Cerebral artery conditional blood velocity in sickle cell disease: a multicentre study and evidence for active treatment

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ABSTRACT

Objective To obtain multicentre data on the prevalence of normal, high or conditional (intermediate) blood velocity in the cerebral arteries among children with sickle cell disease (SCD) in Nigeria.

Design A prospective observational study in five tertiary healthcare institutions. By transcranial Doppler (TCD) ultrasonography, cerebral artery peak systolic blood velocity (PSV) was determined in 193 children with SCD and time averaged mean of the maximum blood velocity (TAMMV) in a different cohort of 115 children. This design was to make the findings relevant to hospitals with TCD equipment that measure either PSV or TAMMV.

Setting Nigeria.

Participants 308 children (126 girls, 182 boys; age 2–16 years).

Main outcome measures Percentage of children with SCD who have normal, high or intermediate (often termed conditional) PSV or TAMMV.

Results In the cohort of 193 children, PSV was normal in 150 (77.7%), high in 7 (3.6%) and conditional in 36 (18.7%). In the cohort of 115 children, TAMMV was normal in 96 (84%), high in 7 (6%) and conditional in 12 (10%). There were no significant differences in gender or age distribution between the PSV and TAMMV cohorts. Altogether, cerebral artery blood velocity was normal in 246/308 children (80%), high in 14 (4.5%) and conditional in 48 (15.5%).

Conclusion Since conditional blood velocity in cerebral arteries can progress to high values and predispose to stroke, the proportion of children with SCD who are affected (15.5%) raises the question of whether regular monitoring and proactive intervention ought to be the standard of care.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In children with sickle cell disease, high blood flow velocity in the cerebral arteries is associated with an increased risk of stroke, and intermediate (often termed conditional) blood velocity in the cerebral arteries may progress to high values in a significant proportion of children with sickle cell disease.

⇒ Currently, there is no generally accepted standard of care for children with sickle cell disease and conditional cerebral artery blood flow velocity.

⇒ Single-centre studies of the percentage of children with sickle cell disease in Nigeria who have cerebral artery high or conditional blood flow velocity have yielded variable results.

WHAT THIS STUDY ADDS

⇒ This study provides multicentre data on the proportion of children with sickle cell disease in Nigeria who have conditional blood velocity in the cerebral arteries. These data are more likely to reflect the general situation in this country that has the highest birth rate of children with sickle cell disease.

INTRODUCTION

High blood velocity in the cerebral arteries of children who have sickle cell disease (SCD) is associated with increased risk of ischaemic stroke.[1–9] Transcranial doppler (TCD) ultrasonography is used to determine the time averaged mean of the maximum blood velocity (TAMMV). Normal, high and intermediate (often termed conditional) values of cerebral artery blood velocity in children with SCD had been established in previous studies[4 9] and are used in routine clinical practice. The TAMMV in the internal carotid artery (ICA) or middle cerebral artery (MCA) is normal in a child with SCD if the highest value is <170 cm/s.[4 9] A normal TAMMV in the ICA/MCA is associated with a clinically overt stroke risk of <1% per year in childhood SCD.[4 9] The TAMMV in the ICA or MCA in a child with SCD is high if the highest value is >200 cm/s.[4 9] A high TAMMV in the ICA/MCA is associated with a clinically overt stroke risk of 10% per year in childhood SCD.[4 9] Highest TAMMV values in the ICA/MCA 170–199 cm/s in childhood SCD are described as intermediate or conditional because they might subsequently increase to abnormal values.[4 9] Conditional TAMMV in the ICA/MCA is associated with

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HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings from this study could guide the development of policies on standards of care for children with sickle cell disease and high and conditional blood velocity in the cerebral arteries.
⇒ Information from this study will enable paediatricians to have a more accurate picture of cerebral artery blood velocity. A more informed appreciation of this issue could prompt proactive intervention in clinical practice.
⇒ The results of this multicentre study of cerebral artery blood velocity in children living with sickle cell disease in Nigeria might serve as reference data for future nationwide epidemiological research.

a stroke risk of 3%–4% per year in childhood SCD.[4 9] Some TCD machines determine peak systolic blood velocity (PSV) in the cerebral arteries.[10–12] The normal PSV is <200 cm/s, high >250 cm/s and conditional 200–249 cm/s. The standard of care for high blood velocity in the ICA/MCA is regular blood transfusion to prevent stroke,[1–9] but active intervention is not generally considered the standard treatment for conditional blood flow velocity. Conditional blood flow velocity does progress in a significant proportion of children to abnormal values that are associated with increased risk of ischaemic stroke.[11 12] In a previous evaluation of the benefits of active intervention with 3 months of multimodal therapy comprising omega-3 fatty acids and potassium thiocyanate, progression of conditional blood velocity to abnormal values occurred in none (0%) of treated children relative to 14% of the control group on standard care of SCD only, and PSV reduced to normal values in 79% of the treatment compared with 43% of the control group.[12] Two other studies showed reduction of conditional blood velocity to normal values following hydroxycarbamide therapy.[13 14] If a considerable percentage of children with SCD have conditional blood velocity in the cerebral arteries, proactive intervention with treatment modalities not associated with the hazards of regular blood transfusion or the potential cytotoxic side effects of hydroxycarbamide might be justifiable to reduce the number that progress to abnormal velocity.

In Nigeria, the country that has the largest population of people with SCD (3 million) and the highest SCD birth rate of 150 000 per year,[15–18] previous studies of the percentage who have conditional blood velocity in the cerebral arteries have been in single healthcare institutions and yielded variable results.[19–24] The objective of this study is to obtain multicentre data to represent the general situation in the country and so facilitate the development of policy on the care of children with SCD who have conditional blood velocity in the cerebral arteries.

MATERIALS AND METHODS

Study design and population

Following approval by the Health Research Ethics Committee, informed consent by the legal guardians and assent by the children as appropriate, this prospective study was done in five tertiary healthcare institutions in Nigeria. The main outcome measure was the proportion of children with SCD who have normal, high or conditional PSV or TAMMV in the cerebral or internal carotid arteries. Although it was not possible to calculate the minimum sample size required for this study because the prevalence in Nigeria of cerebral artery conditional blood velocity in childhood SCD is not certain, a previous study in this country recruited 232 children.[12] Guided by the previous report, the minimum sample size for this study was increased to 300. We studied 308 children with SCD (126 girls and 182 boys) aged 2–16 years. The haemoglobin phenotype had been confirmed by high performance liquid chromatography. In one cohort of 193 children with SCD (76 girls, 117 boys) cerebral artery PSV was determined by TCD. In another cohort of 115 children with SCD (50 girls, 65 boys), TAMMV in the cerebral arteries was determined. The design to determine PSV or TAMMV was deliberate to make the research findings useful to hospitals with TCD equipment that measure either parameter. Children with SCD who had stroke, or were on regular blood transfusion or hydroxycarbamide to prevent primary or secondary stroke, were excluded from this study. Sociodemographic data on the participants, including age and gender, were documented.

TCD ultrasonography

Trained personnel (two radiologists and one paediatrician) did the ultrasonography in all participants while in steady state SCD. To reduce interobserver variation,[25] ultrasonography was done following a written protocol. On each participant, two sessions of ultrasonography were performed, separated by a minimum interval of 30 min. This is to increase the reliability and reproducibility of the measurements at the specific time point. The average scan time was 15 min. Prior to the commencement of sonography, the procedure was explained to the participant and guardian. The participant was asked to lie in the supine position on a clinical examination couch and keep awake throughout the procedure. The sonographer sat comfortably on a chair near the head of the couch close to the TCD machine. The ultrasonic gel was applied to the 2 MHz transducer and placed at the temporal window (2–3 cm in front of the tragus of the ear). Adjustments were made to identify and optimise the spectral signals.

In accordance with current standards of care, children with high TAMMV or PSV in the anterior cerebral, middle cerebral or internal carotid artery were started on a blood transfusion programme to prevent ischaemic stroke. To determine PSV, TCD was done with a non-imaging (non-duplex) system: the Multigon Neurovision TOC 1M TCD system (Multigon Industries, Inc, Elmsford, NY, USA). The sample volume was 6–12 mm, the scale extended to more than 250 cm/s, acquisition commenced at 50 mm or near the bifurcation and peak velocities saved at an increment or decrement depth of 2 mm. Anatomical segments were identified by their depth, direction of flow, traceability, audio signal and spectral waveform. The anatomical segments of the MCA were primarily identified in this non-imaging TCD based on the distance from the bifurcation of the distal ICA. Ultrasonography was done on arteries of the left and right cerebral hemispheres. The highest PSV in the MCA, anterior cerebral artery or ICA were recorded. The distal ICA and its main branch the MCA were used in the study because most significant lesions occur in these arteries. The long linear tract of the MCA allows for ease of accessibility and reproducibility of the findings in a non-imaging study. For TAMMV, we used a non-imaging (non-duplex) system: the DWL Multidop T (DWL MDT 2419, Germany). The sample volume was 6 mm, the scale extended to more than 250 cm/s or as appropriate for the examination. Acquisition commenced at the distal MCA where signal is detected (≥30 mm) towards the bifurcation of the ICA, TAMMV saved at an incremental depth of 2 mm and terminated at the bifurcation of the ICA. Anatomical segments were identified by their depth, direction of flow, traceability, audio signal and spectral waveform. TAMMV for the distal ICA was recorded

from the bifurcation with angulation of the probe inferiorly. The highest value of TAMMV in the MCA or the distal ICA and the anatomical segment depth for each side were documented.

Those with normal PSV or TAMMV were reassured and booked for repeat TCD ultrasonography after 1 year. Children with conditional blood velocity were rescanned at 3-monthly intervals. In accordance with the standard of care, those with high velocity were started on regular blood transfusion to prevent stroke.[1–4]

Statistical analysis

Data generated were collated and analysed with the Statistical Package for Social Sciences (SPSS V.23, IBM, Armonk, NY, USA). Frequencies, means and SD for demographic and ultrasound parameters were calculated. The two-tailed independent sample t-test was used to evaluate differences between parameters, and a p value of <0.05 taken as indicating a statistically significant difference.

RESULTS

A total of 308 children with SCD participated in this study: 126 girls and 182 boys. The age range for all participants was 2–16 years, the mean age was 8.86 years and the SD 3.98 years. Since two types of TCD machines are used in Nigeria,[10–12] PSV and TAMMV were measured in separate cohorts used to make the findings clinically relevant and useful to hospitals with either PSV or TAMMV equipment. The TAMMV cohort had 115 children (50 girls, 65 boys) with an age range of 3–16 years, mean±SD 8.78±3.37 years. The PSV cohort included 193 children (76 girls and 117 boys) with age range 2–16 years and mean±SD of 8.91±4.32 years. There was no statistically significant difference in age or gender distribution between the TAMMV and PSV cohorts (p>0.05). The proportions of children with normal, abnormal (high) or conditional (intermediate) blood velocity in each cohort is shown in table 1.

There was no difference in frequency of conditional velocity between the left and right cerebral hemispheres (table 2 and figures 1 and 2).

Supplementary data

Individual cerebral artery blood velocities in all the 308 children who participated in this study are accessible in online supplemental tables 1 and 2.

DISCUSSION

Stroke in a child adversely affects the life of the patient and that of an adult relative or guardian (usually the mother) who provides personal care for the child. In a child with SCD, stroke significantly increases the burden of care, the time and material resources expended and the adverse effects on family life; such as the inevitable reduction in attention paid by parents to the siblings of a child who has this haemoglobinopathy. So, stroke increases the psychological burden associated with SCD. Time devoted by the parents to care for their child who has a stroke usually translates to less time at work and loss of income to the family. By extension, this means a reduction in economic productivity, both nationally and globally. Medically, a cerebrovascular accident is a very serious complication that affects the outcome of SCD, especially if it recurs.[1 2 12 18 26–29] Therefore, considered together, the medical, psychological, social and economic implications of stroke in a child with SCD are such that all care ought to be taken to prevent the accident in each individual at risk.

This multicentre study in five tertiary health centres in Nigeria found a prevalence of 15.5% for conditional (intermediate)

Table 1 Blood velocity in the cerebral arteries of children with sickle cell disease

Cohort	Normal	Abnormal (high)	Conditional (intermediate)
TAMMV n=115	96 (84%)	7 (6%)	12 (10%)
PSV n=193	150 (77.7%)	7 (3.6%)	36 (18.7%)
All participants n=308	246 (80%)	14 (4.5%)	48 (15.5%)

PSV, peak systolic velocity; TAMMV, time averaged mean of the maximum velocity.

Table 2 Comparison of blood velocity in arteries of the left vs right cerebral hemispheres

	TAMMV cohort n=115		PSV cohort n=193	
Blood velocity	Left cerebral hemisphere	Right cerebral hemisphere	Left cerebral hemisphere	Right cerebral hemisphere
Conditional (intermediate)	12	11	15	21
Abnormal (high)	5	3	1	6
Normal	98	101	177	166
Total	115	115	193	193

PSV, peak systolic blood velocity; TAMMV, time averaged mean of the maximum blood velocity.

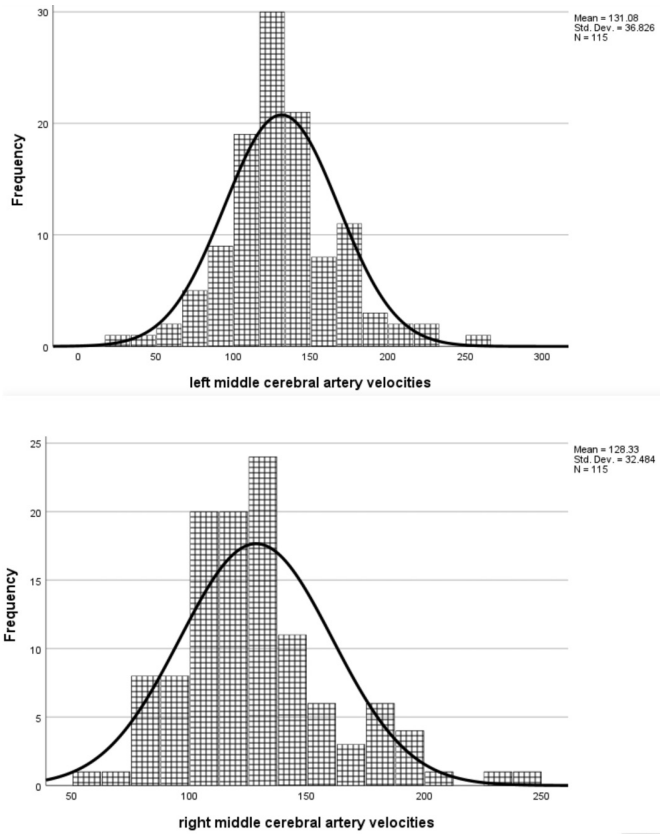

Figure 1 Frequency distribution of time averaged mean of the maximum blood velocity (cm/s) in the left (top) and right (bottom) middle cerebral arteries of children with sickle cell disease.

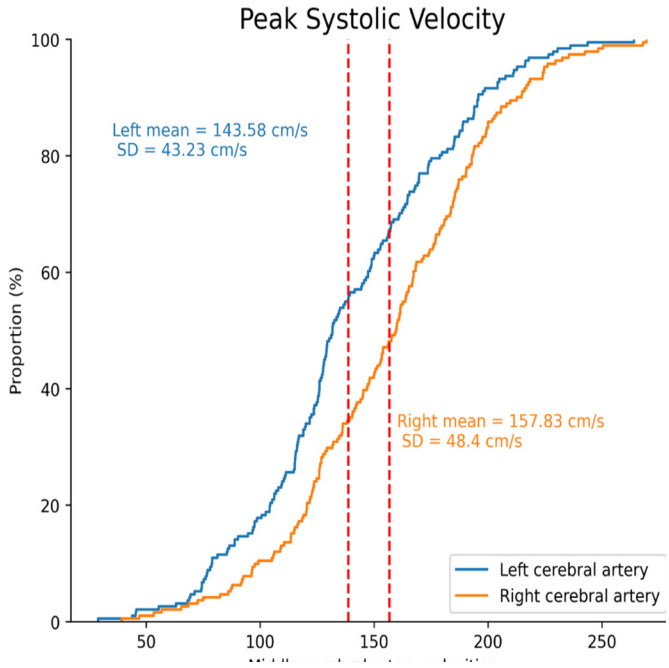

Figure 2 Cumulative frequency curves for peak systolic blood velocities (PSV, cm/s) in the middle cerebral arteries (MCAs) of children with sickle cell disease. Left MCA: curve to the left. Right MCA: curve to the right. Vertical dotted line to the left indicates mean PSV in left MCA; vertical dotted line to the right indicates mean PSV in right MCA.

blood velocity in at least one cerebral artery in children with SCD. This proportion differs from single-institution data of 25.6%[22] and 21.9%[24] previously reported in Nigeria. Coexistent genetic factors in the study population, sample size, whether TAMMV or PSV was measured, and geographical spread of the participants might contribute to variation in the proportion of children with SCD who have conditional blood velocity in the cerebral arteries. A single-institution study in Nigeria showed that the coexistence of alpha thalassaemia trait protects against a rise in cerebral artery blood velocity, whereas no significant association with glucose-6-phosphate dehydrogenase was observed.[23] That the parameter used could affect the proportion with conditional velocity is suggested by the similarity in the percentage in the TAMMV cohort in this study (10%) and that of 9.9% from another multicentre survey of children with SCD in Brazil during which TAMMV was measured.[30]

Children with conditional blood velocity can progress to abnormal (high) values that are associated with increased risk of stroke or cerebrovascular accident.[12 13] In situations when thousands of individuals are at risk, the adverse effects of cerebrovascular accidents are multiplied accordingly. This is the situation in countries where thousands of children are born with SCD every year. For example, an estimated 150 000 children are born with SCD every year in Nigeria.[15–18 31 32] Data from this study suggest that 15.5% of these could develop conditional blood velocity in at least one cerebral artery by the age of 16 years. This translates to an absolute number of over 20 000 children. Findings from a previous study of the benefits of proactive treatment of cerebral artery conditional blood velocity in SCD suggest that, untreated, this condition could progress to abnormal (high) velocity in 14% of affected Nigerian children.[12] The absolute number would be around 3000 children at increased risk of stroke. The same number would be added every year. So, the population of children with SCD and abnormal (high) blood velocity in cerebral arteries would cumulate. Health service resources would be stretched to provide care for such a large population of children. In Brazil, 9.9% of children with SCD had conditional TAMMV.[30] Meta-analysis of data showed a 10.6% prevalence of conditional blood velocity across Africa.[26] Therefore, there is a strong case for active treatment of conditional blood velocity in SCD, and various studies have demonstrated its benefit.[12–14]

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Contributors All authors contributed to data collection, drafting the manuscript, reviewing the revised drafts for accuracy and intellectual content, approved the final version of the manuscript as submitted and agree to be accountable for all aspects of the work. EM, BC and NI performed transcranial Doppler ultrasonography on the study participants. AM and CN-E carried out statistical analyses of the study data. IO conceptualised, designed the study and acted as guarantor.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. Supplementary material: individual cerebral artery blood velocities in all the 308 children who participated in this study are accessible as online supplemental data in tables 3 and 4.

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Supplementary Data

Table 1. Timed averaged mean of the maximum cerebral artery blood velocity in children with sickle cell disease

Identity Number	**Age (yrs)**	**Sex**	**Left**			**Right**		
			TAM (cm/s)	Artery	Depth (cm)	TAM (cm/s)	Artery	Depth (cm)
1	5	M	227	MCA	50	192	MCA	42
2	6	M	180	MCA	46	212	MCA	40
3	12	F	204	MCA	40	154	MCA	60
4	5	M	259	MCA	36	85	MCA	36
5	8	M	207	MCA	42	189	MCA	50
6	9	M	224	MCA	52	240	MCA	52
7	3	M	190	MCA	44	227	MCA	48
8	7	F	170	MCA	48	173	MCA	44
9	11	M	179	MCA	52	174	MCA	40
10	7	M	177	MCA	52	183	MCA	48
11	4	M	184	MCA	40	181	MCA	44
12	4	F	171	MCA	42	188	MCA	48
13	5	F	178	MCA	44	176	MCA	48
14	9	F	192	MCA	42	179	MCA	46
15	10	M	174	MCA	48	170	MCA	46
16	2	F	170	MCA	44	196	MCA	46
17	7	M	176	MCA	54	114	MCA	42
18	6	M	176	MCA	48	183	MCA	48
19	5	M	176	MCA	42	179	MCA	42
20	12	M	118	MCA	48	140	MCA	52
21	9	M	118	MCA	42	127	MCA	44
22	5	F	163	MCA	44	160	MCA	48

23	10	F	130	MCA	48	156	MCA	58
24	11	F	33	MCA	52	96	MCA	48
25	10	F	148	MCA	48	133	MCA	44
26	7	F	80	MCA	50	82	MCA	52
27	10	F	79	MCA	54	115	MCA	50
28	10	F	137	MCA	50	132	MCA	48
29	12	M	152	MCA	46	126	MCA	52
30	11	F	104	MCA	48	84	MCA	36
31	6	F	101	MCA	52	100	MCA	40
32	12	M	107	MCA	44	108	MCA	50
33	12	M	102	MCA	52	84	MCA	40
34	4	F	122	MCA	28	123	MCA	46
35	10	F	118	MCA	48	123	MCA	44
36	6	F	127	MCA	50	115	MCA	42
37	12	M	146	MCA	50	137	MCA	48
38	5	F	119	MCA	38	127	MCA	48
39	11	F	118	MCA	56	154	MCA	46
40	10	M	130	MCA	44	111	MCA	52
41	11	M	138	MCA	50	131	MCA	52
42	7	F	128	MCA	36	111	MCA	40
43	8	F	124	MCA	46	104	MCA	48
44	9	M	145	MCA	46	125	MCA	50
45	10	M	113	MCA	46	121	MCA	40
46	10	F	121	MCA	40	85	MCA	40
47	9	M	161	MCA	50	136	MCA	44
48	9	M	124	MCA	50	108	MCA	54
49	3	M	148	MCA	48	132	MCA	32
50	9	M	108	MCA	60	146	MCA	58
51	8	F	121	MCA	48	97	MCA	44

52	6	F	64	MCA	56	133	MCA	50
53	13	F	110	MCA	42	129	MCA	46
54	9	F	124	MCA	54	91	MCA	58
55	4	F	143	MCA	38	141	MCA	44
56	3	F	132	MCA	48	131	MCA	44
57	9	M	144	MCA	48	132	MCA	52
58	8	M	150	MCA	48	145	MCA	44
59	8	F	132	MCA	42	118	MCA	44
60	8	M	143	MCA	44	134	MCA	44
61	4	M	161	MCA	44	147	MCA	44
62	11	M	96	MCA	42	134	MCA	52
63	12	M	97	MCA	52	98	MCA	48
64	7	M	148	MCA	48	146	MCA	44
65	15	F	117	MCA	52	104	MCA	42
66	14	M	118	MCA	52	123	MCA	58
67	4	M	144	MCA	38	144	MCA	42
68	6	F	113	MCA	48	147	MCA	46
69	9	F	136	MCA	46	127	MCA	46
70	6	M	108	MCA	50	109	MCA	46
71	12	F	162	MCA	50	61	MCA	60
72	16	F	100	MCA	58	109	MCA	54
73	14	M	127	MCA	50	123	MCA	48
74	12	M	119	MCA	46	102	MCA	44
75	16	M	119	MCA	50	123	MCA	50
76	5	M	107	MCA	40	124	MCA	52
77	5	M	152	MCA	40	74	MCA	52
78	11	F	136	MCA	42	126	MCA	50
79	14	M	126	MCA	48	89	MCA	58
80	10	F	142	MCA	42	122	dICA	54

81	12	M	150	MCA	48	139	MCA	44
82	10	F	66	MCA	50	108	MCA	42
83	13	M	75	MCA	38	108	MCA	50
84	6	M	146	MCA	28	120	MCA	54
85	2	M	110	MCA	48	101	MCA	44
86	10	M	147	MCA	42	121	MCA	50
87	5	M	124	MCA	48	111	MCA	46
88	11	M	95	MCA	48	76	MCA	46
89	14	M	157	MCA	58	132	dICA	60
90	7	F	106	MCA	50	101	MCA	50
91	8	F	73	dICA	60	114	MCA	44
92	12	F	122	MCA	54	107	MCA	48
93	9	F	116	MCA	41	115	MCA	55
94	4	M	104	MCA	52	129	MCA	42
95	2	M	122	MCA	36	114	MCA	42
96	8	F	91	MCA	30	157	MCA	52
97	12	M	153	MCA	50	150	MCA	50
98	11	M	85	MCA	44	85	MCA	44
99	15	M	130	MCA	46	125	MCA	48
100	12	M	113	MCA	48	95	MCA	54
101	14	M	91	MCA	48	135	MCA	44
102	15	M	130	MCA	46	111	MCA	50
103	11	M	113	dICA	52	132	MCA	46
104	10	M	135	MCA	44	119	MCA	40
105	6	F	114	MCA	48	124	MCA	44
106	6	F	86	MCA	52	101	MCA	42
107	7	F	44	MCA	38	86	MCA	44
108	12	F	104	MCA	52	104	MCA	50
109	6	M	84	MCA	32	142	MCA	46

110	11	F	143	MCA	46	136	MCA	50
111	12	F	68	MCA	40	90	MCA	50
112	12	F	148	MCA	48	148	MCA	48
113	6	M	130	MCA	46	116	MCA	56
114	10	M	111	MCA	44	92	MCA	42
115	5	M	121	MCA	44	104	MCA	42

Total 115	Abnormal ≥200cm/s	Conditional 170-199cm/s	Normal <170cm/s
M: Males 65	7 (6%)	12 (10%)	96 (84%)
F: Females 50			

MCA: middle cerebral artery dICA: distal internal carotid artery

Supplementary Data

Table 2. Peak systolic blood velocity in cerebral arteries of children with sickle cell disease

Identity Number	Age (Yrs)	Sex	RMCA	RICA	LMCA	LICA	Comment
116	13	M	272	103	214	133	A
117	8	F	181	265	169	155	A
118	10	F	129	148	117	71	
119	6	M	114	52	82	82	
120	12	M	181	36	189	57	
121	3	F	205	152	248	117	C
122	16	F	141	74	149	201	C
123	8	M	214		172	102	C
124	16	M	134	125	144	139	
125	8	M	158	109	155	132	
126	11	F	199	221	196	193	C
127	9	M	239	163	169	175	
128	15	M	147	143	160	136	
129	13	M	116	115	104	107	
130	8	M	176	87	156	162	
131	9	F	198	81	188	198	
132	14	F	146	101	141	107	
133	6	M	178	95	96	92	
134	13	M	166	100	108	105	
135	6	M	169	195	176	173	
136	3	F	149		192	195	
137	5	F	218		234	221	C
138	13	M	162	172	159	107	

139	11	M	132	103	202	201	C
140	5	M	164	132	159	181	
141	5	M	168		136		
142	5	F	168		131		
143	12	M	166	180	220		C
144	13	M	128	141	153	146	
145	10	F	116		152		
146	13	M	133		127		
147	4	F	139	157	156	157	
148	5	M	208	185	190	182	C
149	16	F	110	112	128	155	
150	10	M	136	104	155	182	
151	11	M	112	58	137	128	
152	9	M	106	99	141	158	
153	6	F	180	183	204	204	C
154	5	M	139	145	151	164	
155	10	F	176	172	175	179	
156	9	F	192	172	162	187	
157	10	M	300	224	161	132	A
158	7	M	220	120	130	189	C
159	9	F	226	194	198	188	C
160	10	F	214	258	136	99	C
161	16	F	103	51	96	65	
162	5	M	324	248	241	240	A
163	16	M	199	144	124	104	
164	14	M	185	181	63	93	
165	5	M	64	70	75	103	

166	14	F	218	209	186	193	C
167	2	M	151	128	122		
168	6	M	186	163	159	153	
169	14	F	211		204	200	C
170	16	M	144	148	127	143	
171	13	M	157	119	157	130	
172	15	M	175	122	91	157	
173	3	M	162	161	144	191	
174	4	F	202	141	180	146	
175	14	F	240	246	224	61	C
176	16	F	146	178	112	82	
177	10	M	114	84	156	114	
178	15	M	189				
179	12	M	169		114	105	
180	11	M	154		152		
181	3	M	230	178	198	211	
182	12	M	128	136	148	85	
183	3	M	151	159	70	105	
184	4	M	280	313	129	286	A
185	5	F	146	168	90	118	
186	3	F	139	150	120	219	C
187	9	F	125	174	56	104	
188	10	F	120	122	128	173	
189	3	M	84	118	58	145	
190	2	M	184	206	131	192	C
191	9	M	184	126	142	129	
192	2	M	108	174	174	138	

193	14	M	34	95	57	83	
194	12	M	126	110	142		
195	15	M	145	115	111	80	
196	5	F	53	60	80	60	
197	14	F	145	57	84	109	
198	10	F	236	219	97	61	C
199	16	F	50	63	90	78	
200	7	F	202	225	180	103	C
201	9	M	200	234	181	179	C
202	6	F	236	213	182	182	C
203	5	F	141	108	139	139	
204	10	M	213	108	91	89	C
205	13	M	150	153	177	162	
206	15	M	94	107	121	108	
207	14	F	160	81	83	161	
208	7	M	181	178	177	160	
209	8	F	177	181	177	177	
210	16	F	177	139	122	177	
211	16	F	90	113	139	96	
212	8	F	173	168	175	138	
213	7	F	152	98	161	90	
214	5	F	145		129		
215	8	F	228		186	162	C
216	3	F	120	197	135	176	
217	7	F	112	63	149	231	C
218	5	M	248	227	263	140	A
219	5	F	155	65	171	138	

210	3	F	222	208	144	219	C
211	6	M	105	177	150	143	
212	7	M	152	163	182	157	
213	2	M	80	66	79	102	
214	5	M	143	115	98		
215	3	M	133		148	149	
216	8	F	204			206	C
217	5	F	174	70	118	48	
218	9	M	211	179	156	191	
219	3	M	73	142	94	61	
220	7	M	106	110	145	161	
221	5	M	155	142	103	125	
222	8	M	124	101	173		
223	6	M	132	77	76	151	
224	4	F	239	94	237	207	C
225	7	M	184	126	142	129	
226	6	M	155		147	199	
227	14	M	185	179	121	154	
228	11	M	163	149	140	183	
229	11	M	177	169	163	192	
230	15	M	149		164	205	
231	9	M	181	171	174	177	
232	5	M	174	165	184	130	
233	6	M	167	169	171	188	
234	3	F	147		146		
235	8	F	197		80		
236	15	M	141	121	178	177	

237	15	F	182	141	163	105	
238	4	M	144	87	113	84	
239	10	F	187	89	51	71	
240	3	M	69	98	94	94	
241	15	M	137	154	98	74	
242	4	M	184	169	162	209	C
243	12	F	175	120	111	86	
244	13	F	83	73	80	72	
245	8	F	215	234	238	211	C
246	2	M	128	123	119	98	
247	16	F	52	110	91	94	
248	6	M	162	149	162		
249	4	F	202	158	202		C
250	13	M	178	127	64	115	
251	8	M	106	89	90	118	
252	6	M	129	138	104	90	
253	13	M	86	68	105	183	
254	16	F	41	94	85	134	
255	16	F	87	83	65	86	
256	16	M	102	98	89	89	
257	12	M	98		82		
258	16	M	109	92	98	103	
259	8	F	117	127	125	128	
260	10	M	208	196	193	208	C
261	6	M	250	213	215	125	A
262	6	M	190	182	195	172	
263	6	F	131	141	138	131	

264	4	M	176	168	184	188	
265	16	M	160	160	143	147	
266	3	F	157		130		
267	13	M	115	107	93	119	
268	9	F	182	106	119	106	
269	12	M	219	150	216	136	C
270	10	F	124	172	152	179	
271	2	F	196	165	173	165	
272	14	F	190	167	162	151	
273	4	M	125	155	123	83	
274	3	M	155	154	175	171	
275	2	M	74	160	106	95	
276	16	M	136	140	148	151	
277	11	F	163	164	114	143	
278	10	F	170	155	149	118	
279	2	F	125	134	179	175	
280	9	F	151	206	111	134	C
281	11	F	170	160	164	138	
282	9	M	163	153	118	120	
283	2	M	127	105	169	149	
284	15	M	171	175	167	164	
285	7	M	99	112	79	73	
286	5	M	80	123	112	85	
287	9	M	112	101	104	113	
288	14	M	143	143	186	159	
289	10	M	90	81	109	103	
290	12	M	168	108	206	83	C

291	8	M	89	81	113	81	
292	10	F	160	130	159	131	
293	4	M	219	157	246	246	C
294	12	M	126	135	160	116	
295	5	M	228	162	172	128	**C**
296	6	F	173	95	123	104	
297	5	F	182	128	152	139	
298	14	M	179	92	171	151	

Total Number of children: 193 Males (M):117 Females (F): 76

A: Abnormal ≥ 250cm/s C: Conditional 200-249 cm/s Normal <200 cm/s

7 (3.8%) 36 (19.7%) 150 (76.5%)

RMCA: right middle cerebral artery LMCA: left middle cerebral artery

RICA: right internal carotid artery LICA: left middle cerebral artery