Original Article

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Association between Sickle Cell Disease and Malocclusion among A Sample of Sudanese Children

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Abstract

Background: Sickle cell disease is an autosomal recessive hemoglobinopathy predominant among Afro-descendants, and has been categorized as a public health issue as it affects a significant percentage of the world's population. The objective of this study was to determine the association between malocclusion and sickle cell disease in a sample of Sudanese children compare to healthy controls children. *Methods:* Malocclusion traits was recorded for 212 sickle cell disease children aged 3-15 years old, matched with 212 control healthy children in Khartoum, Sudan. Statistical analysis was done using statistical software SPSS 17.5 version. Chi square test was used for the comparison of study and control groups, the level of significance was set at $p<0.05$. The relative risk was estimated for malocclusion. *Results:* Malocclusion was significantly higher in sickle cell disease children than healthy control children. The common malocclusion traits were Angle's Class II with increased over jet followed by anterior open bite. The malocclusion traits and relative risk were significantly more among sickle cell disease individuals 12-14 years old compared to the control group. *Conclusion:* Sudanese sickle cell disease children had high prevalence of malocclusion than healthy children. Early recognition of malocclusion, preventive and interceptive dental treatment was recommended.

Keyworld: Sickle Cell; Malocclusion; Children.

Introduction

Sickle Cell Disease defined as hereditary autosomal recessive blood disorder, characterized by hemoglobin gene mutation caused by amino acid substitution in the gene coding valine is encoded instead of glutamic acid results in the production of hemoglobin S rather than hemoglobin A[1, 2].

Two types of sickle cell disease were recognized; homozygous and heterozygous. Homo- zygous have S-type haemoglobin (Hb-SS), and sickle-cell disease develops as a result. Heterozygous (Hb-SA) have a sickle cell trait with 40% of S-type haemoglobin (Hb-SS), which define milder characteristics concerning the disease[1, 3-6].

In Sudan, sickle cell disease is following the natural extension of West African sub- Saharan belt. The most prevalent variant among the African and Sudanese population is the HbSS variant [3-5].

Recurrent painful crisis (vaso-occlusive crisis) the common symptom of sickle cell disease result from obstruction of small blood vessels by the suckled red blood cells which leads to local oxygen depletion, acidosis, necrosis and severe pain[1, 6].

Malocclusion in sickle cell disease patients is due to Bone marrow hyperplasia, and compensatory expansion of medullar spaces manifest as mid face protrusion and maxillary expansion[7-17]. Although the etiology of malocclusion is multifactorial, it include genetic, environmental and local factors the difficulty of separating these factors is obvious [18].

Material and Methods

This is a retrospective cohort study, as sickle cell disease is genetic disease thus the exposure occurs at birth. A total of 212 children 4-14 years old attended Jaafer Ibn Oaf hospital with confirmed diagnosis of

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sickle cell disease (HbSS genotype) was selected through simple randomization for this study, matched to randomly selected kindergarten and primary school children selected through multistage sampling was applied on the basis of birth date and gender.

All examination of the study group and the control group were carried out at Jaafer Ibn Oaf hospital and schools respectively at the office under artificial light, while the child sitting in an up-right position in front of the examiner, and the examination of malocclusion was done while the teeth in the maximum intercuspation using a plane dental mirror and ruler.

Age stratification was used, according to the WHO [19] into three age groups; age group one that includes children aged 4-6 years old. Second age group, this includes children aged 7-11years old and third age group includes children aged 12-14 years old. Approval from Research Committee of the University of Khartoum- Faculty of Dentistry was obtained prior to the conduction of the study. Clinical calibration of the investigator in the clinical examination was carried out in 20 cases. All Kappa values were considered acceptable according to the qualitative classification of kappa values as the degree of agreement [20, 21].

Data were Collected, Summarized, Cleaned and Coded; then Entered to the Statistical

Package for Social Sciences (SPSS) program (version 20). Frequency tables and descriptive statistic were done. Chi square test was used P-value of less than 0-05 was considered as significant. 95% confidence interval (CI) for malocclusion was estimated and compared using Chi- square. The association between sickle cell disease and malocclusion was estimated by the adjusted relative risk (RR) and respective 95% CI were calculated.

Ethical Consideration

Approval from research Committee University of Khartoum- Faculty of Dentistry was obtained prior to the conduction of the study. A written permission to carry out the study was obtained from the directors of Jaafer Ibn Oaf hospital and the head masters of the schools. The consent was obtain from each child and child's caregiver.

All the participants were given oral hygiene education and motivation instruction after examination. During examination, all children with dental problems were referred to Pedodontics clinic the faculty of dentistry, University of Khartoum for appropriate management.

Results

The number of children examined in the present study was 424 (226 boys and 198 girls) within age range 4-14 years old, and it comprised of two equal groups; sickle cell disease and control (healthy) group (Table 1).

It was clear that the number of boys was more than girls and the majority in the age group 4-6 years old while low percentage in the age group 7-11 years old.

Table 2 showed the distribution of malocclusion trait among 4-6 years old sickle cell disease children and control children. It is obvious that control group had a flush terminal plane, and no malocclusion was recorded except anterior open bite (1.3%). Whereas, sickle cell disease children showed a minor increase in crowding, horizontal overbite and vertical overbite relationship. A significant association between sickle cell disease group and control group using Chi-square test was noted in all examined malocclusion traits except the vertical overbite relationship. In the terminal plane relationship, a significant association recorded (P=0.014) through Fisher exact test that was used instead of Chi-square. Although there is no significant association about vertical overbite (P=0.06), the sickle cell disease group showed increased relative risk (6.1).

Age Group7-11years

Concerning age group 7-11 years old, more or less the same findings had been recorded about malocclusion traits as the 4-6 years age group in the control group. The sickle cell disease group had increased incidence of Angle's Class II malocclusion (19.7%), increased horizontal overbite (30.3%), increased vertical overbite (10.6%) and anterior open bite relationship (24.2%).

Significant associations were reported in relation to all malocclusion traits between the two examined groups, the sickle cell disease children had a greater risk of malocclusion, Angle's classification (6.5) and vertical overbite (7.6) than those in control group (T able 3).

Age Group 12-14 Years

Table 4 showed the distribution of malocclusion trait among study sample 11-14 years old. It is obvious that, the control group had slight increase in malocclusion compared to the younger groups; Angle's class III malocclusion (1.4%), spacing of the anterior teeth in the maxilla (2.9%) and anterior open

Table 1: Distribution of the gender and mean age

Variable	Sickle cell disease N=212	Control group N=212
Gender		
Male	113 (53.3%)	113 (53.3%)
Female	99 (46.7%)	99 (46.7%)
Mean age	8.5+3.7	8.3+3.5

Table 2: Distribution of malocclusion trait among the age group 4-6 years old children

Malocclusion Trait	Sickle cell Group	Control Group	Chi square P-Value	RR	Fisher exact test
Terminal Plane			---		0.014
Mesial	4 (5.3%)	0			
Flush	70(92.1%)	76 (100%)		–-	
Distal	2 (2.6%)	0			
Spacing Condition of Maxilla					
Non spaced	76 (100%)	76 (100%)	----	---–	
Spaced	0	0			
Crowded	0	0			
Spacing Condition of Mandible					
Non spaced	75 (98.7%)	70 (100%)	0.000	**---**	
Spaced	0	0			
Crowded	1 (1.3%)	0			
Horizontal Overbite					
Normal	67 (88.2%)	70 (100%)			
Increased	6 (7.9%)	0	0.002	**---**	
Reduced	3 (3.9%)	0			
Vertical Overbite				RR = 6.1 95%	
Normal	70 (92.1%)	75 (98.7%)		CI:	
Increased	2 (2.6%)	0	0.063	L =0.8	
Anterior open bite	4 (5.3%)	1 (1.3%)		U =49.3	

*P-Value significant at ≤ 0.05

Table 3: Distribution of malocclusion trait among 7-11 years old children

Malocclusion Trait	Sickle cell Group	Control Group	Chi-square P-Value	RR
Angle's Classification				
Class I	52 (78.8%)	62 (94%)	0.002	RR=6.5 95% CI:
Class II	13 (19.7%)	2 (3%)		L=1.5
Class III	1 (1.5%)	2 (3%)		U =27.39
Spacing Condition of Maxilla				**
Non spaced	58 (87.6%)	66 (100%)	0.004	
Spaced	5 (7.9%)	0		
Crowded	3 (4.5%)	0		
Spacing condition of Mandible				
Non spaced	54(81.8%)	66 (100%)	0.000	**
Spaced	3 (4.5%)	0		
Crowded	9 (13.6%)	0		
Horizontal Overbite				
Normal	44 (66.7%)	66 (100%)		
Increased	20 (30.3%)	0	0.000	**
Reduced	2 (3%)	0		
Vertical Overbite				
Normal	43 (65.2%)	63 (95.5%)		RR = 7.6 95% CI:
Increased	7 (10.6%)	0	0.000	L =2.4, U
Anterior open bite	16 (24.2%)	3(4.5%)		=23.9

Chi-square test was insignificant

Table 4: Distribution of malocclusion trait among 12-14years old children

Malocclusion Trait	Sickle cell Group	Control Group	Chi-square P-Value	RR
Angle's Classification				
Class I	54 (77.1%)	68 (98.6%)	0.000	RR=15.5 95%CI:
Class II	16 (22.9%)	0		L=2.11
Class III	0	2 (1.4%)		U=113.9
Spacing Condition of Maxilla				RR=6.5 95%
Non spaced	61 (87.1%)	68 (97.1%)	0.000	CI:
Spaced	2 (2.9%)	2 (2.9%)		L =4.5
Crowded	7 (10%)	0		U =20.1
Spacing condition of Mandible				
Non spaced	59(84.3%)	70 (100%)	0.001	**
Spaced	1 (1.4%)	0		
Crowded	10 (14.3%)	0		
Horizontal Overbite				
Normal	39 (55.7%)	70 (100%)		
Increased	30 (42.9%)	0	0.000	**
Reduced	1 (1.4%)	0		
Vertical Overbite				
Normal	44 (62.9%)	67 (95.7%)		RR = 8.7 95%
Increased	11 (21.4%)	0	0.000	CI: L =2.8
Anterior open bite	15 (15.7%)	3(4.3%)		U =27.3

**RR relative risk cannot be computed.

Table 5: Association between sickle cell disease and Angle's classification among examined groups

Examined groups		Angle's Classification Class I	Class II	Class III	Total	RR	Chi Square P-value
7-11	Sickle cell	52	13				0.002
	group	62	2	1	66	RR = 6.5 95%	
					66	CI:	
	Control group			2		L =1.5,	
						U =27.39	
12-4	Sickle cell	54	16				0.000
	group	68	0	1	70	RR= 15.5 95%	
					70	CI:	
	Control group					L=2.11,	
				2		U=113.9	

Table 6: Association between sickle cell disease and vertical bite relationship among different age groups

Age Group		Vertical Overlap Normal	Abnormal	Total	RR	Chi-square P-value
5-6 years	SCD	70	6	76	RR	
	Normal	75	1	76	RR = 6.1 95% CI: L =0.8, U =49.3	0.063
7-10	SCD	43	23	66	RR	
	Normal	63	3	66	RR = 7.6 95% CI: L =2.4, U =23.9	0.000
11-14	SCD	44	26	70	RR	
	Normal	67	3	70	RR = 8.7 95% CI: L =2.8, U =27.3	0.000

bite (4.3%). Whereas the sickle cell disease group showed increased prevalence of malocclusion traits; Angle's class II malocclusion (22.9%), increased horizontal overbite (42.9%), increased vertical overbite (21.4%) and anterior open bite (15.7%).

A significant statistical correlations were observed in relation to all examined malocclusion traits between sickle cell disease group and control group using the Chi-square test, the individuals in

sickle cell disease group had a greater risk of developing Class II Angle's classification malocclusion (RR=15.5), spacing of anterior teeth in the maxilla (RR=6.5) and vertical overbite malocclusion (RR=8.7).

When comparing the malocclusion traits among two older age groups it was clear that, Angle's classification showed significant association with these groups, the relative risk of developing malocclusion was more severe in the older age group (Table 5).

In table (6), the results showed a significant association in the vertical bite relationship except for the age group 4-6 years, it was noticed that relative risk was the lowest for age group 4-6 years and increased with increase in age (table 6), while that means the age affect the association between sickle cell disease and vertical bite relationship.

Discussion

The null hypothesis of this research was rejected, children with sickle cell disease showed remarkable findings in malocclusion. Also, there was a higher risk of developing malocclusion than individuals without the disease. Although the findings of the mixed dentition stage do not have precedents in the literature [12], they were in agreement with other studies that suggested an association between sickle cell disease and malocclusion was co n- ceivable.[9, 14, 16, 22-24]

Jaafer Ibn Ouf hospital is pediatric governmental hospital in Khartoum, which receives referred cases throughout the country from different ethnic and socioeconomic status. We emphasize that the sickle cell disease children belonged to only Jaafer Ibn Ouf hospital, may not be representative of all sickle cell disease children in Sudan, although the number of the children enrolled in the study was consistent with the number of participant in previous studies concerning malocclusion.[7, 9, 14, 16, 22-28]

In this study, age 4-6 years old group showed 7.9% increased over jet and 5.3% open bite. In contrast to a study carried out among Brazilian children, in which high prevalence of increased over jet 28.6% and open bite 17.1% were reported among five-year-old children.[12] In Africa, a study conducted in Nigeria sickle cell disease population showed 30% prevalence of over jet without age stratification.[10]

Furthermore, Oredugba et al carried out a study among 1-18 years old sickle cell disease individuals and the results revealed that about one-third of the participant had increased over jet and overbite[10]. Which was on the line with obtained results among 7-11 yearsold Sudanese children, 30.3% showed increased over jet, and 24.2% increased overbite, although different age group were examined.

In the present study, Angle's Class II malocclusion among sickle cell disease children was reported 19.7% among 7-11 years old children and 22.9% among 12-14 years old, which was more or less similar to the results obtained by Oredugba et al; Angle's Class II malocclusion was 21% in 1-18 years old sickle cell disease children[10]. Moreover, a high prevalence of Angle's Class II malocclusion among sickle cell disease patients was re ported by Mendes et al and Da Costa et al, 32% in Brazil and 88.5% Nigeria [14, 29].

The variation in the prevalence of Angle's Class II malocclusion among the sickle cell disease population may be partially attributed to differences in the study age group as well as the methodology applied. The etiological factor of Angle's Class II malocclusion in sickle cell disease patients may be due to Bone marrow hyperplasia, and compensatory expansion enlarged medullar spaces manifested by maxillary expansion and protrusion [16, 30].

In the current study, the spacing in the anterior segment of the maxilla and mandible among the age group 12-14 years old sickle cell disease children, was found to be 2.9% and 1.4% respectively. Whereas a higher percentage of spacing was reported by Da Costa et al among Nigerian sickle cell disease children, which was 49% in the maxilla and 30.8% in the mandible[14]. In contrast, much higher percentage of crowding was reported among the Brazilian sickle cell population, 79.6% in the maxilla and 60.2% in the mandible[31]. However in the present study, the percentage of crowding was reported only 10% in the maxilla and 14.3% in the mandible. This variation in the results may be partially due to differences in the age of the study sample and ethnic background as well as environmental factors.Increased over jet among sickle cell disease population had been reported in previous studies as one of the most common malocclusion traits [12, 31]. In the present study, in- creased over jet was reported 42.9% among 12-14 years old sickle cell disease group, which inconsistent support to the results of previous studies[12, 31]. In agreement with the present results, Da Costa et al conducted a study among Nigerian population, the in- creased over jet was reported in 48.2% of the sample[14]. Moreover, two studies carried out recently in Brazil among sickle

cell disease by Alves et al and Costa et al revealed a high percentage of an over jet, 63.9% and 67.7% respectively[12, 31].

In contrast, less percentage of increased over jet as 30% and 35% was reported by Taylor et al and Okafor et al among the sickle cell population[24, 30]. The increased over jet may be explained by increased bone marrow activity and maxillary dysplastic growth among sickle cell disease patients[9].

In current study, 15.7% of the 12-14 years old children had anterior open bite, this finding was in line with the results obtained by Costa et al, 12.9% of sickle cell disease group had open bite[31]. Moreover, Alves et al in 2013 reported very low percentage (0.4%) of anterior open bite in sickle cell disease patients [12].

In contrast, a high percentage of anterior open bite was reported 56%, 35% and 48.2% of sickle cell disease patients in Nigeria respectively [14, 24, 30]. These differences may be partially due to a different age of the study sample, study design, ethnic background and environmental factor.

The results obtained from this study showed increased risk of Angle's Class II malocclusion (15.5), anterior spacing of the maxilla (6.5), anterior open bite and increased over jet (8.7). These findings were in agreement with a study conducted by Cost a et al, in which sickle cell disease was assessed as risk factor for severe dental malocclusion, the obtained results revealed that the sickle cell disease was associated with increased risk of Angle's classification (RR= 1.57), anterior spacing (RR = 1.66), increased over jet (RR = 1.87) and anterior open bite (RR = 1.94) [31].

Conclusion

The obtained results revealed a high prevalence of malocclusion and in children with Sickle cell disease.

The sickle cell disease appears to be a risk factor for malocclusion especially when related to Angel's Class II malocclusion and anterior open bite.

Competing interest

The authors declare that they have no competing interests.

Author's Contribution

All authors have read and approved the final manuscript.

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