA_PI	-.867-	.000
WBCs (x103/mm3) * ACA_PI	-.629-	.000
CRP (mg/ml) * ACA_PI	-.761-	.000
PRISM score * ACA_PI	.136	.527
Glasgow Coma Scale * ACA_PI	-.273-	.196
ACA_RI * ACA_PI	.961	.000

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, PSV: peak systolic volume, SBP: systolic blood pressure, CRP: C-reactive protein, RI: resistivity index

Comments

Significant negative correlations are observed between ACA_PI and heart rate, respiratory rate, temperature, white blood cell count, and C-reactive protein. Conversely, ACA_PI has strong positive correlations with systolic blood pressure and diastolic blood pressure, showing that higher ACA_PI corresponds to higher blood pressure values. The correlation between ACA_PI and ACA_RI is extremely strong. Age and grades of sepsis show weak and non-significant correlations with ACA_PI. Similarly, the PRISM score and Glasgow Coma Scale (GCS) do not exhibit significant correlations with ACA_PI

Table 7: Correlation between ACA_RI and other variables.

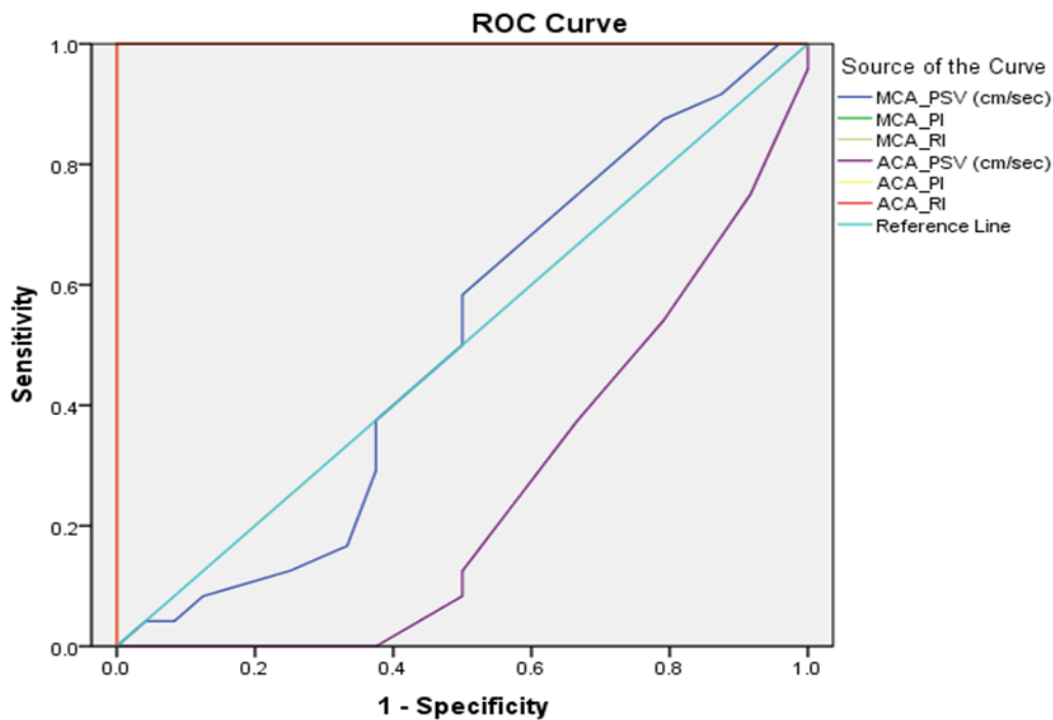
Correlation	Pearson's correlation	
	R	P-value
Age (months) * ACA_RI	-.092-	.533
Grades of sepsis (days) * ACA_RI	.074	.732
Heart rate (beat/min) * ACA_RI	-.729-	.000
Respiratory rate (/min) * ACA_RI	-.822-	.000
SBP (mmHg) * ACA_RI	.856	.000
DBP (mmHg) * ACA_RI	.759	.000
Temperature (0C) * ACA_RI	-.857-	.000
WBCs (x103/mm3) * ACA_RI	-.650-	.000
CRP (mg/ml) * ACA_RI	-.766-	.000
PRISM score * ACA_RI	.075	.727
Glasgow Coma Scale * ACA_RI	-.252-	.235

Table Legends

ACA: The Anterior Cerebral Artery, MCA: middle cerebral artery, PSV: Peak Systolic Velocity, PI: The Pulsatility Index, SD: Standard Deviation, PSV: peak systolic volume, SBP: systolic blood pressure
 CRP: C-reactive protein, RI: resistivity index

Comments

Significant negative correlations are observed between ACA_RI and heart rate, respiratory rate, temperature, white blood cell count, and C-reactive protein. Conversely, ACA_RI shows strong positive correlations with systolic blood pressure and diastolic blood pressure, suggesting that higher ACA_RI is linked to higher blood pressure. Weak and non-significant correlations are found between ACA_RI and age, grades of sepsis, PRISM score, and Glasgow Coma Scale



Diagonal segments are produced by ties.

Figure 1: ROC curve results

DISCUSSION

Despite being somewhat older than the control group (19.46 ± 4.139 months), the mean age of patients in the sepsis group (20.13 ± 5.511 months) in our study is not statistically significant. In terms of the distribution of sexes, the sepsis group had 37.5% females compared to 45.8% females, and 62.5% males compared to 54.2% in the control group. Regarding gender, there was no statistically significant difference (P value= 52.2%) of patients were male, and the majority (66.3%) were under the age of six, according to Humoodi et al. (7). Comorbidities were present in 75.2% of patients and this was consistent with the findings of our investigation.

Additionally, according to Sediqi et al. (8), when the prevalence of sepsis was examined by gender, it was discovered that the prevalence was 34.24% in women and 65.75% in men.

The Middle Cerebral Artery (MCA) peak systolic velocity (PSV) did not differ statistically significantly between septic patients and controls, according to our study. The septic group's pulsatility index (PI) and resistance index (RI), however, were noticeably lower.

Anterior Cerebral Artery (ACA) measures in septic patients revealed significantly lower PI and RI with a slightly higher PSV, which is consistent with MCA findings. The inflammatory effects of sepsis on cerebral autoregulation may be the cause of the reduced PI and RI in our investigation, which could suggest diminished cerebrovascular resistance.

The results of Schramm et al. (9), who employed TCD to evaluate cerebrovascular autoregulation in critically sick pediatric patients with severe sepsis or septic shock in conjunction with sepsis-associated delirium (SAD), are consistent with these findings. They observed a strong correlation between the development of SAD later on and compromised cerebrovascular autoregulation on the first day of intensive care unit admission.

Accordingly, Refaat et al. (10) found that all three of the main cerebral arteries had increased peak systolic velocity (PSV). Compared to neonates in the control group, neonates with EONS showed significantly decreased resistance (RI and PI), vasodilatation, and higher peak systolic velocity (PSV) in MCA & ACA. This suggests that a widespread rise in CBF is an early response to sepsis.

This is also in line with Basu et al. (11), who found that neonates with EONS had reduced resistance (RI and PI), vasodilatation, and (ICA, VA, and MCA)

within 24 hours of birth, suggesting a generalized rise in CBF as an early response to sepsis. Koch et al. (12) reported that their infants with chorioamnionitis (HC) had reduced resistance in the majority of the major cerebral vessels when compared to controls, with HC males being more affected than HC females.

On the other hand, it has been previously documented that septic shock and severe sepsis are associated with elevated cerebral vascular resistance as measured by TCD calculated PI and RI (13).

This also contradicts the findings of Algebaly et al. (14) who demonstrated that PI and RI were considerably greater in juvenile septic patients with sepsis-associated encephalopathy (SAE) than in those without SAE.

Furthermore, a research by Crippa et al. (15) found a strong correlation between impaired cerebral autoregulation identified by TCD and brain dysfunction linked to sepsis.

MCA_PI and MCA_RI demonstrated high positive associations with blood pressure and strong negative correlations with temperature, heart rate, and respiratory rate in our study. This implies that cerebral blood flow becomes less pulsatile and resistive as sepsis severity grows (shown by elevated heart rate, respiration rate, and temperature, as well as decreased blood pressure).

These results are consistent with those of Brasil et al. (16), who examined brain hemodynamics in critical illness and found comparable associations.

The idea of widespread cerebral hemodynamic alterations in sepsis was further supported by the correlations that ACA_PI and ACA_RI showed with those of MCA.

The Glasgow Coma Scale and the PRISM score did not significantly correlate with TCD characteristics in our investigation.

Algebaly et al. (14) on the other hand, found a correlation between PI and the PRISM III-estimated degree of disease. The Full Outline of Unresponsiveness score (FOUR) and PI had a highly significant negative correlation ($p = 0.016$). This indicates that when coma deepens (the FOUR score decreases), cerebrovascular resistance (CVR) rises.

Pierrakos et al. (17) found that patients with high PI on the first day of ICU admission also had a lower Glasgow coma scale (GCS) at the onset of sepsis, with no correlation to the severity of the illness as measured by the Acute Physiology and Chronic Health Evaluation (APACHE) II score. This is in contrast to previous adult data. However, not every

adult in their study had septic shock or severe sepsis, unlike our group of kids.

In contrast, several investigations have found that increased CVR is associated with more delirium or disruption of consciousness (18, 19).

Increased BFV was linked to mild vasospasm of the basal cerebral arteries, according to Straver et al. (2), who also found a substantial correlation between TCD anomalies and the severity and consequences of the condition.

CONCLUSION

Children with sepsis can have alterations in their brain hemodynamics detected by TCD, a noninvasive technique. PSV rises, PI and RI fall, and cerebral blood flow rises as a result of neonatal sepsis, which raises the risk of intraventricular hemorrhage in the sepsis group relative to the control group.

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Consent for publication

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Competing interests

The authors declare that they have no competing interest.

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