


Assessment Implementation of Transcranial Doppler Imaging as a Screening Tool in Pediatrics with Sickle Cell in Prince Sultan Military Medical City

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Abstract

Stroke is one of the irreversible neurological complications of sickle cell disease. Early diagnosis and appropriate treatment of neurological complications of sickle cell anemia require hematological and neurological expertise. Stroke prevention guidelines for sickle cell disease (SCD) recommend transcranial Doppler Imaging (TCDI) screening to identify children at risk for stroke. However, this study provides a baseline assessment of TCDI implementation rates as it is the first study of its kind in Prince Sultan Military Medical City. This study aimed to assess whether TCDI was successful or not as a screening tool to identify children at risk for stroke at Prince Sultan Military Medical City in Riyadh City, Saudi Arabia. From January 2023 to December 2023, a retrospective cohort study design was conducted. Ethical approval was obtained from the institutional board to waive the consent forms since it is a retrospective study and we are collecting normal routine data. Only the primary investigator had access to the patient's medical records. The data will be extracted during the period from the initial launch of transcranial Doppler imaging TCDI as a screening tool tile January 2023. Variables collected from the hospital medical record department and a picture archiving and commu-

nication system (PACS), include the participants' age at the TCDI initial transcranial screening exam and patient TCDI results which are categorized into 3 main categories: **Normal** (if the highest reading of Time Average Maximal Mean Velocity TAMMV) is less than 170 cm/sec and more than 70 cm/sec, **Low conditional** if the highest reading of TAMMV was more than 170 cm/sec and less than 200 cm/sec. **High Conditional (Abnormal) which indicated the group at high risk of stroke** if TAMMV highest velocity is more than 200 cm/sec and their recommended close follow up. The adherence to annual follow-ups in normally reported patients and close follow-ups with TCDI and confirmatory MRA/I is low conditional and abnormal once. Data was collected in an Excel sheet and analyzed using IBM SPSS Statistics 25 (SPSS, Inc., Chicago, IL). This study reflects a good level of compliance to TCDI follow-up and MRA/I among patients with abnormal results compared to those with normal results, where more efforts are needed to investigate barriers to adherence for successful implementation.

Keywords

Stroke Prevention, Sickle Cell, Transcranial Doppler Imaging, TCDI

1. Introduction

Sickle cell disease is one of many inherited diseases characterized by a mutated gene that alters Red Blood cell morphology and function [1]. The normal function of RBC is to supply the human body with oxygen and nutrients in a shape that serves its function [2]. The mutated gene results in deformed and fragile erythrocytes that have a characteristic crescent shape (half-moon) and reduced lifespan (from 120 days to 10 - 20 days) [3].

These sickle-shaped erythrocytes clog the microvascular circulation, leading to tissue ischemia and infarcts. In addition to vascular occlusion, sickle cell degradation leads to chronic hemolytic anemia, which increases the production of free hemoglobin [2].

This disease manifests in wide signs and symptoms. The defining characteristic of Sickle Cell Disease is pain, either acute or chronic, which is an accountable reason for repeated ER visits and admission [4].

Patients with SCD may experience severe pain during infancy, childhood, and adulthood. Pain is usually the major cause of hospitalization and negatively impacts the patient's health-related quality of life [3].

Most frequent complications originate from hemolysis, infection, or vas occlusion in the abdomen Organ-specific symptoms are the spleen (such as infarction, abscess formation, sequestration), the kidneys (such as papillary necrosis, infarction), the pancreas (such as pancreatitis), the gastrointestinal tract (such as infarction), the reproductive organs (testicular atrophy) (e.g., acute chest syndrome, infarction there are a variety of gastrointestinal symptoms associated with sickle cell

disease [3].

Among other complications with degrees of severity ranging from minor liver discomfort and increasing jaundice to severe sickle cell hepatic crisis, sickle cell intra-hepatic cholestasis, or acute hepatic sequestration and death [5].

Chronic anemia reduces the blood's ability to carry oxygen, which causes an increase in cardiac output, primarily through a higher stroke volume. All heart chambers enlarge as a result of chronic volume overload, and eccentric hypertrophy forms in response to elevated wall tension. However, SCD can result in higher venous return, higher filling pressures, and the syndrome of high-output heart failure [6].

Cerebrovascular complications, including changes in silent infarction (SI), transient ischemic attack, and clinical stroke, are common and affect nearly half of the patients from birth to 14 years old [7].

Without intervention, the risk of stroke in a child with sickle cell disease is 333 times higher than in a healthy youngster without heart disease. The risk is significant before the age of 20; about 11% of sicker patients get clinically noticeable strokes. The first ten years of life have the highest risk of stroke, with the age range between two and five years being the most significant [8].

In a study involving 411 participants, Brazilian researchers calculated the total prevalence of overt stroke to be 5.1% in Sickler pediatrics with sickle cell disease. The overall stroke prevalence in the German registry was 4.2%, and an overall rate of 3.8% in the United Kingdom.

In Africa, a prevalence of 6.8% (24/351) was discovered in several research studies conducted between 2004 and 2008 in different cities in Nigeria.

With only 4 out of 222 patients from the Gulf states (Oman, Qatar, and United Arab Emirates) suggests that stroke is less common where only stroke occurred (1.8%). The stroke had the lowest prevalence reported in Kuwait, with 1.4% in pediatrics with sickle cell disease [8].

While in Saudi Arabia, research that included parts of Southwest Saudi Arabia revealed 8/400 (2%) over the course of three years. Nonetheless, among a group of children from Medina, 9/90 (10%) experienced a clinical stroke [9].

The risk of a second stroke recurrence in untreated sickle cell patients can range from 60% to 92% [8].

However, since even one stroke can result in irreversible brain damage, it would be better to prevent the first one. Using Transcranial Doppler imaging as a screening tool in pediatrics to evaluate stroke risk and treat high-risk individuals appropriately seems to have been beneficial in preventing primary stroke [10].

In 1986, transcranial Doppler ultrasonography (TCD) was initially used in clinical settings. Measuring the blood flow velocity from the Willis polygon arteries allows for the determination of the ideal blood flow velocity for sickle cell disease patients. More importantly, the measurement indicates which blood flow velocity is associated with an increased risk of stroke with a sensitivity of 90% and specificity of 100% [11].

This technique used Doppler sonography, which was applied to the temporal region of the scalp, and probe manipulation enabled sonication of the internal carotid artery (ICA), MCA, PCA, and ACA. The measurements included peak systolic, end-diastolic, and time-averaged maximal Mean velocity (TAMMV) [11].

Highlighting the risk of stroke was linked to those patients with cerebral blood flow velocities (Time Average Maximum Mean Velocity TAMMV) beyond normal cut-off values, which is also important since it is well documented that children with stroke are at increased risk of recurrence unless they receive the proper intervention that will reduce the risk of stroke from 10% per year to less than 1% [12].

The obtained Velocity TAMMV stratifies the patient into three main categories corresponding to their risk of stroke: **Normal** (if the highest reading of time-averaged maximal Mean velocity) is less than 170 cm/sec and more than 70 cm/sec, the patient will be recommended for annual follow up, **Conditional** if the highest reading more than 170 cm/sec and less than 200 cm/sec, patient will be recommended for a closer follow up in one to three months and **Abnormal** if TAMMV highest velocity is more than 200 cm/sec patient will have to show up for even closer follow up in one to four weeks. And arrange MRA/I for those patients beyond the normal range [13].

Most of the recommendations came after the utilization of TCD as a screening tool, but the most recent ultrasound machines are equipped with a TCDI imaging technique, which did not show much difference in velocity accuracy [14].

Non-imaging transcranial Doppler (TCD) sonography can accurately predict the risk of stroke in children with sickle cell disease by measuring intracranial arterial blood velocity. TCD screening is not widely used, except in large sickle cell centers, due to a lack of suitable technology and skilled workers.

Although most centers have sonography equipment, they may lack the necessary dedicated transducer to perform duplex TCD and imaging (TCDI). Because the image transducer is far less expensive than a nonduplex TCD machine, many centers are likely to take advantage of it.

Independent of the equipment used, because these examinations are technically hard, and optimization of velocity measurements needs careful attention to the auditory signal, the velocity readings, and the probe position [15].

TCDI enables the visualization of the vessels under examination and the outline of parenchymal structures. These characteristics can enhance the accuracy of accurately identifying vessels and accurately positioning the sample volume into a specific vascular segment. As a result, TCDI is used by many centers since they believe it offers similar velocity information [16].

Prince Sultan Military Medical City, one of Riyadh's biggest medical cities, offers medical services to those affiliated with the military sector as well as to its personnel and their families both inside and outside of Riyadh. as the screening with TCDI was not available in the primary care setting ultrasound department.

In Prince Sultan Military Medical City (PSMMC), earlier in 2013, utilized TCDI as a screening tool to screen pediatrics from 2 to 14 years old with SCD at risk of stroke in an outpatient setting.

Before beginning the exam, the sonographer will meet with the patient's parent or guardian to go over a pre-exam preparation checklist provided by the Paediatric Radiology Department.

During the exam, the sonographer will follow a predesigned protocol using a transtemporal window, Readings of MCA, ACA, PCA, and Term ICA should be taken 3 at least and records the highest TAMMV Interpret the reading in a predesigned worksheet that categories the patient into **Normal** (if the highest reading of time-averaged maximal Mean velocity) is less than 170 cm/sec and more than 70 cm/sec and the patient subsequently be booked for annual screening, **Conditional high** if the highest reading more than 170 cm/sec and less than 200 cm/sec **conditional low** (below 70 cm/sec) patient will be booked for close TCDI follow up 1 or 3 months as the radiologist recommends and **Abnormal high** if TAMMV highest velocity is more than 200 cm/sec **Abnormal low** below 40 cm/sec patient will have to wait for the radiologist to contacted the hematology in service doctor for the arrangement of confirmatory MRI/MRA and book patient for in a week close TCDI follow up.

The level of compliance has not been evaluated since the TCDI screening program began. This research paper will investigate the adherence to TCDI screening protocol and guidelines as a primary stroke preventive measure since it was launched in 2022 in Prince Sultan Military Medical City.

2. Study Objectives

A) Asses the age of pediatrics with sickle cell disease at the initial TCDI screening examination.

B) Evaluate compliance with annual follow-ups of patients with normal readings.

C) Evaluate adherence to the close follow-up with TCDI and confirmatory MRI/A in patients who reported as conditional or abnormal (high or low) as recommended.

Literature Review

Stroke has been the subject of decades' worth of research since it is one of the most fatal and incapacitating consequences for children with sickle cell disease. In the absence of screening or preventative care, the incidence is high [17].

A study conducted by Adams *et al.* in 190 pediatrics with sickle cell disease in 1986 aimed to evaluate the accuracy of TCD in detecting the risk of stroke in symptomatic sickler pediatrics.

The result in TCD showed increased blood flow velocities in 23 of the participants, with recorded velocity reaching 170 cm/sec in 21/23 patients had a single velocity that exceeded 170 cm/sec, and 2 had recorded velocities in both the right and left side, six of seven strokes reported in this group where one of the reported strokes was not in the abnormally reported TCD group [18].

Since then, the utilization of TCD as screening of elevated CBFV as predictive of high risk of stroke has increased.

Later, The Stroke Prevention Trial in Sickle Cell Anemia STOP and STOP II in 1995 and 2005 a multicentre trial conducted in specialized centres to care for paediatrics with sickle cell disease, located in the United States and Canada.

Provide what is later known as the STOP protocol, which Stratifies the patients at risk of stroke according to TAMMV obtained from TCD screening, followed by suggested rescanning frequency [19].

Result of TCD	TAMMV	Frequency of exam
Normal	if TAMMV < 170 cm/sec	annual screening
Conditional	if TAMMV Between 170 - 199 cm/sec	should prompt more frequent TCD *Younger children and those with TCD velocities closer to 200 cm/sec getting more TCD
Abnormal	if TAMMV is equal to or greater than 200 cm/sec	early repeat (within 4 weeks) TCD should be performed

After that, many guidelines and recommendations for implementing TCD screening among the Sickler pediatrics population have been established.

The American Society of Hematology, as well as the National Heart, Lung, and Blood Institute. released a strong recommendation for annual screening of Sickler pediatrics aged from 2 - 16 years annual TCD screening [20] (Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014|NHLBI, NIH, n.d.)

Guidelines regarding the implementation of TCD and the frequency of low (below 170 cm/sec) normal and conditional (low and high conditional TCD) based on TCD results were established by the Brazilian guidelines that emphasize special patient criteria that may alter the result of TCD, patient awake, a febrile and delay screening with TCD for one month after acute events and blood transfusions [21].

Low compliance to TCD screening in pediatrics with sickle cell disease to evaluate the risk of stroke in many studies. Even in resourceful nations as well, the TCD screening is not well adopted. Annual TCD exams are administered to fewer than 50% of eligible pediatrics in Europe [22].

As shown in a large-scale study, the DISPLACE (Dissemination and Implementation of Stroke Prevention Looking at the Care Environment) study, which included 5116 patients from 28 sites, was conducted to evaluate the application of TCD screening. The mean age at initial TCD was 5.9 years; all sites showed inadequate TCD screening rates (mean 49.9%; range 30.9% - 74.7%) in all sites. The TCD result was conditional in 495 individuals (13.5%) and abnormal in 104 (2.8%) patients [23].

In Tanzania, they evaluate the implementation of TCDI screening among 200 Tanzanian pediatrics; they consider 150 cm/sec as the upper cutoff value for high results and below 50 cm/sec as low velocity and slightly elevated (150 - 169 cm/s),

conditional (170 - 199 cm/s), and abnormal (CBFv \geq 200 cm/s).

They found that 105 of the patients were within normal cut-off values and almost one-third abnormal high in 67 (34%) children, of whom 28 (14%) had elevated CBFv, sixteen had slightly elevated CBFV (150 - 169 cm/s), 11 (5.5%) had conditional CBFv (170 - 199 cm/s), but only one, who had already had a clinical stroke, had an abnormal high CBFv (>200 cm/s) and low CBFV in 39 (20%) had CBFv < 50 cm/s.

Among those with high CBFv, only 18 (27%) of patients with CBFv beyond normal did not undergo MRI, while only 49 patients had an MRI done; MRI results came positive in 21 (43%) as this study did not elaborate on the patient compliance to annual screening in the normal proportion of the close follow up in those beyond normal limits [24].

In Europe, a study conducted across 5 European countries aimed to assess TCD screening and stroke prevention programs found that only 28% of all patients with tier results reported as (normal) and requested annual follow-up successfully complied with annual screening [25].

Most of the available literature discusses the evaluation of TCD as screening to reflect the sickle pediatric population according to TCD calcification, evaluate patient response to an intervention (before and after), compare the effectiveness between the two interventions, focus on annual follow-up only, or track the abnormal result and compare the findings to MRA/I.

This study will contribute to the literature and offer useful information; our study will tackle the topic more comprehensively. This work can close a gap in the literature on the assessment of compliance of transcranial Doppler imaging as a screening method for sickle cell disease in pediatric patients.

3. Methodology

3.1. Setting and Design

A retrospective cohort study design was conducted in the Medical Imaging Department at Prince Sultan Medical Military City (PSMMC). Ethical approval was obtained from the institutional board to waive the consent forms since it is a retrospective study and we are collecting normal routine data.

Only the primary investigator had access to the patient's medical records. The data was extracted during the period from the beginning of the screening program to December 2022. The inclusion criteria for the subjects will be pediatric patients diagnosed with sickle cell disease, from 2 to 14 years old, who completed the TCDI exam via temporal window was systematically sampled, and time-averaged maximum. The exclusion criteria will be patients who are non-sticklers under 2 years old or older than 14 years old or/and incomplete TCDI exam.

Mean velocity (TAMMV) was recorded at least three times for four arteries: the middle cerebral artery (MCA), anterior cerebral artery (ACA), internal carotid artery (ICA), and posterior cerebral artery (PCA) on both the right and left sides. Based on the radiologist's report, patients were classified as Normal or Abnormal (low/high

conditional) and recommended for a follow-up scan or confirmatory MRA/MRI.

TCDI was performed on Philips EPIQ7 or IU21 ultrasound scanners with Sector transducers ranging from 1 - 5 MHz in frequency and any MRA/I imaging cerebral magnetic resonance imaging (MRI)/magnetic resonance angiogram (MRA) for abnormal TCDI. The patient results were collected from the hospital medical record department, and pediatric Ultrasound Transcranial reports were extracted from a picture archiving and communication system (PACS).

3.2. Data Collection

Data was collected in an Excel sheet extracted from PACS (Picture archiving and communication system). The collected variables include participants' gender, age at initial screening TCDI, the result of TCDI exams as reported by the radiologist (normal, conditional, high conditional (abnormal)), missed opportunities in annual follow-up in exams reported as normal, exams reported as normal and the patient was compliant to the annual follow up. TCDI follow-up for conditional and abnormal once and if a confirmatory MRA/I was done or not.

3.3. DATA Analysis and Management

Data was analyzed using IBM SPSS Statistics 25.0 (SPSS, Inc., Chicago, IL). Demographic and descriptive data for categorical variables will be expressed as counts and percentages. Descriptive statistics and other parameters will be used to present the baseline characteristics for the population of this study.

4. Results

All pediatric patients referred from the hematology clinic are to be screened by transcranial Doppler imaging to assess their risk of having a stroke in an outpatient setting. In the study of 438 Sickler pediatrics, 228, 52.1% were male, and 210, 47.9% were females, all meeting the inclusion criteria where no significant differences were noted (**Table 1**).

Where almost half of the participants, 51.1% had their first TCDI screening between ages two and five years, 71, 16.2% of them started screening at the age of three (**Table 2**).

The participants' mean age at their initial TCDI screening was 6.3 ± 3.5 , which is higher than the recommended age to initiate screening (**Table 3**).

TCDI classification: Normal with no single abnormal result, either high or low. F (when a patient has reported exams of low and high velocities), high when the patient had reported exams with high velocities either (low/high conditional), and low when the patient had reported exams with low velocities either (low/high conditional). As the results show, the majority of patients had their exams reported as normal with no single abnormal report, representing 332, 75.8% of patients attending for TCDI screening as shown in (**Table 4**).

In the remaining 106 patients, the majority were patients with all of their reports coming abnormally low either (low/high conditional), representing 77, 17.6%, and

the patients reported as high (low/high conditional) only in 26, 5.9% while 3 patients had their reports fluctuate between high and low (**Table 4**).

Table 1. Patient demographics.

		Frequency	Percent	Valid Percent	Cumulative
Valid	Male	228	52.1	52.1	52.1
	Female	210	47.9	47.9	100.0
	Total	438	100.0	100.0	

Table 2. Frequencies of patient age at initial TCDI screening.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2	58	13.2	13.2	13.2
	3	71	16.2	16.2	29.5
	4	50	11.4	11.4	40.9
	5	45	10.3	10.3	51.1
	6	30	6.8	6.8	58.0
	7	28	6.4	6.4	64.4
	8	24	5.5	5.5	69.9
	9	27	6.2	6.2	76.0
	10	30	6.8	6.8	82.9
	11	28	6.4	6.4	89.3
	12	24	5.5	5.5	94.7
	13	17	3.9	3.9	98.6
	14	6	1.4	1.4	100.0
	Total	438	100.0	100.0	

Table 3. Descriptive statistics of patient age at initial TCDI screening.

	N	Minimum	Maximum	Mean	Std. Deviation
Age at Initial TCDI	438	2.0	14.0	6.315	3.5141
Valid N (listwise)	438				

Table 4. Patient's status according to the radiologist's report.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	3	0.7	0.7	0.7
	H	26	5.9	5.9	6.6
	L	77	17.6	17.6	24.2
	N	332	75.8	75.8	100.0
	Total	438	100.0	100.0	

Out of 1325 TCDI exams that were reported as normal, only 602 had annual follow-ups, which represents overall compliance to annual follow-ups among normal exams of 45.43%, as shown in (Table 5).

Table 5. Overall compliance with annual follow-up.

		Total Normal TCDI Exams	Total Number of Normal TCDI with Annual F/U	Compliance to Annual Follow-Up
N	Valid	438	438	602/1325
	Missing	0	0	
Sum		1325.0	602.0	45.433%

95 patients had shown up for a single TCDI with no follow-up, and only 3 had annual follow-up. Out of 79 patients who had 2 normal TCDI exams, only 45, 43.7% of them had 1 annual follow-up. Of 78 patients who had 3 normal TCDI exams, the majority had one or a maximum of two annual follow representing 38, 36.9%, 24, 29.3% respectively, where 40.2% complied with 2 annual follow-ups only in patients who had 4 normal TCDI. Patients who had 5 or 6 normal TCDI showed high compliance to at least 4 annual screenings at 48.3% and 37.9%, respectively.

Seven out of Eleven patients had 7 normal TCDI exams and succeeded in showing up for 5 annual follow-ups representing 63.6%. Only 4 patients had eight total normal TCDIs representing 0.9%. Each one had at least 4 annual follow and only one had shown up for all his/her annual screenings and only 4 patients had a total of 8 normal TCDIs, where each one had 4, 5, 6, 8 annual follow-ups accordingly (Table 6).

Table 6. Compliance with annual follow-up after normal TCDI exam.

		Number of normal TCDI with Annual F/U								Total	
		0.0	1.0	2.0	3.0	4.0	5.0	6.0	8.0		
Total-Norman/TCDI	0	Count	15	0	0	0	0	0	0	0	15
		% within Normal with Annual F/U	9.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.4%
	1	Count	95	3	0	0	0	0	0	0	98
		% within Normal with Annual F/U	58.3%	2.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	22.4%
	2	Count	32	45	2	0	0	0	0	0	79
		% within Normal with Annual F/U	19.6%	43.7%	2.4%	0.0%	0.0%	0.0%	0.0%	0.0%	18.0%
	3	Count	16	38	24	0	0	0	0	0	78
		% within Normal with Annual F/U	9.8%	36.9%	29.3%	0.0%	0.0%	0.0%	0.0%	0.0%	17.8%

Continued

	Count	4	12	33	17	2	0	0	0	68
4	% within Normal with Annual F/U	2.5%	11.7%	40.2%	37.0%	6.9%	0.0%	0.0%	0.0%	15.5%
	Count	1	4	17	19	14	1	0	0	56
5	% within Normal with Annual F/U	0.6%	3.9%	20.7%	41.3%	48.3%	9.1%	0.0%	0.0%	12.8%
	Count	0	1	5	9	11	2	1	0	29
6	% within Normal with Annual F/U	0.0%	1.0%	6.1%	19.6%	37.9%	18.2%	33.3%	0.0%	6.6%
	Count	0	0	1	1	1	7	1	0	11
7	% within Normal with Annual F/U	0.0%	0.0%	1.2%	2.2%	3.4%	63.6%	33.3%	0.0%	2.5%
	Count	0	0	0	0	1	1	1	1	4
8	% within Normal with Annual F/U	0.0%	0.0%	0.0%	0.0%	3.4%	9.1%	33.3%	100.0%	0.9%
Total	Count	163	103	82	46	29	11	3	1	438
	% within Normal with Annual F/U	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

For patients with results beyond normal (high), the radiologist classifies the patient as high or low conditional and recommends TCDI screening more frequently than once a year if the patient is younger and TAMMV is high (around 200 cm/sec).

For patients with low conditional high velocities, most radiologists recommend a Three-month follow-up and MRI/A.

The compliance to close F/U and MRA/I increases as the patient repeatedly has abnormally high TCDI results. Out of 10 patients who have at least one low conditional high velocity, 4 only complied to close TCDI follow-up, and even fewer, 3 only had their MRA/I done, as shown in (Table 7).

Table 7. Compliance to close follow-up and MRA/I after high low-conditional TCDI exam.

	Close TCDI/F/U						MRI-A						
	Done		Not Done		Not Applicable		Done		Not Done		Not Applicable		
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
	0	0	0.0%	0	0.0%	422	100.0%	45	10.7%	45	10.7%	332	78.7%
Number of High (Low-Conditional) Exams	1	4	40.0%	6	60.0%	0	0.0%	3	30.0%	7	70.0%	0	0.0%
	2	2	66.7%	1	33.3%	0	0.0%	2	66.7%	1	33.3%	0	0.0%
	3	1	100.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%	0	0.0%
	4	2	100.0%	0	0.0%	0	0.0%	1	50.0%	1	50.0%	0	0.0%

For abnormal high-conditional, based on the radiologist's recommendation, the patient must have a close TCDI F/U that varies from week to one-month F/U.

The patients show high compliance to TCDI close F/U as they had repeated high conditional TCDI exam results. The patient reported that, with more than one high conditional velocity, he/she tends to show up for the coming TCDI and MRA/I follow-up (**Table 8**).

Table 8. Compliance to close follow-up after high-conditional TCDI exam.

		Close TCDIF/U						MRI-A					
		Done		Not Done		Not Applicable		Done		Not Done		Not Applicable	
		Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %
Number of High (High-Conditional) Exams	0	0	0.0%	0	0.0%	417	100.0%	37	8.9%	48	11.5%	332	79.6%
	1	4	50.0%	4	50.0%	0	0.0%	6	75.0%	2	25.0%	0	0.0%
	2	5	100.0%	0	0.0%	0	0.0%	2	40.0%	3	60.0%	0	0.0%
	3	3	100.0%	0	0.0%	0	0.0%	2	66.7%	1	33.3%	0	0.0%
	4	4	100.0%	0	0.0%	0	0.0%	4	100.0%	0	0.0%	0	0.0%
	5	1	100.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%	0	0.0%

In patients with low velocities, the radiologist followed the same classification of (low/high) conditional low velocities. A low (low-conditional) is when the velocities are less than 70 and more than 40. A three-month close TCDI is recommended by the radiologist, and a low (high-conditional) is when the recorded velocity is equal to or below 40, where a TCDI follow-up is recommended closer in four weeks to one week in addition to MRA/MRI confirmatory Exam.

No significant difference in the compliance to close follow-up in patients with low (low conditional) velocity from those with high low-conditional velocities where the patient tended to adhere to close follow-ups as he/she had more abnormal low TCDI velocities; the same compliance pattern was noticed in the adherence to MRA/I (**Table 9**).

Table 9. Compliance to close follow-up after low (low-conditional) TCDI exam.

		Close TCDIF/U						MRI-A					
		Done		Not Done		Not Applicable		Done		Not Done		Not Applicable	
		Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %
Low (Low-Conditional)	0	0	0.0%	0	0.0%	359	100.0%	15	4.2%	12	3.3%	332	92.5%
	1	16	33.3%	32	66.7%	0	0.0%	20	41.7%	28	58.3%	0	0.0%
	2	18	75.0%	6	25.0%	0	0.0%	12	50.0%	12	50.0%	0	0.0%
	3	3	60.0%	2	40.0%	0	0.0%	3	60.0%	2	40.0%	0	0.0%
	4	2	100.0%	0	0.0%	0	0.0%	2	100.0%	0	0.0%	0	0.0%

Out of five patients reported with low (high-conditional) velocities 3 patients, 60% only had close TCDI F/U done, whereas the majority 4 patients were more compliant with MRA/I follow-up (**Table 10**).

Table 10. Compliance to close follow-up after low (high-conditional) TCDI exam.

	Close TCDIF/U						MRI-A						
	Done		Not Done		Not Applicable		Done		Not Done		Not Applicable		
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
Low	0	0	0.0%	0	0.0%	433	100.0%	48	11.1%	53	12.2%	332	76.7%
(High-Conditional)	1.0	3	60.0%	2	40.0%	0	0.0%	4	80.0%	1	20.0%	0	0.0%

5. Discussion

This study aimed to evaluate the implementation of transcranial Doppler TCDI imaging as a primary preventive measure for stroke among the Sickler pediatrics population at Prince Sultan Military Medical City. The following is a summary of the primary findings: participants' mean at initial TCDI was 6.3 ± 3.5 ; out of 1325 TCDI exams that were reported as normal, only 602 had annual follow-ups, which represents overall compliance to annual follow-up among normal exams of 45.43%.

For the (low conditional) either High or Low velocities exams, the compliance to close F/U and MRA/I increases as the patient repeatedly has abnormally high TCDI results.

In high-conditional high conditional velocities exams, the patients show high compliance to TCDI close F/U as they had repeated high conditional TCDI exam results. The patient reported that with more than one high conditional velocity, he/she tends to show up for the coming TCDI and MRA/I follow-up. In low high conditional low velocities exams, patients tend to be more compliant to MRA/I in 80% compared to TCDI follow-ups in 60%.

Identifying patients with a high risk of stroke allows early intervention to be introduced, especially in patients between the ages of two to five, where the risk of stroke among sickler pediatrics is significant compared to children of an older age.

This retrospective cohort study was conducted on 438 patients to evaluate the implementation of TCDI screening and found the mean age for the first TCDI screening was 6.3 ± 3.5 , which is a bit higher compared to a DISPLACE (Dissemination and Implementation of Stroke Prevention Looking at the Care Environment) study where the mean age was 5.9.

Almost 51.1% of patients had their first TCDI before the age of 5, as shown in **Figure 1**, which reflects a strong understanding of the importance of early screening. Similar to the studies mentioned before [23]-[25].

The screening result showed that almost 332, 75.8% of the participants were considered normal according to their TAMMV.

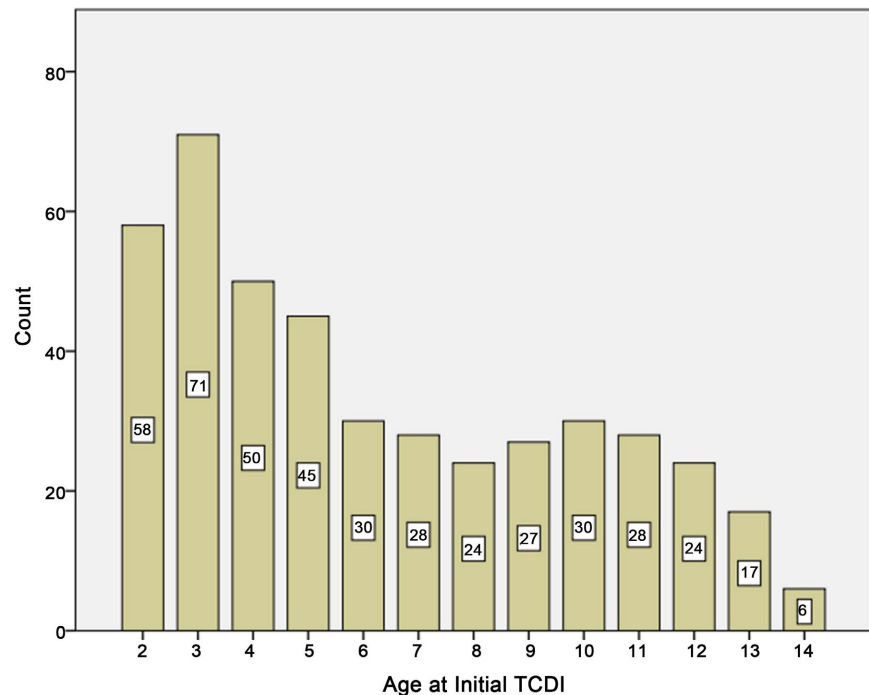


Figure 1. Frequencies of patient age at initial TCDI screening.

The overall compliance to annual follow-up of 45.43% as only out of 1325 TCDI exams reported as normal, 602 exams had annual F/U was also similar to the findings in DISPLACE (Dissemination and Implementation of Stroke Prevention Looking at the Care Environment) [23], with overall compliance to annual F/U was 45.43%.

In the remaining 106, 24% of patients who had at least one result came beyond normal TAMMV cut-off values classified into high (low/high conditional) and low (low/high conditional).

As shown in **Figure 2**, the percentage of abnormal high TCDI exam results was almost 37.69%, and the risk of stroke was 7% in low conditional to 40% in abnormal high conditional patients [11].

It appears to be similar to the reported result from the previously mentioned study 67/200 34% of Tanzanian pediatrics have high TCDI results (28) but still higher than the DISPLACE Study, which reported only 13% of the included participants to have conditional high velocities [23].

In high (low-conditional), this category of patients requires close follow-up and observation due to the higher incidence of strokes, which is 7% compared to patients classified as normal according to the TCDI examination [11].

According to the radiologist's recommendations, they need to be referred to MRA/I and follow up TCDI F/U within one to three months.

As shown in (**Table 7**), The compliance to close F/U and MRA/I increases as the patient repeatedly has abnormally high TCDI results. Out of 10 patients who have at least one low conditional high velocity 4, 40% only complied to close TCDI follow-up, and even fewer 3, 30% only had their MRA/I done.

Distribution of TCDI abnormal Result

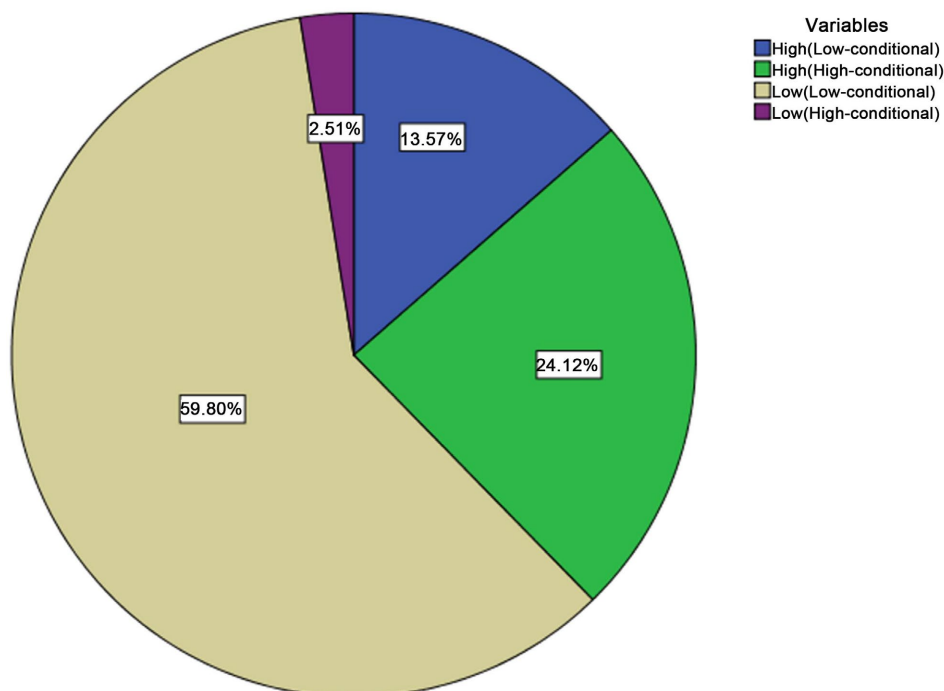


Figure 2. Distribution of abnormal TCDI results in patients.

The percentage of abnormal high (high-conditional) was found to be 24.12%, which is way higher than the Tanzanian study, where only 1/67 1.5% of patients reported having high (high-conditional) results.

For those patients with Abnormal High-conditional, the risk of stroke jumps higher to 40% [11]. Based on the radiologist's recommendation, the patient must have a close TCDI F/U that varies from week to one-month F/U Depending on the patient's age and the recorded TAMMV exceeding 200 cm/sec.

Out of 8 Patients who had only one conditional high velocity 4, 50% only showed up for TCDI close F/U compared to their compliance to MRA/I is higher where 6 of them 75% had their MRA/I done.

The compliance to TCDI noticeably reached 100% as the patient repeatedly had more abnormal high conditional TCDI results. On the contrary, regarding the situation in MRA/I (see [Table 8](#)).

Our result showed that 62.31% of abnormally reported examinations had low-velocity TCDI, which is about three times higher than the previously mentioned study [24].

No significant difference in the compliance to close follow-up in patients with low (low conditional) velocity from those with high low-conditional velocities where the patient tended to adhere to close follow-ups as he/she had more abnormal low TCDI velocities. The same compliance pattern was noticed in the adherence to MRA/I (see [Table 9](#)).

5 patients only reported having one high conditional low velocity. Out of five patients, 3 only showed up for close TCDI F/U, but at the same time, 4.80% com-

plied with MRA/I recommendation.

6. Conclusions

Stroke is one of the most devastating complications for patients with sickle cell disease, especially in pediatrics. The need to implement primary stroke prevention measures is of great value.

Transcranial Doppler imaging has been one of the most highly recommended practices by several guidelines to highlight people at risk of stroke to Ensure that appropriate interventions are implemented.

Our research aimed to assess the implementation of transcranial Doppler imaging among the Sickler pediatric population. Moreover, we investigated the patient age at initial TCDI screening and their compliance for annual follow-ups for those found to be normal in TCDI exams and the compliance in patients beyond normal to close TCDI follow-ups and MRA/I recommendations.

This study reflects a good level of adherence to guidelines TCDI and MRA/I follow-up among patients with abnormal results, but for those with normal results, a lower level of adherence is demonstrated as more efforts are being made to investigate the barriers to adherence with successful implementation.

Investigating causes of non-compliance should be done by offering an educational clinic to families of children about the significance of keeping follow-up appointments, providing exams in primary care facilities, setting up an electronic appointment reminder system, making examination rooms more pediatric-friendly, lowering their anxiety and agitation levels to create a more proper atmosphere.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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