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Clinical Applications of Transcranial Doppler Ultrasound in Septic Children

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Abstract

Systemic vascular resistance (SVR) frequently falls as a result of a Gram-negative sepsis, which is an immune-mediated systemic illness. With an emphasis on its therapeutic uses and possible effects on patient outcomes, this study sought to assess the use of transcranial Doppler ultrasonography (TCD) in critically unwell children with sepsis. This case control study was carried out in the Department of Pediatrics in Zagazig University Hospital on 24 septic children and 24 non septic. The majority of cases group (66.7%) classified as Grade I sepsis, followed by 29.2% with Grade II (severe sepsis), and 12.5% with Grade III (septic shock). The vital signs of septic patients showed significant differences compared to the control group, with higher heart rates, respiratory rates, and temperatures, and lower blood pressures. Our results showed significantly elevated white blood cell counts (WBCs) and C-reactive protein (CRP) levels in septic patients compared to controls. Regarding culture results, 70.8% of the cases were culture-positive, with 20.8% of these being Gram-positive infections and 50.0% being Gram-negative infections, while 29.2% of the cases were culture-negative. 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. Anterior Cerebral Artery (ACA) measurements showed significantly lower PI and RI in septic patients, with a slightly higher PSV. The mean PSV was 66.88. As regard outcome, 66.7% (16 patients) survived, while 33.3% (8 patients) died. MCA_PI and MCA_RI showed strong negative correlations with heart rate, respiratory rate, and temperature, and strong positive correlations with blood pressure. ACA_PI and ACA_RI demonstrated similar correlations to those of MCA. We found no significant correlation between TCD parameters and the PRISM score or Glasgow Coma Scale. Our ROC curve analysis showed that MCA_PI, MCA_RI, ACA_PI, and ACA_RI had the highest diagnostic accuracy for sepsis, with area under curve (AUC) values of 1.000. While our study found significant differences in TCD parameters between septic patients and controls, we did not observe a significant relationship between these parameters and patient outcomes (survival vs. mortality). Our study demonstrated that TCD can detect significant changes in cerebral hemodynamics in children with sepsis. While prognostic value of these changes requires further investigation, TCD appears to be a promising tool for non-invasive monitoring of brain perfusion in pediatric sepsis. Its integration into clinical practice could potentially improve our understanding and management of this critical condition in children.

Keywords: Transcranial Doppler Ultrasound - Applications – Septic Children

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1. Introduction

Systemic inflammatory response syndrome (SIRS) is a systemic sickness brought on by an infectious pathogen entering the body and causing the production of inflammatory mediators. Sepsis does not have SIRS. It is a general inflammatory process that can follow burns, pancreatitis, infection, trauma, and numerous other illnesses [1]. Globally, sepsis continues to be a major cause of illness and mortality. About 60% of deaths in children under age of five are caused by infectious illnesses [2]. In children with a variety of conditions, such as traumatic brain injury, intracranial hypertension, vasospasm, stroke, cerebrovascular disorders, central nervous system infections, and brain death, bedside transcranial Doppler (TCD) may offer crucial diagnoses and prognoses regarding cerebrovascular hemodynamics. The Doppler spectrum can be used to determine 3 key parameters: velocities, flow direction, and artery resistance indices. Latter comprises resistive index (RI) and the pulsatility index (PI). Adult sepsis has shown to raise PI [3]. With an emphasis on its therapeutic uses and possible effects on patient outcomes, this study sought to assess use of Transcranial Doppler ultrasonography in critically unwell children with sepsis.

2. Patients and Methods

2.1. Technical Design

2.1.1. Setting

The present study was case- control study carried out in the Department of Pediatrics in Zagazig University Hospital during the period from April 2023 to October 2023. The study protocol was submitted for approval by Zagazig University Institutional Review Board (IRB) (IRB Number 10405).

2.2. Study Population

2.2.1. Inclusion Criteria

1. Children who are septic. Every child aged 1 month to 14 years who satisfied the sepsis criteria in our study were classified as such [1].

SIRS: The existence of two or more of the four requirements listed below, at least one of which needs to have an abnormal leukocyte count or temperature: The core temperature should be between 38.5°C and 36°C. One definition of tachycardia is a mean heart rate. Bradycardia, defined as a mean heart rate <10th percentile for age in the absence of external vagal stimulus, b-blocker drugs, or congenital heart disease, or otherwise unexplained persistent depression over a 0.5-hour period; or 2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5- to 4-hour period. The average rate of breathing.2 SD higher than typical for the patient's age or mechanical ventilation for an acute procedure unrelated to general anesthesia or underlying neuromuscular illness. A higher or lower-than-normal leukocyte count (not due to chemotherapy-induced leukopenia) or.10% immature neutrophils.

Infection: A clinical syndrome linked to a high chance of infection OR an infection produced by any pathogen that is suspected or confirmed (by positive culture, tissue stain, or polymerase chain reaction test). Positive results from a clinical examination, imaging, or laboratory test (such as white blood cells in a typically sterile bodily fluid, a ruptured viscus, and a chest radiograph that is consistent with pneumonia, petechial or purpuric rash, or purpura fulminans) are examples of evidence of infection. Sepsis SIRS due to or in conjunction with a suspected or confirmed infection.

Extreme sepsis: Acute respiratory distress syndrome, cardiovascular organ dysfunction, or two or more other organ dysfunctions along with sepsis. Table 4 defines organ dysfunctions.

Septic shock: SOFA is for sequential organ failure assessment; qSOFA stands for fast SOFA; and SIRS stands for systemic inflammatory response syndrome.

2. Control children: kids sent to the PICU or hospital for reasons other than sepsis.

2.2.2. Exclusion Criteria

- Traumatic children
- Epileptic children
- Congenital infection

2.3. Methods and Samples

Also, all patients and controls were subjected to the following

- ***rho → Spearman's correlation coefficient***

1. Taking a complete medical history, which includes information on age, sex, domicile, socioeconomic situation, complete nutritional history, and regular dosages of drugs.
2. Clinical assessment: a) Anthropometric parameters, such as height and weight

b) Vitals (blood pressure, blood sugar, heart rate, and respiration rate).

c) A comprehensive examination that looks at the heart, chest, and abdomen.

d) Laboratory tests, such as CRP and complete blood count

e) Cultures from bodily fluids, such as stool, urine, and sputum, as well as blood.

f) Imaging tests, such as computerized tomography (CT), ultrasonography, or X-rays, depending on the patient's preferences.

g) Particular studies: (Doppler ultrasonography of the brain (TCD)

In TCD ultrasonography, a low-frequency transducer (typically ≤ 3–5 MHz) was used. 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 line between the external canthus and the tragus, is the most pertinent scanning view in clinical practice. This window enables the measurement of blood flow velocities, including peak systolic (VS) and end-diastolic (VD) 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. Based on the sepsis criteria, we separated the patients into two groups. Septic group (a) and non-septic group (b). The septic group was then separated into two categories:

a) Sepsis (SIRS and suspected or confirmed infection).

b) Severe sepsis (sepsis and respiratory, cardiovascular, or at least two non-cardiorespiratory organ system dysfunctions).

c) Septic shock (cardiovascular dysfunction and sepsis, characterized by either hypotension, the use of vasoactive drugs, or decreased perfusion in spite of fluid resuscitation).

2.4. 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 (X2) was employed. The mean ± standard deviation, median, and range used to express the quantitative data. Two independent groups' normally distributed variables were analyzed using the student "t" test. Correlation b/w non-parametric variables evaluated using Spearman's correlation coefficient (rho). Risk of association was examined using regression analysis. To find cutoff values with best sensitivity and specificity, a ROC curve was employed. In this study, 0.05 declared level of significance (P <0.05 was deemed significant). Twenty-four children separated into a control group and twenty-four sick children, who were further divided into three groups: Grade I (sepsis) (N = 16), Grade II (severe sepsis) (N = 7), and Grade III (septic shock) (N = 3).

It evaluates the linear association between 2 quantitative variables (one is the independent var. X, and the

other is the dependent var., Y). Value of "r" ranges from -1 to 1
0= no linear correlation
1= perfect positive correlation
-1 = perfect negative correlation
Positive= increase in the independent variable leads to increase in the dependent variable
Negative = increase in the independent variable leads to decrease in the dependent variable.
ROC curve = receiver operator characteristic curve,
P value was considered significant as the following:
* $P > 0.05$: Non significant
* $P \leq 0.05$: Significant

3. Results and discussion

3.1. Results

In terms of demographic information, there was no statistically significant difference between the Sepsis group and the Control group (Table 1). The majority of the patients, 16 out of 24 (66.7%), are Grade I (sepsis). Grade II (severe sepsis) accounts for 7 patients (29.2%), Grade III (septic shock) are 3 patients (12.5%) (Table 2). WBCs in the sepsis group were statistically significantly higher than in the control group (p. value = 0.000). The CRP of the Sepsis group was statistically significantly higher than that of the controls (p. value = 0.000) (Table 3). The PRISM score has a mean of 16.00 with a standard deviation of 6.64. The GCS shows a mean score of 9.45 with a standard deviation of 2.91. Regarding culture results, 70.8% of the cases were culture-positive, with 20.8% of these being Gram-positive infections and 50.0% being Gram-negative infections, while 29.2% of cases were culture-negative. As regard outcome, 66.7% (16 patients) survived, while 33.3% (8 patients) died (Table 4). With a non-significant p-value of.908, the mean middle cerebral artery peak systolic velocity (MCA_PSV) is comparable between the sepsis and control groups.

With a p-value of.000, the sepsis group's middle cerebral artery pulsatility index (MCA_PI) is significantly lower than that of the control group. With a p-value of.000, the sepsis group's middle cerebral artery resistance index (MCA_RI) is likewise lower than that of the control group. With a p-value of.001, the sepsis group's peak systolic velocity (ACA_PSV) is higher than the control group's for the anterior cerebral artery (ACA). With extremely significant p-values of.000 for both indices, the sepsis group's ACA pulsatility index (ACA_PI) and resistance index (ACA_RI) are likewise significantly lower than those of control group (Table 5). There were no statistically significant difference between positive culture and negative culture regarding Transcranial Doppler Ultrasound parameters (Table 6). There was no statistically significant relation between outcome and Transcranial Doppler Ultrasound parameters (Table 7). MCA_PI, MCA_RI, ACA_PI and ACA_RI have the most diagnostic accuracy in sepsis group than MCA_PSV and ACA_PSV (Table 8).

3.2. Discussion

Our results showed significantly elevated white blood cell counts (WBCs) and C-reactive protein (CRP) levels in septic patients compared to controls. This aligns with the findings of Stand age and Wong [4], who reported that these inflammatory markers are typically increased in pediatric sepsis, although they emphasized that these markers alone are not specific for sepsis diagnosis. This is also consistent with other studies El-Mazary et al., [5]. They discovered that WBCs were noticeably more in cases than in controls. In our study, regarding culture results, 70.8% of cases were culture-positive, with 20.8% of these being Gram-positive infections and 50.0% being Gram-negative infections, while 29.2% of cases were culture-negative. Our study found no significant difference in Middle Cerebral peak systolic velocity (PSV) of the arteries (MCA) in septic patients and controls. The septic group's pulsatility index (PI) and resistance index (RI), however, were noticeably lower. 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 inflammatory effects of sepsis on cerebral auto regulation. This is agreed with Basu et al. [6].

They found newborns with EONS had significantly reduced levels of resistance (RI and PI), vasodilatation, and ICA, VA, and MCA within 24 hours after delivery, suggesting a widespread rise in CBF as an early reaction to sepsis, & Koch et al [7].They reported that, in comparison to controls, their newborns with chorioamnionitis (HC) showed reduced resistance in the majority of the major cerebral arteries, with HC males being more impacted than HC females. While our study found significant differences in TCD parameters between septic patients and controls, we did not observe a significant relationship b/w these parameters and patient results (mortality versus survival). The comparatively small sample size or generally lower mortality rate in our cohort could be the cause of absence of correlation in our study. Additionally, this contradicts Algebaly et al. [8] He stated that the non-survivor group's PI and RI values were higher than those of survivor group. Additional research revealed a connection between mortality and a higher CVR. [9-10]. Despite this, clear differences in TCD parameters between septic patients and controls suggest that TCD could be a valuable tool for monitoring cerebral hemodynamics in pediatric sepsis. The non-invasive nature of TCD makes it particularly suitable for use in children, where more invasive monitoring techniques might be challenging or risky.

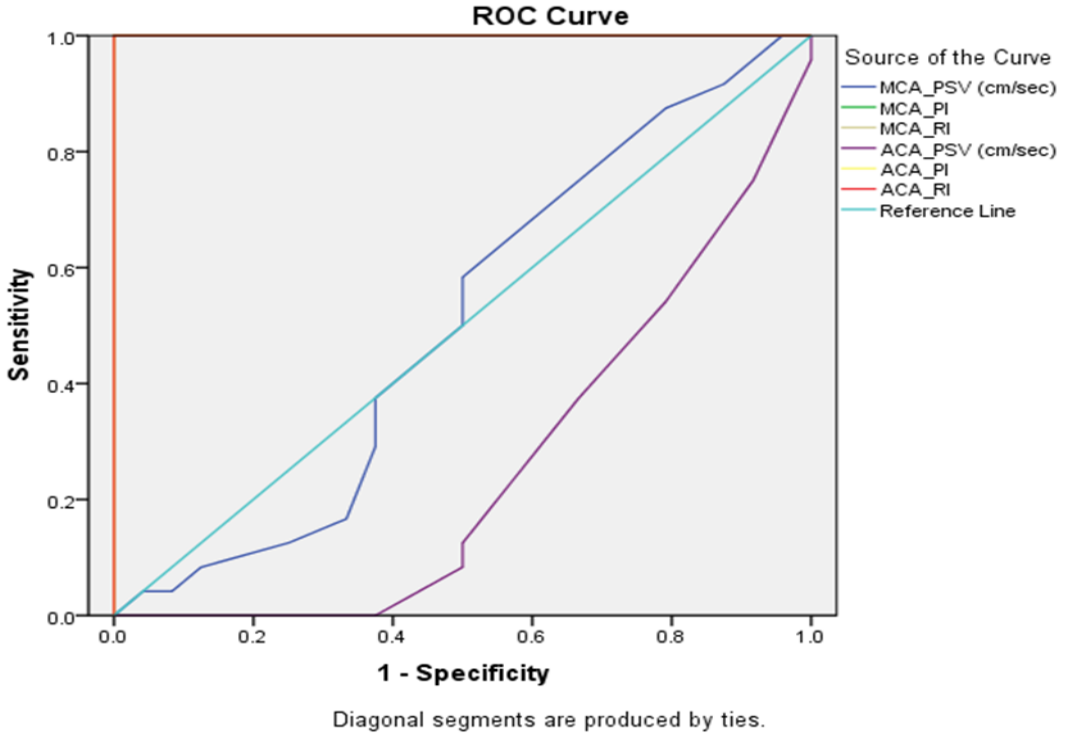

Figure 1: ROC Curve

Table 1: Comparison between Sepsis group and Control group regarding demographic data.

			Sepsis group	Control group	t. test	P. value
Age (months)	**Mean ± SD**		20.13 ± 5.511	19.46 ± 4.139	0.474	0.638
Sex	**male**	**No. %**	15 (62.5%)	13 54.2%	X^2 0.343	0.558
	Female	**No. %**	9 37.5%	11 45.8%		
Socioeconomic status	**Low**	**No. %**	11 45.8%	9 37.5%	X^2 0.771	0.680
	Moderate	**No. %**	9 37.5%	12 50.0%		
	High	**No. %**	4 16.7%	3 12.5%		
Residence	**Rural**	**No. %**	16 66.7%	17 70.8%	X^2 0.097	0.755
	Urban	**No. %**	8 33.3%	7 29.2%		

Table 2: Grades of sepsis.

		No.	%
Grades of sepsis	**Grade I (sepsis)**	16	66.7%
	Grade II (severe sepsis)	7	29.2%
	Grade III (septic shock)	3	12.5%

Table 3: Comparison between Sepsis group and Control group regarding WBCs and CRP.

		Sepsis group	Control group	t. test	P. value
WBCs (x103/mm3)	**Mean ± SD**	18.36± 8.15	8.54± 1.58	5.788	.000
CRP (mg/ml)	**Mean ± SD**	61.15± 34.13	3.60± 1.50	8.250	.000

Table 4: Distribution of sepsis cases regarding PRISM score, Glasgow Coma Scale, Culture and Outcome.

		Mean ± SD	
PRISM score		16.00± 6.64	
Glasgow Coma Scale		9.45± 2.91	
		No.	**%**
Culture	**Negative**	7	29.2
	Positive	17	70.8
	Gram +ve	5	20.8
	Gram -ve	12	50.0
Outcome	**Alive**	16	66.7
	Died	8	33.3

Table 5: Comparison 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 6: Comparison between positive culture and negative culture regarding Transcranial Doppler Ultrasound parameters.

		Positive culture	Negative culture	t. test	P. value
MCA_PSV (cm/sec)	**Mean ± SD**	.692± .058	.681±.045	.439	.665
MCA_PI	**Mean ± SD**	.909±.069	.917± .051	-.264-	.794
MCA_RI	**Mean ± SD**	.540± .554	.021± .023	-1.424-	.168
ACA_PSV (cm/sec)	**Mean ± SD**	66.47± 2.37	67.86± 2.19	-1.327-	.198
ACA_PI	**Mean ± SD**	.871± .066	.921± .066	-1.674-	.108
ACA_RI	**Mean ± SD**	.542± .030	.568±.021	-1.993-	.059

Table 7: Relation between outcome and Transcranial Doppler Ultrasound parameters.

		Alive	Died	t. test	P. value
MCA_PSV (cm/sec)	**Mean ± SD**	.680± .055	.706±.052	-1.091-	.287
MCA_PI	**Mean ± SD**	.906± .072	.921±.044	-.511-	.614
MCA_RI	**Mean ± SD**	.544± .022	.543± .024	.062	.951
ACA_PSV (cm/sec)	**Mean ± SD**	66.63± 2.41	67.38± 2.32	-.725-	.476
ACA_PI	**Mean ± SD**	.885± .070	.887± .071	-.081-	.936
ACA_RI	**Mean ± SD**	.545± .029	.561± .030	-1.248-	.225

Table 8: Diagnostic accuracy

Test Result Variable(s)		Area	Std. Error [a]	Asymptotic Sig. [b]	Asymptotic 95% Confidence Interval	
					Lower Bound	Upper Bound
dimension0	MCA_PSV (cm/sec)	.503	.086	.967	.336	.671
	MCA_PI	1.000	.000	.000	.000	1.000
	MCA_RI	1.000	.000	.000	1.000	1.000
	ACA_PSV (cm/sec)	.256	.071	.004	.116	.396
	ACA_PI	1.000	.000	.000	.000	1.000
	ACA_RI	1.000	.000	.000	1.000	1.000

4. Conclusions

Our study demonstrated that TCD can detect significant changes in cerebral hemodynamics in children with sepsis. While the prognostic value of these changes requires further investigation, TCD appears to be a promising tool for non-invasive monitoring of brain perfusion in pediatric sepsis. Its integration into clinical practice could potentially improve our understanding and management of this critical condition in children.

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