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Dr. Einstein Kibet Watenga, MBChB, M.Med ,Paediatrics, Department of Child Health & Paediatrics, Moi University, College of Health Sciences, School of Medicine, P.O. Box 4606- 30100, Eldoret Kenya, Dr. Julia Jerono Songok, MBChB, M.Med, Paediatrics, Lecturer, Department of Child Health & Paediatrics, Moi University, College of Health Sciences, School of Medicine, P.O. Box 4606- 30100, Eldoret, Kenya, Prof. Constance Nalianya Tenge, MBChB, M.Med, Paediatrics, Associate Professor, Department of Child Health & Paediatrics, Moi University, College of Health Sciences, School of Medicine, P.O. Box 4606- 30100, Eldoret Kenya.

Corresponding author: Dr. Einstein Kibet Watenga, MBChB, M. Med, Paediatrics, Department of Child Health & Paediatrics,Moi University, College of Health Sciences, School of Medicine, P.O. Box 4606- 30100,Eldoret Kenya. Email: einkibetz@gmail.com

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E. K. Watenga, J. J. Songok and C. N. Tenge

ABSTRACT

Background information: **Sickle cell disease (SCD) is a genetic disorder that affects the haemoglobin (Hb) molecule. Interventions for SCD needs to be supported by local data.**

Objective: **To determine the prevalence of sickle cell trait (HbAS) among adolescents in Bungoma County.**

Methods: **Public health education on SCD control was offered to adolescent students in 9 schools. Eligible participants were selected randomly from the school registers and consented. Pre-test counselling was done followed by testing for sickle cell gene status using a point of care device (The Sickle scan™). Post-test counselling was offered. Demographics characteristics and test results were documented. Proportions and Percentages were used to describe categorical data, Mean and Median for continuous data. Logistic regression was done and risk ratios (RR) generated. Pearson chi square was used to test for associations. Level of significance was set at P value <0.05 with Confidence interval at 95%.**

Results: **A total of 225 eligible participants consented for testing; Males: 116(51.6%), Females: 109(48.4%). The median age was 17 years (range 13- 19). HbAS prevalence was 18.7% (42) (CI 0.14-0.24). Proportion of males with HbAS was 24/116(20.7%); proportion of females with HbAS was 18/109(16.5%). Proportion of HbAS among students with known family history of SCD was 6/12 (50%). There were no adolescents with HbSS, HbAC, HbCC, HbSC. Those with Family History of SCD were three times more likely to have HbAS. (RR-2.958, p value-0.004, CI:1.561-5.607)**

Conclusion: **Prevalence of HbAS among adolescents is high for intervention for SCD to be put in place.**

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder that affects the haemoglobin molecule, which is constituted by four globin chains. Genes in the α-globin and β-globin clusters on chromosome 16 and 11respectively control the production of globin chains. [1] Due to point mutation, haemoglobin gene variants are present and fall into two broad groups – structured variants in which there is a change in the amino acid sequencing producing unusual haemoglobin (haemoglobinopathy) and thalasaemia in which there is a lower or abolished production of globin chains[2] Sickle cell anaemia is a haemoglobinopathy caused by a point mutation in the β-globin chain causing the hydrophilic amino acid glutamate to be replaced by the hydrophobic amino acid valine at the sixth position.[2]The resulting red blood cells assume an abnormal, rigid sickle shape (sickling) in conditions of low oxygen concentration like dehydration, acidosis, infection, among others.[2]

SCD is inherited in an autosomal recessive fashion. A person who receives two normal genes one from each parent has normal haemoglobin (HbAA) [2]. A person who receives a gene for sickle cell from one parent and a normal gene from the other has the Sickle Cell Trait (Heterozygous state-HbAS). Two genes for the sickle haemoglobin, each one inherited from both parents results in an offspring with the disease (homozygous state HbSS).[3,4,5] If both parents are heterozygous (HbAS), there is a 25% chance per pregnancy of having an offspring with SCD (HbSS) , 50% chance of having a carrier (HbAS) and a 25% chance having the normal Haemoglobin (HbAA).[3,4,5] If one parent is homozygous (HbSS) and the other parent is heterozygous (HbAS), there is a 50% chance per pregnancy of having an offspring with SCD (HbSS) and a 50 % chance of having a carrier (HbAS).[3,4,5] If one parent is homozygous (HbSS) and the other is normal (HbAA), then every pregnancy is likely to result into an offspring who is a carrier (HbAS). If both parents are homozygous (HbSS) then every pregnancy is likely to result into an offspring with sickle cell disease (HbSS).[3,4,5] It is advisable that persons who have the gene for sickle cell (HbAS or HbSS)should have offsprings with persons with normal genes(HbAA) in order to avoid likelihood of getting offsprings with HbSS.[3,4,5]

Other but less common compound heterozygous states include sickle-haemoglobin C (Hb SC), sickle beta-zero thalasaemia (HbSβ°), sickle beta-plus thalasaemia ((HbSβ^{+}), sickle-haemoglobin D-Punjab (Hb SD-) among others. [2]

Individuals with the trait (SCT or Hb AS or Hb SC) are mostly healthy, live a normal life but contribute towards transmission of the gene with a potential of having offspring with Hb SS. [6]

Persons with homozygous state (Hb SS or Hb SC) are symptomatic and have lifelong symptoms which include anaemia, infection and vaso-occlusive crisis such as jaundice, pallor, fever and severe pain as well as chronic organ damage. [7] SCD poses a significant public health burden in sub-Saharan Africa especially in the malaria endemic region where the gene frequency is highest. [8] Sickle cell disease affects millions of people throughout the world. Three quarters of sickle cell disease cases occur in Africa [9]. It affects up to 3% of births and it is estimated that 6 to 9 million infants are born with sickle cell disease in Africa each year [9]. The carrier frequency ranges between 10% to 40% across equatorial Africa decreasing to 1% - 2% on the North African coast and less than 1% in South Africa. [9]. In Kenya, the sickle cell gene is found mostly in the lake regions of Western Kenya and the Coastal areas. [10]

The intervention strategies for SCD are categorized into primary, secondary and tertiary by the World Health Organization (WHO).[11] The tertiary intervention entails

managing the complications (anaemia, vaso-occlussion and chronic organ damage) as the patients present with the signs and symptoms. [11] The secondary intervention entails screening the new-borns, identifying those with SCD, follow them up and provide prophylactic management in terms of giving standard vaccines as well as other special ones (Pneumococcal and Typhoid), haematinic supplementation (folate) and prophylaxis against malaria and other infections.[11] The primary intervention entails preventing birth of sicklers by ensuring persons are aware of their carrier status, there is pre-conception genetic counselling and reproductive choices are made.[11]

This study was conducted in adolescents attending mixed day secondary schools in Bungoma County, Western Kenya. The focus was on the strategy of primary intervention. This involved public health education and screening to ascertain the frequency of the trait.

Testing was done using a rapid immunoassay diagnostic kit called the Sickle Scan™.

MATERIALS AND METHODS

The study population were adolescents aged between 10 and 19 years attending mixed day secondary schools in Bungoma County, Western Kenya. Bungoma County covers an area of 3,032 km^2 and as at the 2009 census had a population of 1,374,627 persons with 347,875(25.3%) being age bracket 10 to 20 years.

During the period of the study, Bungoma County had 275 public and 12 private secondary schools out of which 189 were mixed day secondary with an eligible population of 150,738 students of which 75,597(50.2%) were boys and 75,141(49.8%) girls. The county had 136 health facilities of which 11 were hospitals, 4 nursing Homes, 16 health centres, 78 dispensaries and 27 private clinics.

Stratified random sampling was adopted. Bungoma County has nine constituencies. One mixed day secondary school was randomly picked from each constituency. 25 students per school who met the eligibility criteria were randomly selected from the registers of the selected schools.

The study was conducted over a six-month (January to March 2017, May to July 2017) period that coincided with the school calendar. Public health education was given to the members of the participating schools to inform them about sickle cell disease, its transmission and importance of getting tested and knowing their sickle cell status and the implications of carrying the sickle cell gene.

Informed consent was obtained then a data collection tool was used to collect the demographic characteristics of the participants. The demographic characteristics included the age, gender, ethnicity, family history of SCD plus their residence in terms of constituency, sub-county, location and village.

Pre-test counselling was done followed by testing using the Sickle scan™ device where under sterile conditions and from a finger prick, capillary blood was obtained, mixed with buffer and introduced to a cartridge and results read within five minutes. The screening test results were documented as the various haemoglobin variants. Data collected was cleaned, entered into Microsoft Excel and exported to SPSS version 23, analysed and presented in cross tabulation and histograms.

RESULTS

Public health education on SCD was given to 2389 students.

Data was collected from a total of 225 eligible adolescents with 25 from each of the 9 mixed day secondary schools each

randomly selected from the 9 constituencies of Bungoma County.

Table 1 shows that 116 (51.6%) of the respondents were male, the participants' age ranged between 13 to 19 years and 12(5.3%) had a known family history of SCD. Of those with family history of SCD, 1(8.3%) reported a sibling, 9(75%) reported a cousin and 2(16.6%) reported other relatives.

Table 1

Demographic Characteristics of the Adolescents

Variable	**Values**
Age (years)	
Minimum	13
Maximum	19
Median	17
Mean	16.75 (SD 1.485)
Gender	
Male	116 (51.6%)
Female	109 (48.4%)
Family History of SCD	
Yes	12 (5.3%)
No	213 (94.7%)
If yes to Family History of SCD	
Sibling	1 (8.3%)
Cousin	9 (75%)
Others	2 (16.6%)

Table 2 shows that 183 (81.3%) of the adolescents had the normal haemoglobin variant (HBAA) while 42 (18.7%) had the sickle cell trait (HBAS). None of the other haemoglobin variants (HBSS, HBCC, HBAC and HBSC) were detected.

Table 2

Haemoglobin Variants among Adolescents

Hb Variant	**Number/225**	**Percentage (%)**
HbAA	183	81.3
HbAS	42	18.7
HbSS	0	0
HbAC	0	0
HbCC	0	0
HbSC	0	0
Invalid	0	0
Total	**225**	**100%**

Figure 1 shows that Bumula constituency had the highest (36%; 9/25) burden of SCT, followed by Webuye West (28%; 7/25), Mt. Elgon and Kabuchai had a burden of (20%; 5/25) each, Sirisia and Webuye East a burden of 16%; 4/25) each while Tongaren had 4%; 1/25).

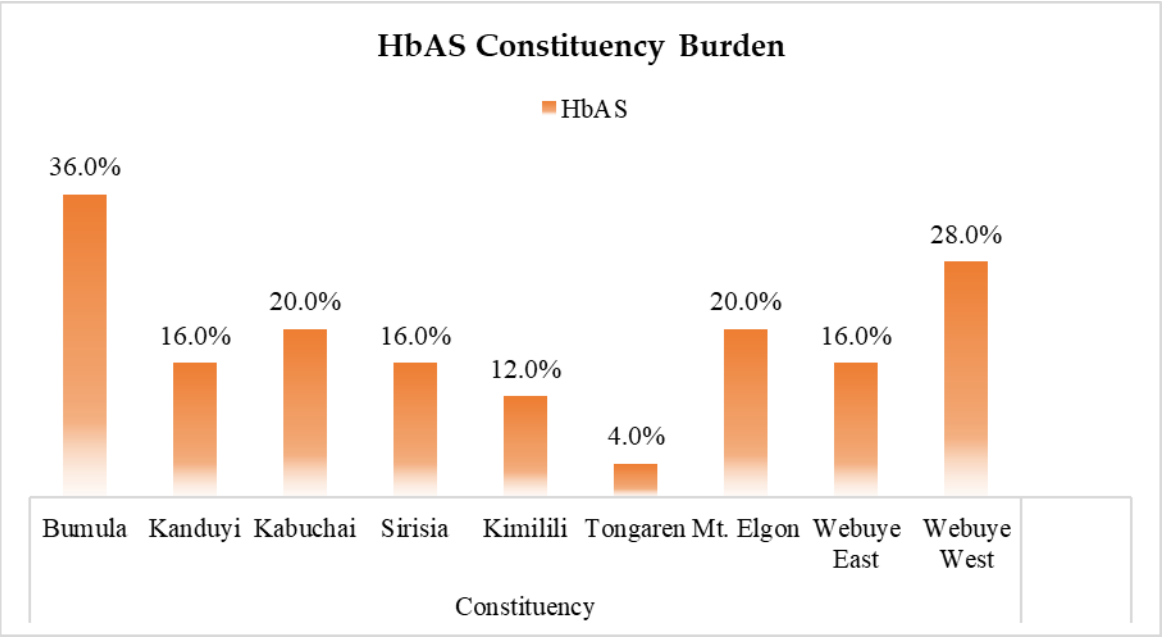

Figure 1: Constituency Burden of Sickle Cell Trait (SCT or HB AS)

Table 3 shows that 24(20.7%) of the 116 male participants while 18 (16.5%) of the 109 female participants had SCT. Statistical analysis further showed that being of the male gender conferred a 1.253 (95% CI: 0.721-2.177) relative risk of having the SCT compared to being female. However, this was not statistically significant (p-value = 0.422)

Table 3

Gender versus Sickle Cell Test Results

Gender	Sickle Cell Test Results		Total	Relative Risk (95% CI)	p-Value
	HbAA	HbAS			
Male	92(79.3%)	24(20.7%)	116(100%)	1.253(0.721-2.177)	0.422
Female	91(83.5%)	18(16.5%)	109(100%)		
Total	183(81.3%)	42(18.7%)	225(100%)		

Table 4 shows that an adolescent who is a resident of Bumula constituency has two-times likelihood of having a sickle cell trait compared to non-Bumula constituency residents, with a risk ratio of 2.182 (95% CI: 1.187-4.010). This was statistically significant (p-value=0.018).

Table 4

Association between constituency and Sickle Cell trait

		Sickle Cell Test Results				
		HbAA	HbAS	Total	RR (95% CI)	P-value
Constituency	**Bumula**	16	9	25	**2.182 (1.187-4.010)**	**0.018**
	Kanduyi	21	4	25	0.842 (0.382-2.161)	0.717
	Kabuchai	20	5	25	1.081 (0.468-2.495)	0.856
	Sirisia	21	4	25	0.842 (0.382-2.161)	0.717
	Kimilili	22	3	25	0.615 (0.205-1.845)	0.364
	Tongaren	24	1	25	0.195 (0.028-1.356)	0.046
	Mt. Elgon	20	5	25	1.081 (0.468-2.495)	0.856
	Webuye East	21	4	25	0.842 (0.382-2.161)	0.717
	Webuye West	18	7	25	1.600 (0.797-3.212)	0.204
Total		**183**	**42**	**225**		

Table 5 shows that 12 (5.3 %) of the 225 had a family history of SCD. Among the 12 with family history of SCD, 6 (50%) had the trait while 36 (16.9%) of the 213 without a family history of SCD had the trait. Further analysis showed that the Adolescents with a family history of SCD were three times more likely to have the trait with a relative risk (RR) of 2.958 (95% CI: 1.561-5.607) than those without a family history. This was statistically significant (p-value = 0.004).

Table 5

Family History of Sickle Cell Disease Vs Sickle Cell Test Results

Family History	Sickle Cell Test Results		Total	Relative Risk (95% CI)	p-Value
	HbAS	HbAA			
Yes	6 (50%)	6 (50%)	**12 (100%)**	**2.958**(1.561-5.607)	**0.004**
No	36 (16.9%)	177 (83.1%)	**213 (100%)**		
Total	**42 (18.7%)**	**183 (81.3%)**	**225 (100%)**		

DISCUSSION

Inherited haemoglobin disorders (sickle cell disorders and thalassaemia) were originally characteristic of the tropics and subtropics but are now common worldwide due to migration though they are particularly common among people whose ancestors lived in tropical and sub-tropical sub-Saharan regions. [12]

The world health organization (WHO 2005) recognized sickle cell as a global public health problem and urged member states to come up with national control programmes for sickle cell disease among them supporting community awareness programs and research. Most programmes in the developed countries have been successful and have demonstrated that where they exist, survival of patients is

steadily improving, affected births are falling and an increasing number of patients are stabilizing. It is high time that the region also embraces this.

Sickle cell disease is a common condition in Western Kenya. Those affected by the disease frequently seek care in the appropriate health facilities (level 3 and above). The services provided mostly dwell on the WHO tertiary intervention strategy in which the complications of the disease are sorted out as the patients present. Screening services for persons to know their 'sickle cell status' are not routinely available in Western Kenya. There is also inadequate knowledge among majority of health care providers in the communities that the inheritance is autosomal recessive whereby the individuals with the homozygous state (HB SS) present with lifelong symptoms. These symptoms require frequent and regular medical attention while those with the heterozygous state (HB AS) lead normal lives, have special protection against severe forms of malaria but can unknowingly transmit the gene and are usually surprised when they get offspring with the homozygous state(HB SS). This has resulted into more and more persons with the homozygous state (HB SS) being born. Therefore, health education, screening for sickle cell and identifying the carriers of the gene is essential in control of the disease as the burden will be quantified in local populations and affected persons are likely to make informed reproductive choices resulting in prevention of birth of children with HBSS.

In this study public health education on SCD was given to 2389 students in the selected mixed secondary schools out of which 225 eligible adolescents participated in the study. The male participants were 116 (51.6%) and 12(5.3%) had a family history of SCD. The prevalence of the sickle cell trait was 18.7%. Statistical analysis showed that being of male gender conferred a 1.253 (95% CI: 0.721-2.177) relative risk of having the SCT compared to being female. However, this was not statistically significant (p-value = 0.422). Further analysis also showed that having a family history of sickle cell disease was three times more likely to have the trait with a relative risk (RR) of 2.958 (95% CI: 1.561-5.607) than those without a family history. This was statistically significant (p-value = 0.004)

The prevalence of the sickle cell trait in this study was almost similar to the one found in a study done Western Kenya villages of Nyando, Kisumu County among 858 children aged 6-35 months where the prevalence was 17.1% as well as in a Kenyan 8-year cohort study in Kilifi which found a HbAS frequency of 14.6% as well as in Eastern Uganda where the prevalence was found to be 17.5% in a study population was 6-60 months [13,14,15] In spite of the differences in the age groups of the participants, the prevalence of the SCT in all the studies falls within what is estimated (10 -40%) across equatorial Africa that has the highest burden of individuals with the homozygous state (HBSS) who usually present with lifelong symptoms.[9]

The findings in this study are different from those in a study in Lebanon- Beirut conducted between 2002 and 2014 from laboratory records of 184,105 study subjects whereby 899 of them were found to have SCT giving a prevalence of 0.49% (95% CI, 0.46-0.52%). Lebanon-Beirut is in a different geographical setting and also has an insignificant burden of individuals with the homozygous state (Hb SS). [16, 17] This low proportion of individuals with the carrier state (Hb AS) can provide a secure approach by regions with high burdens of the sickle cell gene to step up their efforts towards the implementation of the activities recommended for the control of its perpetuation.

In this study, Hb C variants were non-existent. This is consistent with various

studies which found that the geographic range of Hb C is more limited than Hb S. Hb C is thought to have originated as a founder effect in west Africa , West of the Niger river and is more centred in the West and North Western African countries with Northern Ghana having a prevalence of up to 40%, North Ivory Coast up to 50%, Burkina Faso up to 40% (where 2% of the population has SC disease), and around 20% in Togo and Benin, up to 10% in Morocco ad Algeria, 3.5% and 3% in individuals of African descent in the Caribbean and USA respectively , less than 1% in central Africa while generally non-existent in East Africa.[20] The clinical characteristics of individuals carrying the Hb C gene are almost similar to those carrying the Hb S gene.

The proportion of adolescents with the normal haemoglobin variant (HB AA) in this study was 81.3%. These findings are almost similar to those of a Nigerian study among students which found an HbAA prevalence of 80.32%. [18] and slightly lower in another Nigerian study conducted among students in a single university of Lagos department where the HbAA prevalence of 70%. [19]. The knowledge that there is a high proportion of persons with normal haemoglobin should drive public health education and control programmes in encouraging pairing up between persons with normal haemoglobin (HBAA) and those who carry the sickle cell gene (HBAS & HBSS) so as to minimize the carrier states and the persistence of the homozygous states.

Reduction of the burden of sickle cell disease and carrier state requires the implementation of WHO primary intervention strategy through public education, determination of the sickle cell status of individuals, pre-conception genetic counselling and informed reproductive choices. Therefore Availability, Accessibility, Acceptability and Affordability of screening services so that individuals can know their, 'sickle cell status' is a crucial and major milestone in the process implementation.

It is therefore necessary to call upon partners to facilitate public education, identification of genetic risks in the community by recording family disease histories, genetic counselling, awareness and active participation in prevention and care programmes.

CONCLUSIONS AND RECOMMENDATIONS

The study concludes that adolescent sickle cell trait prevalence in Bungoma county is high (18.7%). The Haemoglobin variants found were HBAA and HBAS. There was no HbSS or HbC variant. Having a family history of sickle cell disease was significantly associated with the sickle cell trait.

Public health education activities on sickle cell to encourage residents to get tested and know their sickle cell gene status. There is need to set up genetic counselling and testing centers where residents can get tested and be advised on how to prevent birth of children with sickle cell disease through informed reproductive choices.

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