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## Distribution of Haemoglobin S and C in Ghana – The Role of Ethnic Barriers to Intermarriages

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### Abstract

Using repeated cross-sectional data from the Ghana Ports and Harbours' Authority (GPHA) hospital and cross-sectional household data from the Ghana Living Standards Survey 7, this paper exploits intermarriages between the northern part and southern part of Ghana as a potential underlying factor partly explaining the distribution of haemoglobin S (Hb S) and haemoglobin C (Hb C) in the country. Similar to other studies, we find evidence for a higher prevalence of Hb S and a lower prevalence of Hb C in the southern part of Ghana. We also find that the rate of intermarriage between northern ethnic groups and southern ethnic groups is just about 2.6 per cent, largely leading to the confinement of Hb S to the southern part of Ghana and Hb C to the northern part of Ghana.

**Keywords:** Haemoglobin distribution; Haemoglobin S; Haemoglobin C; Intermarriages.

### 1. Introduction

Haemoglobin (Hb) S accounts for 40 per cent of the world's total haemoglobinopathy carriers and 80 per cent of all haemoglobin disorders.

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About 5.2 per cent of the world's population and 7.0 per cent of all pregnant women possess an abnormal haemoglobin variant. A recently calculated haemoglobinopathy birth prevalence and service indicator revealed that 1.1 per cent of couples across the world are at risk of giving birth to a child with haemoglobin disorders. Moreover, there are about 948000 new abnormal haemoglobin carrier couples annually and 1.7 million pregnancies recorded to all carrier couples annually across the world [12]. This calls for drastic measures to reduce haemoglobinopathies since inheriting haemoglobin S together with any other Haemoglobinopathy results in a haemoglobin disorder. Concerning measures aimed at reducing haemoglobinopathies, the World Health Organization (WHO) suggests that; parents with a history of birthing a child with haemoglobinopathy should be educated to reduce the rate of childbirth due to the 25 per cent possibility of recurrence; prenatal diagnosis should also be done for couples with affected children; the population should be educated and offered carrier screening especially senior high school students and young people who are yet to marry [13]. In Africa, the prevalence of both Hb S and Hb C is relatively high compared to other parts of the world, and Ghana is no exception. The prevalence of abnormal haemoglobin carriers in the Ghanaian population is about 30 per cent [17, 18]. However, the distribution and prevalence of these abnormal haemoglobin disorders appear to vary as one moves from the north to the southern parts of the country. Existing literature indicates that haemoglobin C is very common in the Northern part of Ghana while haemoglobin S is more common in the southern parts of Ghana [1, 6]. While there are several studies on abnormal haemoglobin disorders and its distribution in Ghana, most of these studies have often focused on the relationship between Hb S or Hb C and malaria resistance (see, [3, 10, 11]). This has resulted in very little contemporary literature on the distribution of abnormal haemoglobin variants in Ghana and some of its possible underlying factors. To fill this gap in the literature, the purpose of this study includes the following. First, this study seeks to determine the prevalence of haemoglobin S and C in the Western Region of Ghana which is in the southern part of Ghana. Second, by comparing our results to other studies, we provide a general overview of Hb C and Hb S distribution in Ghana. Third, we explore intermarriages as one of the factors underlying the distribution of Hb C and Hb S in Ghana.

## **2. Methodology**

In analysing the distribution of Hb S and Hb C in the western region (which is in the southern part of Ghana), retrospective research was conducted at the Ghana Ports and Harbours' Authority (GPHA) hospital, Takoradi. Demographic data, as well as haemoglobin electrophoresis results, were retrieved from the record books of the facility's laboratory unit and carefully typed into Microsoft Excel spreadsheet version 13. It is worth mentioning that the Hb electrophoresis test which yielded these results were conducted with either the electrophoretic tank (basic medium) or the Sickle scan electrophoretic Rapid Diagnostic Test (RDT). The information entered onto the Microsoft Excel spreadsheet were cross-checked with the information from the laboratory's record books and any mistakes rectified. The data used in this study covers the period between August 2010 and November 2018. Finally, this study uses the SPSS software version 13 to statistically analyse the data. Ethical clearance was obtained from the hospital's management and the identity of clients whose clinical information is used in this study is kept anonymous. In analysing the effect of intermarriages on the distribution of Hb S and Hb C in Ghana, data was retrieved from Ghana statistical service data catalogue.

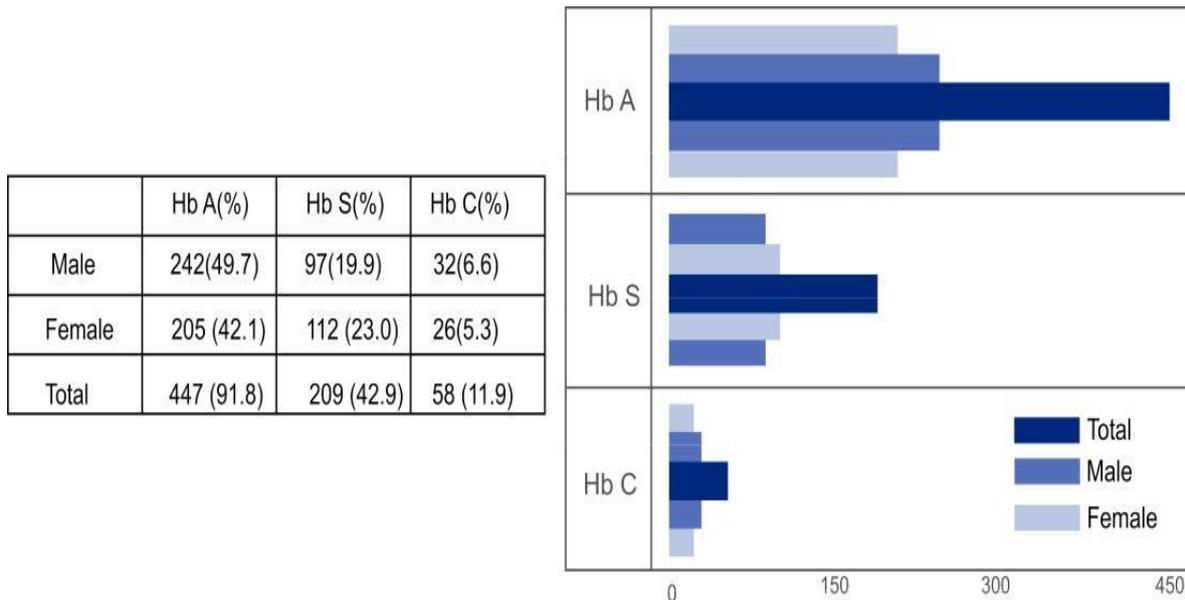
### 3. Results

#### 3.1. Demographics

A total of 487 haemoglobin electrophoresis results were retrieved from available data. Out of this total number, 263 (54 per cent) were males and 224 (46 per cent) were females (Fig 1). The ages of subjects ranged from 1 to 60 years with a mean age of 24.98 (14.342). The modal ages were 1 - 5 years, 25 - 30 years and 30 - 35 years. In the figure below, we see that our sample is fairly distributed between males and females across all the haemoglobin variant types.

#### 3.2. Frequency of Haemoglobin Variants Among Study Subjects

From the figure and table below, we see that haemoglobin variant Hb A is the dominant haemoglobin variant in the sample which is not unusual compared to other parts of the world. However, the frequency of Hb S variant among the study subjects is about 3 times the frequency of Hb C variant - for both males and females. Also, we can see from the figure 1 that the frequency of Hb S variant among the study subjects is about half the frequency of Hb A variant. In short, the proportion of Hb A is about twice the frequency of Hb S while that of Hb S variant is about thrice the frequency of Hb C variant.



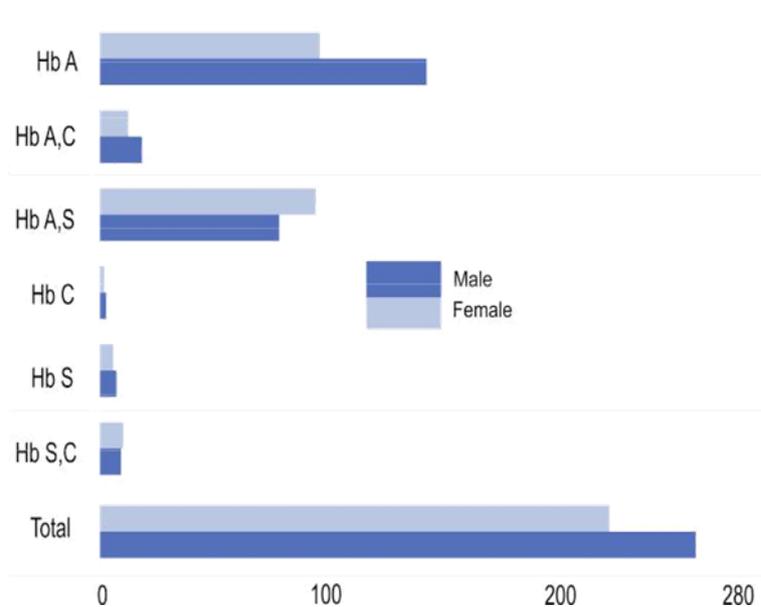
**Figure 1:** Frequency of Various Haemoglobin Variants Among Study Subjects

#### 3.3. Haemoglobin Electrophoresis Results

Among the study subjects, the table and figure below show that Hb C is the least recorded haemoglobin electrophoresis results in our sample. This is somewhat close to the population with haemoglobin electrophoresis results as Hb S. Also, we realized that the number of people with Hb A, S results is about 5 times the number of people with Hb A, C results. The figure below again shows that the number of study subjects that had their haemoglobin electrophoresis recorded as Hb A is about 1.2 times the combined number

of people that had their haemoglobin electrophoresis recorded as Hb A, S and Hb A, C. This suggests that if Ghanaians are to adhere to the education that two carriers of abnormal haemoglobin should not marry each other, then majority of couples would be made up of a homozygous Hb A partner and a heterozygous carrier partner. The advantage here would be that the likelihood of birthing a child with sickle cell disease per pregnancy will be significantly reduced to almost zero per cent while the likelihood of birthing a homozygous Hb A or heterozygous carrier child would be about 50 per cent each.

Haemoglobin electrophoresis	Male	Female
Hb AS (%)	79 (16.2)	95 (19.5)
Hb AC (%)	19 (3.9)	13 (2.7)
Hb A (%)	144 (29.6)	97 (19.9)
Hb SC (%)	10 (2.1)	11 (2.3)
Hb S (%)	8 (1.6)	6 (1.2)
Hb C (%)	3 (0.6)	2 (0.4)
Total (%)	263 (54.0)	224 (46)

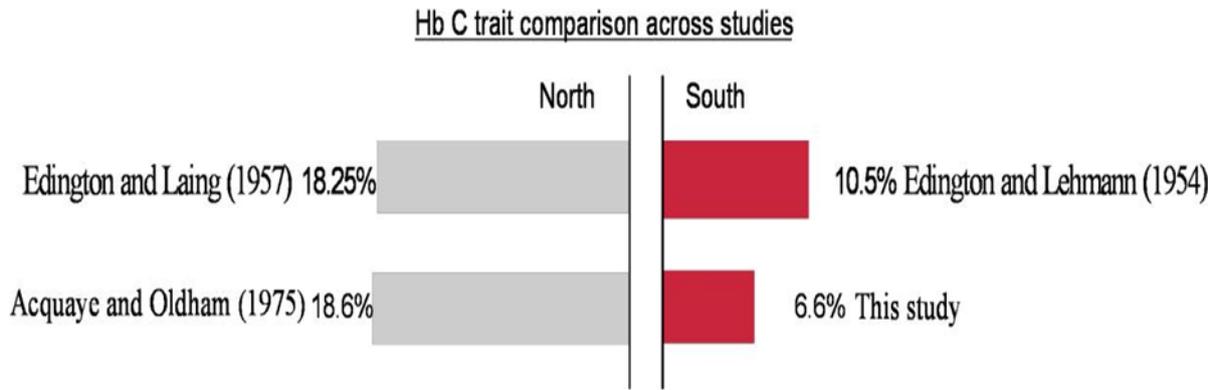


**Figure 2:** Haemoglobin Electrophoresis Results of Study Subjects

#### 4. Discussion

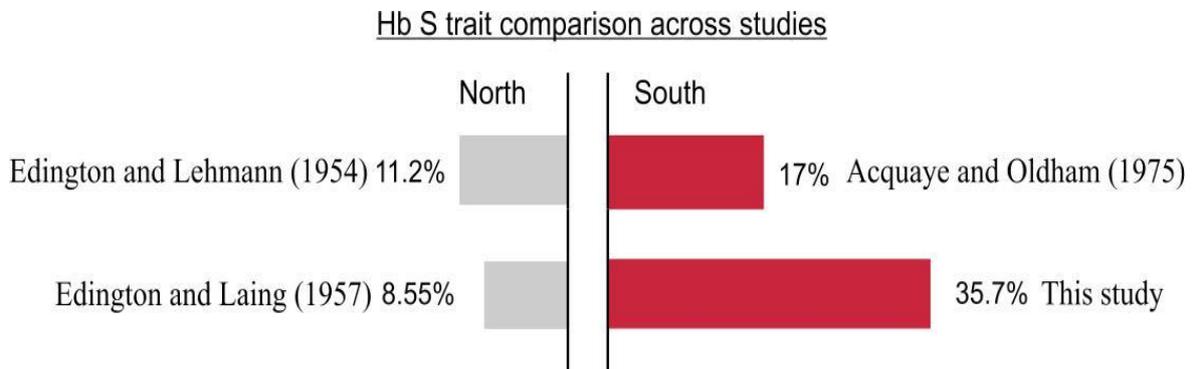
This study revealed a low Hb C trait prevalence of 6.6 per cent in the Western Region of Ghana which is in the southern part of the country. In comparison to other studies in Ghana, the results of this paper confirm that the Hb C trait is relatively less prevalent in the southern part of Ghana compared to the North. Edington and Lehmann [7] found a Hb C trait prevalence of 10.5 per cent in the capital of the country - Accra, which is also in the southern part of Ghana. Acquaye, Oldham and his colleagues[1] reported a Hb C trait of 18.6 per cent in the Northern Region which is in the northern part of Ghana. Similarly, in another study by Edington and Laing [6] conducted in Dagomba in the northern part of Ghana, they also reported Hb C trait of 18.25 per cent. At a glance, one would conclude that haemoglobin C is more prevalent among northern natives while haemoglobin S is more prevalent among the southern natives. The figure below compares the prevalence of Hb C trait in both the northern and southern part of the country across studies.

The low prevalence of the Hb C trait recorded in the southern part of Ghana (relative to the north) could partly be attributed to ethnic barriers to intermarriages between natives of the north and natives of the south. This phenomenon may have confined the Haemoglobin C gene more to the northern part of the country, limiting its prevalence in the south. We will explore this potential underlying factor in more detail in the next section of this study.



**Figure 3:** Hb C Trait Prevalence Comparison Across Studies

In accounting for the high prevalence of Hb C trait in the northern part of Ghana Edington and Lehmann [7] mention that the northern part of Ghana is known over the past 400 to 500 years to be the very origin of the mutation that brought about Hb C variant. As such, neighbouring countries such as Burkina Faso, Togo, Benin, among others also have a high prevalence of the Hb C variant compared to other countries in the sub-region. Using the Bayesian geostatistical model, Piel and his colleagues [16] predicted that the highest frequencies of Hb C exist across Burkina Faso, Togo, Benin, Mali, the northern parts of Ghana, eastern Mauritania, and the southern part of Algeria. According to Piel and his colleagues [16] the average prevalence of Hb C trait in West Africa is pegged at 15 per cent, with a high rate of 17 per cent Hb C trait associated to the northern part of Ghana according to Edington and Lehmann [7].



**Figure 4:** Hb S Trait Prevalence Comparison Across Studies

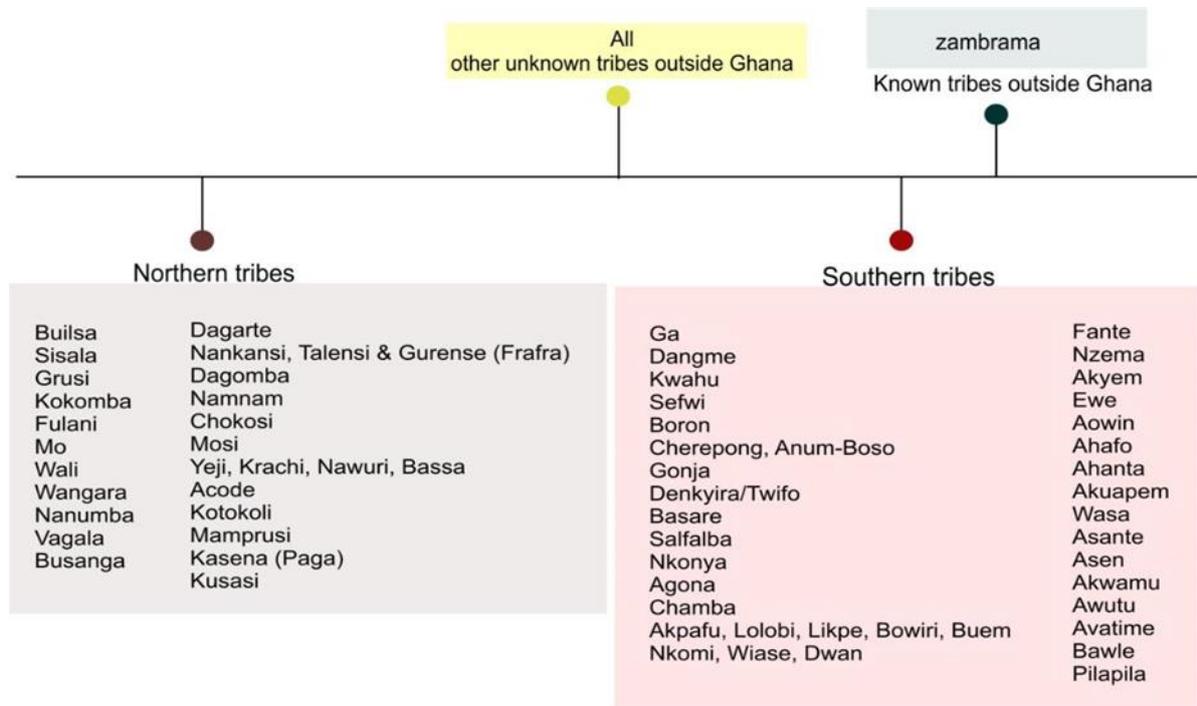
Unlike Hb C trait (Hb A, C), Hb S trait (Hb A, S) seems to have a slightly higher prevalence in the southern part of Ghana compared to the northern part. Two studies conducted in the southern part of Ghana, “Variants of haemoglobin and glucose-6-phosphate dehydrogenase. ii. distribution in northern Ghana” [1] (conducted in Greater Accra region) and our current study (conducted in the Western region) had Hb S trait prevalence of 17 per cent and 35.7 per cent respectively. On the contrary, studies from the northern part of Ghana have reported a slightly lower Hb S trait prevalence. For example, Edington and Lehmann [7] and Edington and Laing [6] have reported Hb A, S prevalence of 11.2 per cent and 8.55 per cent respectively in the northern part of Ghana. Notwithstanding these findings, there is still the need for more contemporary research to strongly affirm this

assertion. Generally, Africa is reported to have a high prevalence of Hb S trait which is about 15 - 30.5 per cent [17]. Science has it that, sickle cell mutation has occurred at least three different occasions in Africa and this is affirmed by the three different haplotypes of the Hb S gene [5]. These are the Benin haplotype, the Senegal haplotype, and the Bantu haplotype in Central-West Africa [9]. Studies by Akhigbe and his colleagues [2], Uzoegwu and Onwurah [19] and Nubila and his colleagues [14] report Hb S trait prevalence of 22.19 per cent, 36.94 per cent and 24.1 per cent respectively for Nigeria. Sinou [17] also reports Hb S trait prevalence of 5 per cent and 40.5 per cent in West Africa and Nigeria respectively. In Northern Africa, Hb S trait was prevalent among 24 per cent newborns in some areas of Sudan and 29 per cent among people who are above five years old [8]. In Egypt, El-Beshlawy and Youssry [4] find that Hb S gene is almost non-existent along the river Nile, however, Hb S trait of about 9 per cent and 22 per cent were recorded in other parts of the country. One significant benefit of the high incidence of Hb S trait or Hb C trait in Africa is the special protection it offers against severe malaria [6]. While both Hb S trait and Hb C trait do not prevent malaria infection, it offers varying levels of protection against malaria infection progressing to severe malaria. This kind of protection is higher in Hb S trait than in Hb C trait. According to a study by Mockenhaupt and his colleagues [11], Hb A, S conferred 90 per cent protection against severe malaria in Ghana while Hb A, C conferred 47 per cent. Hence the high prevalence of Hb S and Hb C in Africa can be regarded as an advantageous hereditary natural selection against Malaria [11]. Moreover, this also possibly explains the low prevalence of Hb C (in comparison to Hb S) in several African countries. For example, according to studies by Akhigbe and his colleagues [2], Nwafor and Banigo [15], Uzoegwu and Onwurah [29], the authors reported Hb C trait prevalence of 5.2 per cent, 1 per cent, 0.12 per cent and 4 per cent respectively for Nigeria. While the sickle cell disease is an established autosomal disease and not sex-linked, Akhigbe and his colleagues [2], asserts that sickle cell disease is sex-linked. They recorded no incidence of Hb S, S, Hb S, C and Hb C, C in males. In another study by Nubila and his colleagues [14] they also observed higher frequency distribution in Hb A, C and Hb S, C in only males while the females dominated in the other haemoglobin variants (Hb A, A, Hb A, S, Hb S, S and Hb C, C). They, however, associated their findings to the higher number of female subjects involved in the study and the cultural belief of polygamous marriage being promoted among the Yuroba men. Our study reports Hb S, S of 1.6 per cent in males and 1.2 per cent in females; Hb S, C of 2.1 per cent males and 2.3 per cent females; Hb C, C of 0.6 per cent males and 0.4 per cent females suggesting a fair distribution of haemoglobin variants across gender. In the next section, we will explore ethnic barriers to intermarriages as a possible factor accounting for the varying degree of prevalence of the Hb S and Hb C traits in Ghana.

#### ***4.1. Intermarriages and its Effect on the Distribution of Haemoglobin S and C in Ghana***

The results of this study as discussed above (together with other studies) seem to support a high prevalence of Hb C and Hb S in the northern and southern part of Ghana respectively. To account for this distribution, we will explore ethnic barriers to intermarriages as an underlying factor to Ghana's abnormal haemoglobin distribution, particularly Hb C and Hb S. While intermarriages and migration are largely known to be one of the factors that increase haemoglobin disorders in the world, could it possibly explain in part why Hb C seems confined to the northern part of Ghana and Hb S to the southern part of Ghana? To answer this question, we group all ethnicities in this study into two big clusters, north and south depending on their location. Using cross-sectional data from the Ghana Living Standards Survey 7 (GLSS 7), we explore the rate of intermarriages among

Ghanaians, especially between people from northern ethnic groups and people from southern ethnic groups. The Ghana Living Standards Survey (GLSS) is a nationally representative household survey which provides reliable, disaggregated and internationally comparable welfare and Living condition statistics in Ghana. In the seventh round of the survey conducted in 2017, section one contains 59864 people of which 18237 are either married or is in a consensual union. 17338 out of the 18237 people have their partners also reported in the survey. These 17338 respondents are distributed across 55 ethnic groups and two other categories (Zambrama, Other tribes). We eliminated households where one of the partners or both partners belong to the Zambrama tribe or some other unknown tribes. The resulting participants used in our analysis were 16756 people (either married or is in a consensual relationship) spread across 55 known Ghanaian ethnic groups. To examine intermarriages between the north and the south, we cluster the 55 ethnic groups into northern and southern clusters. From the 55 ethnic groups in the data, there are 31 ethnic groups in the south and 24 ethnic groups in the north.

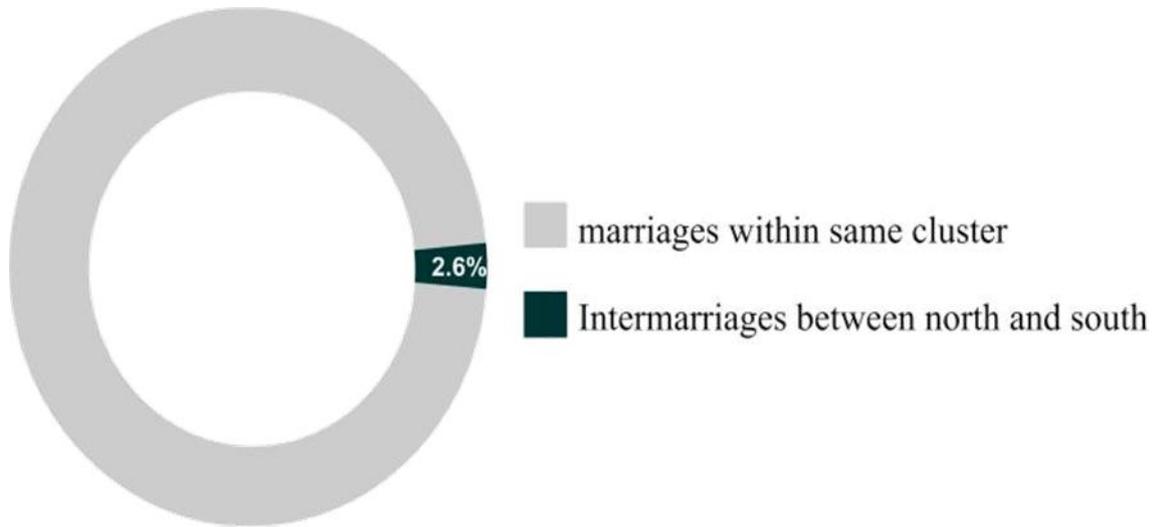


**Figure 5:** Major Tribes in Ghana

From the 16756 respondents (7815 in the south and 8941 in the north) who are married or is in a consensual union, only 436 (2.6 per cent) have a partner or a spouse who does not belong to the same cluster (that is, northern or southern ethnic groups). In other words, the intermarriage rate between northern and southern ethnic groups is just about 2.6 per cent of all marriages reported in the GLSS 7.

Given this small rate of intermarriages between natives of the northern and southern ethnic groups, we assert that this has somewhat contributed to the confinement of Hb C to the northern part of Ghana and Hb S to the southern part of Ghana. In the literature, there have been instances in other parts of the world where intermarriages or migration significantly contributed to the distribution of Hb disorders. Countries like Brazil,

the United States and European capitals which did not have any record of Hb C are now recording the presence of it due to immigration [16].



**Figure 6:** Intermarriage Rate Between The Northern and Southern Tribes

### 5. Limitation of Study

One question that the authors of this study would have also wished to address is to determine whether the prevalence of haemoglobinopathies have increased or decreased in Ghana over the years. Unfortunately, researchers of this study did not find enough literature about the prevalence or distribution of abnormal haemoglobin in Ghana. Haemoglobinopathy studies in Ghana have focused on the relationship between Hb S trait or Hb C trait and their association to malaria resistance and not its prevalence. This has made it difficult to compare our results to many of the existing literature on haemoglobin disorders in Ghana. The above limitation resulted in the comparison of our findings to empirically data from only one region in southern Ghana and two studies from the North. We suggest that more studies on the prevalence of abnormal haemoglobin in different regions in Ghana be conducted. By this, future studies can have access to data from several regions in Ghana. We again suggest that future studies analysing the distribution of Hb C and Hb S traits in Ghana should consider using newborn estimates as it may improve the accuracy of determining the burden of abnormal haemoglobin according to Piel and his colleagues [16]. Notwithstanding these limitations, this study escapes some of the notable biases (often encountered in haemoglobin disorders research), particularly regarding age and small sample size bias. This study uses a sample size of 487 with an age range of 1 to 60 years.

### 6. Conclusion

This study reported a high Hb S trait prevalence of 35.7 per cent and a low Hb C trait prevalence of 6.6 per cent in the western region which is in the southern part of Ghana. This result goes a long way to support the outstanding notion that Hb C is more prevalent in the northern part of Ghana relative to the southern part of Ghana. Furthermore, we assert that the confinement of Hb S and Hb C in the southern part of Ghana and the northern part of Ghana respectively may partly be due to the low rate of intermarriages between northern ethnic

groups and southern ethnic groups. To the best of our knowledge, this study serves as the most current study on the prevalence of abnormal haemoglobin in Ghana and hence could form the basis for determining whether haemoglobinopathies are increasing or decreasing in Ghana. We encourage periodic studies on the prevalence of abnormal haemoglobin across the various regions in the country.

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### **7. Ethical approval**

Ethical approval was obtained from the hospital's management and the identity of clients whose clinical information are used in this study is kept anonymous.

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