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ASSESSMENT OF TRANSCRANIAL DUPLEX IMAGING ABNORMALITIES IN EGYPTIAN CHILDREN WITH SICKLE CELL DISEASE

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Abstract

Stroke has been recognized as a catastrophic clinical manifestation of sickle cell disease SCD, and efforts have been made to identify and treat children at the highest risk. TCD screening has modified the natural history of stroke in children with SCD and emerged as a powerful tool for assessing stroke risk in SCD patients. This cross-sectional study assessed transcranial Doppler imaging (TCDI) velocities in pediatric patients with SCD to identify patients at risk for stroke. Forty-six SCD patients were enrolled (23 males and 23 females), with a median age of 11 years (7.3 - 13.6 years). Thirty-three (71.7%) patients had homozygous SCD, while 28.3% were sickle β-thalassemia. Forty-two (91.3%) patients had normal TCDI findings, and 4 (8.7%) patients had abnormal TCDI findings, including 2.2% of patients who had a conditional TAMMV, while it was low in 6.5% of patients.

Keywords: sickle cell disease; transcranial Doppler ultrasound; children.

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Introduction:

Sickle cell disease (SCD) is the most common monogenic hemoglobin disorder. It is a multiorgan disorder associated with high morbidity, mortality, and poor quality of life [1]. Neurological manifestations of SCD are common and include symptomatic infarction, silent ischemia, and intracranial hemorrhage. About 25% of SCD patients may develop a neurological complication over their lifetime, which may occur in early childhood [2]. Stroke is a devastating complication of the disease because of its high morbidity and mortality. SCD can cause stroke through various mechanisms. Some are linked to the red blood cell (RBC) morphology and others due to vascular endothelial injuries and coagulopathy [3]. It is now possible to identify those at risk prior to a first stroke using transcranial Doppler ultrasound (TCD). TCD is a crucial investigation that can reveal elevated cerebral arterial flow in asymptomatic patients and primary stroke prevention [4]. TCD ultrasound has become a standard of care in screening for asymptomatic vasculopathy [5].

In order to develop criteria for detection of stenotic lesions based on TCD to identify patients with SCD at risk for stroke in 1998, the prospective Stroke Prevention Trial in Sickle Cell Anemia (STOP) trial included patients diagnosed with sickle cell anemia or HbS/β^0-thalassemia (HbS/β^0-thal) [6]. The STOP protocol recommends that children with SCD, ages 2 to 16 years, undergo an annual TCD to identify those individuals with abnormal (high) blood flow who are at high risk of stroke [6,7].

Vascular abnormalities in SCD may be evident even in young children. TCD studies measure flow velocity within the large intracranial arteries, which are the vessels most often involved in sickle cerebral vasculopathy, mainly the distal intracranial portions of the internal carotid artery and the proximal middle cerebral artery (MCA) [2,5]. High blood flow velocity in one or more major arteries indicates vessel narrowing and thus can predict increased stroke risk, and therefore preventive treatment could be started prior to the first stroke [6]. In addition, TCD velocities measurement is convenient because it is painless, non-invasive, requires no sedation, easy to perform, and relatively inexpensive [8]. The aim of the work was to assess abnormal TCD velocities in pediatric patients with SCD to identify patients at risk for stroke.

Patients & Methods:

This cross-sectional study included 46 children with SCD (HbSS, HbSβ) above two years of age, followed at the Hematology outpatient clinic of Alexandria University Children's Hospital in Egypt. SCD was diagnosed by hemoglobin electrophoresis in all patients and confirmed by β-globin gene PCR in 58.7% of patients (data retrieved from patients' files). After approval of the study by the local ethics committee, informed consent/assents were obtained from the patient's legal guardians/patients. Patients were excluded from the study if they had abnormal neurologic symptoms or signs or a history of cerebral thrombotic events, including overt stroke (ischemic or hemorrhagic), transient ischemic attacks, or seizures.

All patients were subjected to a detailed history taking with reviewing medical records (for a period of 2 years), including frequency and severity of vaso-occlusive crises (VOC). VOC was defined as the persistence of pain in the extremities, head, chest, back, or abdomen for two or more hours that could not be explained except by the presence of SCD. The severity of VOC was considered mild if the patient had required or not pain medicines but did not prevent normal daily activity, as moderate when requiring pain medications and changes in daily activities, such as missing work or school. Severe VOC was used for pain episodes requiring a visit to the emergency department, physician's office, or hospitalization [9]. History of blood transfusion was taken, and chronic transfusion was defined as regular transfusions at four to five weeks' intervals [10]. The hydroxyurea (HU) intake, dose, duration, and compliance to treatment (by questioning parents) were noted. A history of silent cerebral infarctions (SCI) in magnetic resonance imaging (MRI) during the preceding last year was recorded.

A thorough clinical examination was done, including a complete neurological examination by a pediatric neurologist. Laboratory investigations included a complete blood count (CBC) with a reticulocytes count, serum ferritin, hemoglobin electrophoresis. A Transcranial Doppler imaging (TCDI) was conducted at the Neurovascular Unit of the Neurology Department at Alexandria University with the patient in the supine position, using a 2 - 4 MHz hand-held probe of Philips Clearvue 350 machine. A transtemporal window was used to measure the highest time-averaged maximum mean velocity (TAMMV) and the highest peak systolic velocity (PSV) of the MCA, anterior cerebral artery (ACA), and posterior cerebral artery (PCA). The cut-off values were defined according to the STOP criteria. These criteria are based on the TAMMV measured in the M1 segment of MCA to assign stroke risk as normal (TAMMV 70-170 cm/s), conditional (TAMMV ≥ 170 cm/sec but < 200 cm/sec), high risk (TAMMV ≥ 200 cm/sec) and low (TAMMV < 70 cm/s). PSV from each segment was recorded at the time of study

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was classified as normal (PSV < 200 cm/sec), conditional (PSV ≥ 200 cm/sec but < 250 cm/sec) and high risk (PSV ≥ 250 cm/sec) [11]. Early studies suggested that TCDI gave lower readings than non-imaging TCD [12], although the consensus is now that readings are similar if both methods are performed using standardized techniques [13]. All TCDI examinations were conducted and analyzed by a single expert.

Non-parametric statistics were adopted, and analysis was performed using IBM SPSS package version 24. Qualitative data were expressed as number and percent. Quantitative data were described using the minimum and maximum, median, and interquartile range (IQR). Kolmogorov-Smirnov test was used to examine the normality of data distribution. Chi-Square, Monte Carlo, and Fisher Exact tests were used for univariate analysis of qualitative variables, while Mann-Whitney and Kruskal Wallis tests were used for quantitative variables. The significance was judged at the 5% level.

Result:

The patient's demographic and clinical data are shown in Table 1. All the patients have received at least one prior packed red cells (PRBCs) transfusion; 20 (61.4%) patients were on a chronic PRBCs regimen transfusion. The median HU dose was 17 mg/kg (range 9 - 35mg/kg), all children on HU were compliant to the drug except 3 (8.6%) patients, with a median duration of treatment of 5 years (range 1-13 years). VOC was reported in 39 (84.8%) patients, of whom 17 (43.6%) had severe VOC. The patient's investigations are shown in Table 2. Forty-two (91.3%) patients had normal TCDI findings, and 4 (8.7%) patients had abnormal TCDI findings; one patient had a conditional TAMMV, while it was low in the three other patients. Regarding the PSV, 4 (8.7%) patients had a conditional velocity, and only one (2.2%) patient had high-risk velocity. Of the 46 evaluated SCD patients, only 2 (4.3%) had a history of SCI by brain MRI. Infarcts were detected in the deep white matter between the ACA and MCA territories. Both patients who had SCIs had a normal TCDI. The results of TCDI and comparison with different clinical and laboratory parameters are shown in Tables 3, 4, and 5.

Table 1. Demographic and clinical characteristics of sickle cell disease patients.

Sickle cell disease patients (n=46)	
Patients' characteristics	**N (%)**
Diagnosis	
Sickle cell disease	33 (71.7)
Sickle β-thalassemia	13 (28.3)
Sex	
Male	23 (50)
Female	23 (50)
Age at the time of the study (years)	
Min. - Max.	2.3 - 17.8
Median (IQR)	11 (7.3 - 13.6)
On chronic transfusion regimen	
Yes	20 (44)
No	26 (56)
VOC frequency	
None	7 (14)
<3 crises per year	5 (10)
≥3 crises per year	38 (76)
Hydroxyurea treatment	
Yes	33 (71.7)
No	13 (28.7)
BMI	
Underweight (<18.5)	38 (82.6)
Normal weight (18.5- 24.9)	7 (15.2)
Overweight (25- 29.9)	1 (2.2)
Median (IQR)	16.2 (14.9 - 18.2)
Min-Max	11.8 - 25.1

IQR: interquartile range, Min. - Max.: minimum - maximum. n= number of patients, N: number, %: percent. VOC: vasoocclusive crises, BMI: body mass index

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Table 2. Laboratory investigations for sickle cell disease patients (n=46).

Laboratory investigations	Min. - Max	Median (IQR)
Complete blood picture parameters		
Hemoglobin (g/L)	6.6 - 10.7	8.45 (7.8 - 9.1)
Total leukocyte count ($\times 10^9$/L)	3.5 - 22.7	10.0 (7.5 - 14.1)
Platelet count ($\times 10^9$/L)	125 - 712	422.5 (251.0 - 544.5)
Mean corpuscular volume (fL)	61.7- 109.6	86.3 (73.8 - 93.7)
Reticulocytes (%)	0.6 - 33.1	5.8 (2.8 - 9.9)
Serum Ferritin (ng/dl)	38.2 - 6,500	585.5 (202.3 - 1,505.3)
Hemoglobin electrophoresis*		
Hemoglobin F (%)	0.0 - 35.7	9.9 (3.3 - 19.1)
Hemoglobin S (%)	26.2 - 94.4	68.8 (53.6 - 83.3)

* at time of the study, IQR: Interquartile range, Min. - Max.: minimum - maximum.

Table 3. TCD imaging velocities of sickle cell disease patients (n=46).

Artery	TAMMV (cm/s)			PSV (cm/s)		
	N	**Min. - Max**	**Median (IQR)**	**N**	**Min. - Max**	**Median (IQR)**
Right MCA	46	53.1 - 172	98.6 (84.3 - 113.3)	46	83.4 - 236	140 (123.8 - 165.3)
Left MCA	45	56.2 - 168	104 (90.9 - 113)	46	79.2 - 250	142 (128 - 158)
Right ACA	43	40.4 - 137	74.4 (57.8 - 92.3)	44	57.3 - 172	103 (84.1 - 121.5)
Left ACA	44	29.6 - 144	80.5 (67.2 - 99)	45	42.5 - 174	105.5 (86 - 131)
Right PCA	44	15 - 98.5	57.5 (47.4 - 65.4)	45	27.3 - 218	77.4 (64.8 - 88.2)
Left PCA	43	29 - 126	60 (48.9 - 76.2)	44	41.9 - 158	81.6 (64.8 - 98.9)

TAMMV: Time-averaged maximum mean velocities, PSV: Peak systolic velocities, IQR: Interquartile range, Min. - Max.: minimum - maximum, N: number of patients, MCA: middle cerebral artery, ACA: anterior cerebral artery, PCA: posterior cerebral artery.

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Table 4. Relation between TAMMV of MCA and different clinical parameters

TCDI findings in MCA	Diagnosis		
	Sickle cell anemia (n=33)	**Sickle Thalassemia** (n=13)	***p*-value**
Right TAMMV (n=46)			
Median (IQR)	99.2 (87.5 - 113.3)	89.1 (68.5 - 115.5)	*P* = 0.414
Min. - Max	69.3 - 172.0	53.1 - 136.0	
Left TAMMV (n=45)			
Median (IQR)	104.5 (94.8 - 113.5)	98.5 (75.3 - 113.0)	*P* = 0.234
Min. - Max	77.4 - 168.0	56.2 - 140.0	
	Age		
	<10 years old (n=19)	**>10 years old** (n=27)	
Right TAMMV (n=46)			
Median (IQR)	106.0 (92.8 - 119)	89.1 (75 - 108)	*P* = 0.013*
Min. - Max	74.9 - 172	53.1 - 136	
Left TAMMV (n=45)			
Median (IQR)	109.5 (104.3 - 120.5)	94.9 (78 - 108)	*P* = 0.001*
Min. - Max	94.7 - 168	56.2 - 140	
	Current blood transfusion		
	No (n=26)	**Yes** (n=20)	
Right TAMMV (n=46)			
Median (IQR)	93.6 (75.3 - 108)	104.0 (85.6 - 118.8)	*P* = 0.187
Min.-Max.	53.1 - 167.0	72.5 - 172.0	
Left TAMMV (n=45)			
Median (IQR)	97.5 (80.5 - 107)	109.5 (99.4 - 118.8)	*P* = 0.012*
Min.-Max.	56.2 - 168.0	77.4 - 150.0	
	Hydroxyurea intake		
	No (n=32)	**Yes** (n=14)	
Right TAMMV (n=46)			
Median (IQR)	93.6 (75.1 - 110.5)	103.3 (84.4 - 114)	*P* = 0.459
Min.-Max.	63.0 - 167.0	53.1 - 172.0	
Left TAMMV (n=45)			
Median (IQR)	103.3 (77.9 - 115.3)	104 (92.9 - 111)	*P* = 0.912
Min.-Max.	63.5 - 168.0	56.2 - 150.0	

	BMI			
	Underweight (<18.5) (n=38)	**Normal weight (18.5-24.9)** (n=7)	**Overweight (25- 29.9)** (n=1)	
Right TAMMV (n=46)				
Median (IQR)	102 (88.4 - 116)	84.4 (72.5 - 103.0)	75.5	*P* = 0.160
Min.-max.	53.1 - 172.0	63.0 - 136.0	-	
Left TAMMV (n=45)				
Median (IQR)	106.0 (96.3 - 114.5)	86.3 (75.1 - 92.9)	77.4	*P* = 0.021*
Min.-max.	56.2 - 168.0	63.5 - 140.0	-	

* Statistically significant at $p < 0.05$. IQR: Interquartile range, MCA: middle cerebral artery, n: Number of patient, TAMMV: time average maximum mean velocity, Min.-Max: Minimum-maximum, BMI: body mass index.

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Table 5. Relation between TAMMV of the MCA and some clinical and laboratory parameters.

	TAMMV of MCA		
	Normal (n=42) **N (%)**	**Abnormal** (n=4) **N (%)**	***P*-value**
Sex			
Female	21 (50)	2 (50)	*P* = 1.000
Male	21 (50)	2 (50)	
Diagnosis			
Sickle cell disease	32 (76.2)	1 (25)	*P* = 0.111
Sickle β-thalassemia	10 (23.8)	3 (75)	
VOC frequency			
None	6 (14.3)	1 (25)	
<3 crises per year	3 (7.1)	0 (0)	*P* = 1.000
≥3 crises per year	33 (78.3)	3 (75)	
VOC severity (n=39)			
Mild	10 (27.8)	0 (0)	
Moderate	12 (33.3)	0 (0)	*P* = 0.113
Severe	14 38.9)	3 (100)	
Hydroxyurea intake			
Yes	29 (69)	3 (75)	*P* = 0.805
No	13 (31)	1 (25)	
Chronic transfusion			
Yes	19 (45.2)	1 (25)	*P* = 0.435
No	23 (54.8)	3 (75)	

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Brain MRI			
Normal	40 (95.2)	4 (100)	*P* = 1.000
Abnormal	2 (4.8)	0 (0.0)	
Hemoglobin (gm/dl)			
Median (IQR)	8.4 (7.8 - 9.1)	8.7 (8.3 - 9.7)	*P* = 0.200
Min. - Max.	6.6 - 10.7	8.6 - 10.6	
Reticulocytes (%)			
Median (IQR)	5.8 (2.6 - 9.8)	8.9 (3.4 - 19.5)	*P* = 0.585
Min. - Max.	0.6 - 33.1	1.5 - 19.7	
Hb F at the time of the study			
Median	9.9 (3.3 - 19.1)	8.2 (2.5 - 17.7)	*P* = 0.866
Min. - Max.	0.0 - 35.7	0.38 - 23.8	

TAMMV: Time average maximum mean velocity, MCA: Middle cerebral artery, Hb F: Hemoglobin F, Min: minimum, Max: Maximum, IQR: Interquartile range, n: Number of patients, VOC: vaso-occlusive crises.

Discussion:

Stroke has been recognized as a catastrophic clinical manifestation of SCD, and efforts have been made to identify and treat children at the highest risk [14]. TCD screening has modified the natural history of stroke in children with SCD [15,16] and emerged as a powerful tool for assessing stroke risk in SCD patients [17]. However, no single clinical tool to identify children who will certainly have a stroke is available. Furthermore, some children with abnormal TCD readings are really prone to stroke events, whereas others are not, and prophylactic blood transfusions are unnecessarily provided. Therefore, refined methods for the primary prevention of stroke in children with SCD are required [18].

In the current study, none of the patients had a TAMMV greater than 200 cm/s, only one (2.1%) patient had a conditional velocity, and 3 (6.5%) patients had low velocity (< 70 cm/s). Several recent Egyptian studies have studied TCD in SCD children in different parts of the country and showed variable results. Abou-Elew et al. [19] reported that 26.9% of patients had abnormally high TCD flow velocities (TCD velocities ≥170 cm/s) among 52 patients with SCD aged 3 - 18 years from Cairo. Moeen et al.'s [20] involved 40 patients with sickle cell anemia (SCA) aged 16 - 22 years from Assiut; 12.5% of patients had conditional TCD velocities and 5% of patients had high risk (>200 cm/s) TAMMV. Bakr et al. 's study [21] conducted on 100 patients with SCD aged 2 - 39 years from Cairo showed that 6% of patients had conditional TCD velocities and 2% had high risk (>200 cm/s). El Sissy et al. [22] showed that only 5% of 500 patients with SCD (mean age of 14.07 ± 9.62 years) had an abnormal velocity (≥170 cm/s). Abd-Allah et al. [23] revealed that 20.5% of the 83 included patients with SCD, aged 3 - 18 years, had abnormal TCD findings, 8.4% had high-risk findings, and 12.1% had conditional findings. Also, Tantawy et al.'s [24] study conducted on 22 patients with SCD, aged 3 - 18 years, showed that all patients had normal velocity. Salama et al.'s [25] study involved 78 children with SCD aged >2 years; 1.28% of patients had had high-risk TCD velocities while 6.4% patients had conditional TCD velocities. Yassien et al. [26] showed that 2% of patients had conditional TCD flow velocities, 8% of patients had high velocity (TCD velocities ≥200 cm/s), a study conducted on 50 children with SCD aged 2-18 years from Tanta in the Delta region. The overall percentage of abnormal TCD in Egypt among children with SCD was low. Conversely, the STOP study reported abnormal results in 9.7% of the pediatric age group (2-16 years) [6]. Moreover, a more recent study of patients with SCD, with a mean age of 9.97 ± 5.02 years, reported that 69 (17.4%) patients had elevated TCD velocities ≥ 170cm/s; of whom 50 (12.6%) had conditional risk velocities of 170-199cm/s, 19 (4.8%) had abnormal risk velocities of ≥ 200cm/s and four patients (1.0%) had abnormally low TCD [27]. There are several reports from the Arabian region of a lower TCD results compared to the STOP trial, even in patients who developed stroke; a study from the Peninsular Arab area involving four countries found that none of the studied SCD patients had high risk TCD results, whereas only 13 (3.1%) had conditional values in the right MCA and seven (1.7%) in the left MCA [28]. A similar finding was observed in a study from Brazil involving 85 children aged 2 - 18 years, which revealed one abnormal result (1.6%) and five conditional results (8.1%) [29]. In contrast, in Nigerian children with SCD aged 3 - 18 years (n=48), a conditional rate as high as 31.5% was reported and a high-risk percentage of 7.6% [30]. The difference in abnormal TCD findings may be explained by the different and relatively small sample sizes and the heterogeneity of the SCD genotypes, as the African genotype is

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commonly associated with a severe phenotype of SCD [23]. Moreover, the discrepancy of data may be explained by anemia that can cause a generalized increase in velocities [31]. In patients on regular transfusion therapy, a higher pretransfusion hemoglobin level may be associated with the normalization of flow velocities [32].

It is also worthy to note that the TCD velocity thresholds for stroke risk determination in SCD were set based on studies conducted in the developed world; these thresholds may not be appropriate in children living in Africa, where the vast majority of SCD children reside. If this is true, then many SCD children at high risk of stroke are missed in Africa despite TCD screening and risk categorization hinged on extraneously determined cut-off points. Hence, further studies are warranted to determine the appropriate TCD velocity thresholds for proper risk stratification and their associated risk factors in children with SCD living in Africa where severe HbSS phenotypes predominate and Middle Eastern countries where HbS/βThal phenotypes are common [17,33].

In the current study, we used the color duplex imaging TCDI protocol to measure TAMMV in cerebral blood vessels. In comparison, the non-imaging TCD technique has been reported to give velocity readings of up to 10% lower than those acquired using the non-imaging protocol [33]. The TCDI results showed that 6.5% of patients had low velocity (< 70 cm/s) in the MCA. Yassien et al. 26 showed that 15 (56%) patients had low velocities (< 70 cm/s). El-Shanshory et al.'s [34] conducted on 30 patients with SCA aged 6 -18 years revealed that 86.7% of study patients have low velocity (< 70 cm/s) and 13.3% having very low velocity (< 10 cm/s). Buchanan et al. [35] described five children with SCD, whose antecedent screening TCD velocities were measured to be ≤ 70 cm/s, but all patients in that study developed some form of cerebral insults, an overt cerebral infarction, silent stroke, or transient ischemic attack. A TAMMV of < 70 cm/s may be associated with an increased number of cerebral insults [36].

TAMMV of < 70 cm/s identifies groups of children at risk for cerebrovascular disease and hence is considered another type of 'abnormal' TCD, prompting more sensitive evaluations such as a brain MRI and magnetic resonance angiography (MRA) for the presence of central nervous system vascular disease [36].

In concordance to what has been reported by other authors, [6,37] this study found the highest TAMMV to be in the MCA (right 53.1 - 172 cm/s and left 56.2 - 168 cm/s), followed by ACA (right 40.4 - 137 cm/s and left 29.6 - 144 cm/s), and PCA (right 15 - 98.5 cm/s and left 29 - 126 cm/s). Moeen et al, [20] reported also the highest velocity in the MCA (right 100.2 - 293.2 cm/s and left 102.2 - 210.8 cm/s), followed by ACA (right 96.6 - 200.5 cm/s and left 96.3 - 202.3 cm/s), and PCA (right 102.6 - 203 cm/s and left 102.4 - 207 cm/s).

In our study, although HbSS patients had higher TCD velocities compared to HbS/βthal patients, this difference was not statistically significant. In contrast, Yousef et al. [38] showed a significant difference between the TCD velocities in patients with HbSS and HbS/βthal with higher velocities in patients with HbSS.

This study revealed significantly lower right and left TAMMV in children more than ten years compared with the younger age group, ($p = 0.013$ and 0.001, respectively). The blood flow velocity varies naturally with age; it is low after birth in the MCA and increases rapidly during the first days of life. Velocities of 100 cm/s are reached between the ages of 4 to 6 years; after this age, the blood flow velocity gradually decreases throughout the rest of life [39].

In the current study, the TAMMV in children receiving HU therapy was slightly higher than those not receiving HU but was within the normal range (<170cm/sec), except for one child who had a conditional velocity ($p = 0.459$ and $p = 0.912$ in the right and left MCA). In contrast, an Indian study conducted on 120 children with SCD showed that the mean blood flow velocity in patients in the HU group was significantly lower than the HU naïve group; the mean blood flow velocity was within the normal range in both groups [40]. Moeen et al. [20] also stated that patients receiving HU therapy had lower TCD velocities.

This study revealed higher right and left TAMMV in children receiving blood transfusion than in those not receiving transfusions; it was statistically significant in the left MCA ($p = 0.012$). This finding was similar to a study by Adekile et al. [28] that showed that a history of blood transfusion did not influence TAMMV and that TAMMV values were significantly higher in the left and right MCA among the transfused group. In contrast, Yassien et al. [26] reported a positive relation between regular blood transfusion in SCD patients and decreased risk for ischemic stroke and abnormal TCD TAMMV.

The current study revealed a higher median TCDI velocity in the MCA among underweight children than normal weight and overweight children; it was only statistically significant for the left TAMMV. It has been previously shown that severe malnutrition was not associated with lower abnormal TCD measurements [41] and that cerebral flow velocities decreased with increasing body mass and age [42].

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The current study showed that out of the 46 TCD examinations, four (8.7%) patients had a conditional velocity and only one (2.2%) patient had high-risk velocity by PSV criteria. The one that was conditional by TAMMV was also conditional by PSV criteria. Therefore, TAMMV criteria would not have identified four (8.7%) patients with abnormal velocities by PSV. This indicates that the PSV could be a valuable measurement for TCD screening [43].

The incidence of SCI in our patients was 4.3%. There are several reports for the incidence of SCI in SCD, as Lotfy et al. [44] found that the incidence was 15% among 20 Egyptian patients with SCD, similar to a French cohort of 173 children (5 - 15 years) with SCD. [45] Pegelow et al. [46] found that up to 37% of their patients with SCD had silent infarction. The variation in the incidence of SCI among different studies may be due to different and usually small sample sizes, different treatment regimens, as it has been documented that chronic blood transfusion reduces the risk of SCI and acute stroke. In the current study, there was a non-significant relation between abnormal TCDI and SCIs (p = 1.000). Similarly, DeBaun et al. [47] did not found an established relationship between SCI and abnormal TCD measurements; neither did Jacob et al. [48].

This study revealed an insignificant relation between abnormal TCDI and hematological parameters (hemoglobin concentration, reticulocyte, and hemoglobin F). Our data are consistent with another Egyptian study that showed that hematological parameters have a statistically insignificant effect on TCD results [23]. In contrast to Leite et al. [49] who demonstrated a negative correlation between Hemoglobin and abnormalities in TCD studies. Ismail et al. [17] showed a significant positive correlation between TAMMV in MCA and reticulocyte count, serum LDH and total and direct bilirubin, while hematocrit and HbF levels were negatively correlated with the TAMMV. Another study reported that the cerebral blood velocities had a statistically positive correlation with total white blood cell count, platelets, and reticulocytes, and there was no significant negative correlation with hematocrit level and hemoglobin concentration [38].

Conclusion:

This study of SCD patients confirmed a low prevalence of abnormal/high TCDI velocities, which may be explained by the prevalence of HbS/βthal genotype and that most children were on HU therapy or chronic transfusion regimens. Adapted national clinical and radiological guidelines, as well as locally defined cut-off values of TCDI, are warranted.

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