

Trans cranial Doppler Ultrasonography to Predict Stroke Risk in Sickle Cell Disease Pediatric Patients in Sudan

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Abstract: *Evaluation of sickle-cell anemia (Hb SS) patients without a history of clinical stroke were screened by TCD at Sudan sickle cell anemia center to determine the risk of stroke. Risk stratification of stroke by TCD was based on the time-averaged mean of the maximum velocity (TAMM) in the proximal middle cerebral artery. The results show that a correlate between gender with time-averaged mean of the maximum velocity in the right middle cerebral artery were the number of male patients was 43 and the female number was 53, and the more frequent time-averaged mean of the maximum velocity in RMCA was 37 then 91-110 cm/s while the lowest frequent time-averaged mean of the maximum velocity in RMCA 50-70 cm /s and 151-170 cm/s. And correlate between gender with time-averaged mean of the maximum velocity in the left middle cerebral artery were the time-averaged mean of the maximum velocity in LMCA ranged from 70-190cm/s, and the more frequent time-averaged mean of the maximum velocity was 111-130 cm/s and the lowest frequent was 171-190 cm/s. The study conclude that the highest time-averaged mean of the maximum velocity in the right and left middle cerebral arteries for majority of cases, within a normal TCD range (MCA TAMMX < 170 cm/s) then re-scanned annually until 16 years old.*

Keywords: Trans cranial Doppler TCD, middle cerebral artery, Sickle Cell Disease

1. Introduction

Rates of SCA and trait varied in different areas in Sudan with the highest rates reported from Western and Eastern Sudan where one in every 123 children born in Messeryia tribe in Western Sudan is at risk of having SCD. [1]. Children with SCA are at increased risk for cerebrovascular complications. The most severe manifestation is stroke, which is defined as “a focal neurologic deficit resulting from cerebrovascular compromise that persists for more than 24 hours, and has neuroimaging evidence of a cerebral infarct corresponding to the focal deficit [2.3]. Children with SCD have a 410-fold increase in ischemic stroke risk as compared to their peers [4.5]. Highest risk of first overt ischemic stroke is within the first decade of life. [6]. and children with sickle cell disease (hemoglobin SS) have a significant risk of developing ischemic stroke, with 11% of HbSS patients suffering a stroke before the age of 20. [7]. In the absence of prevention programs, stroke accounts for up to 10% of deaths in SCD [8]. Which overall results in a reduction of 25 to 30 years of life expectancy. [9.10].

Trans cranial Doppler ultrasound (TCD) is used in children with sickle cell anemia (SCA) to detect increased risk of arterial ischemic stroke (AIS). [11.12] The Stroke Prevention in Sickle Cell Disease (STOP) study, [12-13] which screened children with sickle cell disease who had never suffered a stroke, demonstrated that tran-scranial Doppler (TCD) could be used to identify children who were at high risk for development of stroke. The risk determination in TCD is

measured by a parameter called the time-averaged mean of the maximum velocity (TAMM) [11.14]. The stroke risk from SCD goes up in direct proportion to increasing time-averaged mean of the maximum velocity (TAMMvel) in the distal internal carotid artery (dICA) or proximal middle cerebral artery (MCA). [11.14]. Based on results from the STOP trial which used a non imaging transcranial Doppler US technique The National Heart, Lung, and Blood Institute (NHLBI) recommends that children with homozygous sickle cell anemia who are between the ages of 2 and 16 years be screened for stroke risk with a transcranial Doppler US examination [15]. STOP trial also demonstrated that if these high-risk children were treated with transfusion to maintain the hemoglobin S at less than 30%, their risk of developing a stroke was decreased by 90% when compared to the high-risk group that received standard care. According to the French and U.S. guidelines [16.17], children with SCA should be screened with TCD from the second year of life and then re-scanned annually until 16 years old if normal (i.e. highest TAMX of any artery <170 cm/s), quarterly if conditional (TAMX of at least one artery 170–199 cm/s), and regular transfusions should be initiated in case of abnormal TCD (TAMX in at least one artery ≥200 cm/s).

2. Method and Material

A study was conducted to sickle-cell anemia (Hb SS) without a history of clinical stroke were screened by TCD at Sudan sickle cell anemia center to determine the risk of stroke. A 100 patients enrolled, four could not be evaluated because of

inadequate temporal bone windows and uncooperative. The 96 patients who could be evaluated included 43(45%) boys and 53 (55%) girls with age range of 2 –16 years with a mean of 8.4 ± 3.9 years were involved in the study. The average weight was 20.4 ± 7.4 kg. Age, gender, and weight were collected. Weight (kg) was measured on the day of US study.

Risk stratification of stroke by TCD was based on the time-averaged mean of the maximum velocity (TAMMvel) in the proximal middle cerebral artery. To calculate the blood-flow velocities of the brain vessels, examine both sides of the head using the trans temporal window to identify the maximum velocity (TAMMvel) in MCA. The evaluation explained to the patient and his parents. The child should be awake and cooperative during the examination, because if the patient becomes sleepy, CO2 level increases and can elevate the velocities, resulting in an inaccurate stratification of stroke risk. The children underwent TCD examination with a non-imaging technique using the Color Trans cranial Doppler system TCD, 2-MHZ pulsed Doppler instrument. First assess the TAMM velocity According to the STOP protocol; the highest velocity should be obtained in order to determine the TAMM. The TAMM velocity calculates manually, by placing the horizontal cursor so that the area above the line and under the peak of the waveform outline (A) is the same as the area below the line and above the waveform outline (B), and determining it over time.

3. Results

Table 1: Show statistical parameters for demographic and measurement information all patients:

| | Mean | Median | STD | Min | Max |
|--------------|--------|--------|-------|-----|-----|
| Age | 8.40 | 8 | 3.93 | 2 | 16 |
| Weight | 20.35 | 19 | 7.37 | 9 | 41 |
| TAMMV - RMCA | 110.50 | 111 | 19.59 | 55 | 158 |
| TAMMV - LMCA | 111.96 | 114 | 20.33 | 73 | 180 |

Table 2: Show correlate between gender with time-averaged mean of the maximum velocity in right middle cerebral artery:

| Gender | Time-Averaged mean of the Maximum Velocity- RMCA | | | | | | Total |
|--------|--|-------|--------|---------|---------|---------|-------|
| | 50-70 | 71-90 | 91-110 | 111-130 | 131-150 | 151-170 | |
| Male | 1 | 10 | 14 | 13 | 5 | 0 | 43 |
| Female | 1 | 3 | 16 | 24 | 7 | 2 | 53 |
| Total | 2 | 13 | 30 | 37 | 12 | 2 | 96 |

Table 3: Show correlate between gender with time-averaged mean of the maximum velocity in left middle cerebral artery

| Gender | Gender * Time-Averaged Mean of the Maximum Velocity in LMCA Crosstabulation | | | | | Total |
|--------|---|--------|---------|---------|---------|-------|
| | Time-averaged mean of the maximum velocity LMCA | | | | | |
| | 70-90 | 91-110 | 111-130 | 131-150 | 171-190 | |
| Male | 6 | 12 | 19 | 4 | 2 | 43 |
| Female | 9 | 14 | 23 | 7 | 0 | 53 |
| Total | 15 | 26 | 42 | 11 | 2 | 96 |

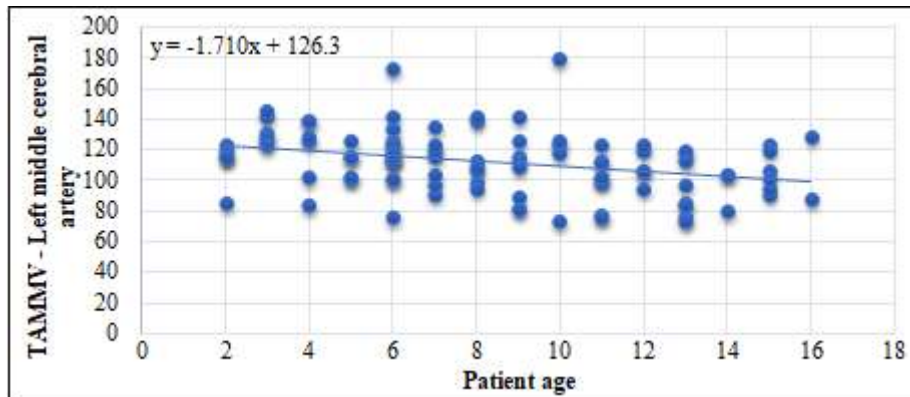


Figure 1: Show correlate between time-averaged mean of the maximum velocity in left middle cerebral artery and patients age

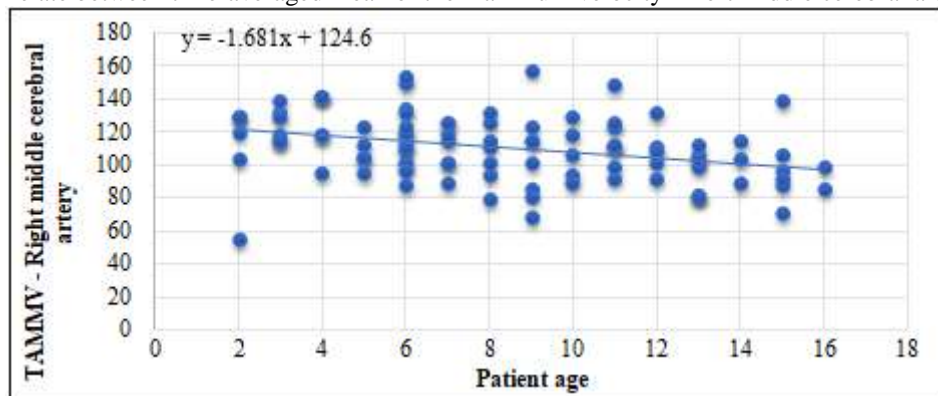


Figure 2: Show correlate between time-averaged mean of the maximum velocity in right middle cerebral artery and patients age

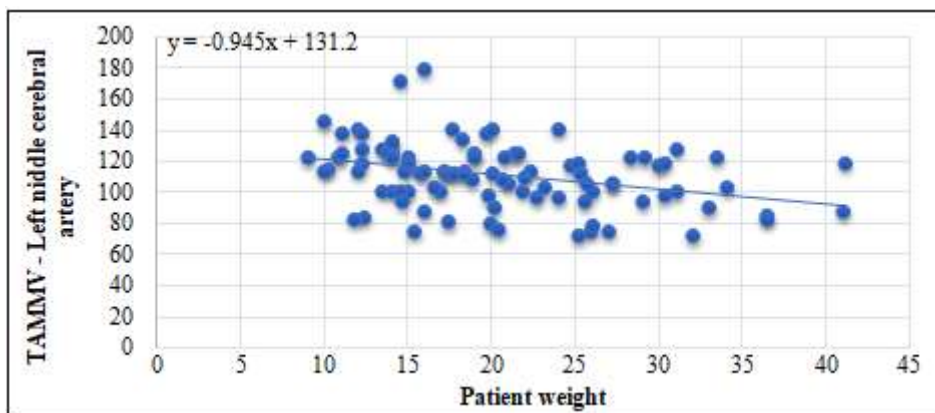


Figure 3: Show correlate between time-averaged mean of the maximum velocity in left middle cerebral artery and patients weight

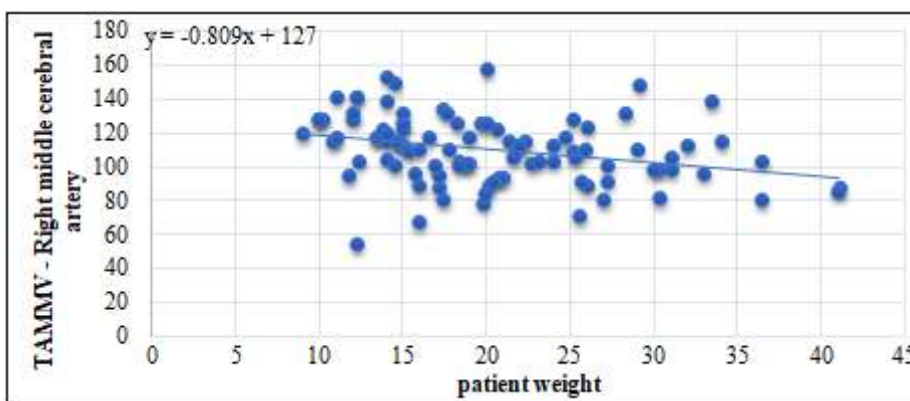


Figure 4: Show correlate between time-averaged mean of the maximum velocity in right middle cerebral artery and patients' weight

4. Discussions

Table 1. show statistical parameters for demographic and measurement information all patients were presented as mean, median, standard deviation, minimum and maximum. For age the mean \pm STD was 8.40 ± 3.93 , for weight, time-averaged mean of the maximum velocity in RMCA and LMCA were 20.35 ± 3.37 , 110.50 ± 19.59 and 111.96 ± 20.33 respectively.

Correlate between gender with time-averaged mean of the maximum velocity in the right middle cerebral artery were the number of male patients was 43 and the female number was 53, and the more frequent time-averaged mean of the maximum velocity in RMCA was 37 then 91-110 cm/s while the lowest frequent in time-averaged mean of the maximum velocity in RMCA 50-70 cm/s and 151-170 cm/s as shown in table 2.

Table 3. show correlate between gender with time-averaged mean of the maximum velocity in the left middle cerebral artery were ranged from 70-190cm/s, and the more frequent was 111-130 cm/s and the lowest frequent was 171-190 cm/s. Fig 1. Show correlate between time-averaged mean of the maximum velocity in the left middle cerebral artery and patients age, were the time-averaged mean of the maximum velocity in the left middle cerebral artery was decrease by rate 1.7109 for each year. Fig 2. Show correlate between time-

averaged mean of the maximum velocity in the right middle cerebral artery and patients age, were the time-averaged mean of the maximum velocity in the right middle cerebral artery was decrease by rate 1.6813 for each year. Fig 3. Show correlate between time-averaged mean of the maximum velocity in the left middle cerebral artery and patients' weight, were the time-averaged mean of the maximum velocity in the left middle cerebral artery was decrease by rate 0.9454 for each kg. Fig 4. Show correlate between time-averaged mean of the maximum velocity in the right middle cerebral artery and patients' weight, were the time-averaged mean of the maximum velocity in the right middle cerebral artery was decrease by rate 0.8092 for each kg.

5. Conclusion

Evaluation of sickle-cell anemia (Hb SS) patients without a history of clinical stroke were screened by TCD at Sudan sickle cell anemia center to determine the risk of stroke. Risk stratification of stroke by TCD was based on the time-averaged mean of the maximum velocity (TAMMvel) in the proximal middle cerebral artery.

The results show that a correlate between gender with time-averaged mean of the maximum velocity in the right middle cerebral artery were the number of male patients was 43 and the female number was 53, and the and the more frequent

time-averaged mean of the maximum velocity in the RMCA was 37 then 91-110 cm/s while the lowest frequent time-averaged mean of the maximum velocity in the RMCA 50-70 cm/s and 151-170 cm/s. And correlate between gender with time-averaged mean of the maximum velocity in the left middle cerebral artery were the time-averaged mean of the maximum velocity in the LMCA ranged from 70-190 cm/s, and the more frequent time-averaged mean of the maximum velocity was 111-130 cm/s and the lowest frequent was 171-190 cm/s. Using linear regression equation showed the correlation between time-averaged mean of the maximum velocity in the left middle cerebral artery and patients age, were the time-averaged mean of the maximum velocity in the left middle cerebral artery was decrease by rate 1.7109 for each year. And a correlation between time-averaged mean of the maximum velocity in the right middle cerebral artery and patients age, were the time-averaged mean of the maximum velocity in the right middle cerebral artery was decrease by rate 1.6813 for each year. Also the correlation between time-averaged mean of the maximum velocity in the left middle cerebral artery and patients' weight, were the time-averaged mean of the maximum velocity in the left middle cerebral artery was decrease by rate 0.9454 for each kg. And correlate between time-averaged mean of the maximum velocity in the right middle cerebral artery and patients' weight, were the time-averaged mean of the maximum velocity in the right middle cerebral artery was decrease by rate 0.8092 for each kg.

The highest time-averaged mean of the maximum velocity in the right and left middle cerebral arteries for majority of cases, within a normal TCD range (MCA TAMMX < 170 cm/s) then re-scanned annually until 16 years old.

And the time-averaged mean of the maximum velocity in the right and left middle cerebral arteries can be estimated from patients age and weight using linear equations as shown below:

TAMMV left middle cerebral artery = $-1.7109 (\text{age}) + 126.32$
 TAMMV right middle cerebral artery = $-1.6813 (\text{age}) + 124.62$
 TAMMV left middle cerebral artery = $-0.9454 (\text{Kg}) + 131.23$
 TAMMV right middle cerebral artery = $-0.8092 (\text{Kg}) + 127$

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