Evaluation of Acute Painful Episodes with Foetal Hemoglobin Level and Other Haematological Parameters in Sickle Cell Patients in Abuja Nigeria

ABSTRACT

Introduction: Heterogeneity in sickle cell anaemia manifestations ranges from near asymptomatic cases to severe illness.

Objective: This study determined the relationship between foetal haemoglobin F level, other haematological parameters and acute painful episode score of sickle cell disease patients in FCT Abuja Nigeria.

Methods: 60 Sickle cell patients were selected for the study. 20 severe crises, 20 non-severe crisis SS were enrolled in the study. Control group comprised 20 apparently healthy haemoglobin AA individuals. Data were analysed descriptively.

Results: Hb F level increased significantly in non-severe crisis sickle cell anaemia (7.12 %± 3.6) and severe crisis (5.30 %±2.3) groups, compared to the control group (0.32±1.8). This trend was also observed in RDW, MCHC and MCV. The mean Hb concentration and haematocrit (Hct) were significantly lower for both non- severe crisis and severe crisis SCA groups. There was no significant correlation between HbF and any of the haematological parameters in both non severe crisis and severe crisis groups. Patients with SCA had higher levels of HbF than matched controls. HbF had no correlation with any of the haematological parameters in both severe and non-severe SCA groups studied.

Conclusion: Further studies should focus on environmental factors contributing to this variability.

Keywords: severe, Sickle Cell, Anaemia, Crisis, Red Cell.

1. INTRODUCTION

Sickle cell anaemia, the most common form of haemogobinopaathy is inherited in an autosomal recessive fashion [1]. An estimated 4 million Nigerians are affected by sickle cell disease. In the west African sub region, sickle cell disease is responsible for 5% to 16% below age 5 mortality WHO [2]. Among sickle cell patients there is a notorious heterogeneity [3] in the manifestations of disease ranging from near complete asymptomatic to severe debilitating illness [4]. The environment, genetic variation among patients, intrinsic, and extrinsic to the sickle erythrocyte, account for the phenotypic differences among sickle cell patients [5]. Sickle cell anaemia is said to be notorious for its clinical heterogeneity [3]. Variation in fetal haemoglobin (HbF) levels in different individuals is believed to be one of the main modifiers that contribute to the clinical heterogeneity observed in Sickle cell disease patients. Polymerisation of sickle red cell is the major pathophysiologic process in sickle cell disease crisis. This process is inhibited by foetal haemoglobin [6, **7**].

Acute pinful episodes has been identified as the most common complication in sickle cell anaemia [3] hence is known as the hallmark of the disease. Acute Painful episodes also known as painful crisis are defined as severe pain that lasts for 2 or more hours. Frequent crisis (defined as 2 or more painful events per year for three years) is considered to be associated with poor quality of life and increased risk of death [6]. Foetal haemoglobin (Hb F) levels in sickle cell patients varies with disease manifestations. It was discovered that any increment in HbF level led to increased survival in sickle cell anaemia patients,[8, 9]. HbF level is an important factor that has been described to influence the clinical course and severity of sickle cell anaemia. Those with higher Hb F levels, like the people in eastern Saudi Arabia have less severe sickle cell anaemia with fewer complications [1] and better survival [10]. In response to treatment with hydroxyurea, patients whose HbF level rises most, fared best [9, 10]. In this study severity was limited to only the number of acute painful events per year. Hence individuals having 2 or more painful crises per year for three consecutive years were grouped

as severe and those having 0-1 crises per year for three consecutive years were grouped as none severe.

It is possible for acute events to be quiescent while sickle vasoocclusion and the hemolytic anemia continue relentlessly [4]. This study aimed at evaluating haemoglobin F level with some haematological parameters in relation to the number of crisis as defined in this study per year. In addition, there is need to generate more data on fetal haemoglobin levels of sickle cell patients [11]

2. MATERIALS AND METHODS

2.1 Study area

Federal capital territory is located in the center of Nigeria and has a land area of 8,000 square kilometers. It falls within latitude 7 45'and 7 39'. It has a climate that is neither too hot nor too cold all year round. The high altitude and undulating terrain of the FCT makes it a specially interesting location for haematological studies.

2.2 Patients

Sickle cell patients (age 5-43 years) in steady state, were selected from both Gwagwalada municipal area council in the Federal Capital Territory Abuja and Babajide Olowodola Sickle cell foundation Jabi, Abuja. A total of 60 participants; 20 patients with severe crisis (severity defined as 2 or more crises per year), 20 non-severe crisis patients (non-severity defined as 0-1 crises per year) and 20 apparently healthy age and sex matched individuals with HbAA were recruited as control. The sample size was calculated using power analysis software. Stat Mate version 2.0. 80% power was used.

2.3 Sample collection

Five millilitres of blood were drawn into ethylene diamine tetra acetic acid bottles from each participant, gently mixed stored at 4 degrees Celsius.

2.4 Full Blood Count

The full blood count was performed using an automated haematology analyzer Mythic 22 model according to the manufactures instructions.

2.5 Foetal Haemoglobin levels

Foetal Haemoglobin levels were determined using cation exchange High performance liquid chromatography method by Bio-Rad Variant Haemoglobin Analyser.

2.6 Statistical Analysis

One-way ANOVA was used to determine difference between means of various groups and Pearson product moment correlation was used to determine correlation between groups. Statistical significance was set at a *p*-value =0.05. Data obtained were presented using tables.

3. RESULT

The result from this study shows that the Hb value (7.68±1.6 and 8.09±1.4) for both severe crisis and non-severe crisis SCA respectively were lower than the control (12.77±1.4). This trend was also observed for HCT values. Whereas RDW values (22.31±2.7 and 20.9±2.2) for both severe and non-severe SCA respectively were significantly higher than the control (14.76±1.5). This trend was also observed for MCHC, MCV and Hb F. The significantly raised Hb F-values for both severe (5.30±2.3) and non-severe (7.12±3.6) SCA patients compared with the control (0.32±0.10), establishes the fact that HbF values are increased in sickle cell patients (Table 1).

There was no significant correlation between Hb F and any of the haematological parameters in both non severe and severe groups Hct (r = 0.37, P = -0.108), Hb concentration (r = 0.39, P = 0.081) red cell distribution width (r = -0.1719, P = 0.4687), mean cell volume (r = 0.15, P = 0.514), mean cell haemoglobin concentration (r = -0.03, P = 0.897) similar values were obtained for the severe group.

Table 1: Haematological Parameters for Non-Severe crisis SCA, Severe crisis SCA and Control Group

GROUPS	NON-SEVERE crisis SCA	SEVERE crisis SCA	CONTROL
Hb(g/l)	8.09±1.4	7.68±1.6	12.77±1.4
HCT%	23.80±4.1	23.39±5.3	40.32±3.9
MCV (fl)	85.82±10.2	81.60±4.4	79.70±24.9
MCHC (g/l)	34.18±1.4	33.14±1.2	32.50±0.9
RDW %	20.9±2.2	22.31±2.7	14.76±1.5
HBF%	7.12±3.6	5.30±2.3	0.32±0.1

Values given as Mean±SD

Table 2: Relationship between haemoglobin F and Haematological parameters in the groups

HP	HbF			
	Severe crisi SCA		Non- Severe crisi SCA	
	(cor. co-eff.; r)	p- value	(cor. co-eff.; r)	p- value
HGB	-0.12160	0.609	0.39870	0.081
HCT	-0.09416	0.692	0.37070	-0.107
MCV	-0.16750	0.4804	0.15470	0.514
MCHC	-0.15600	0.511	-0.30680	0.897
RDW	-0.03910	0.8700	-0.17190	0.468

Hp; haematological parameters, Cor.co-eff; correlation coefficient

4. Discussion.

In this study the mean foetal haemoglobin(HbF) levels in both severe and non-severe groups of sickle cell patients agrees with findings from a study in Ibadan Nigeria where the researchers discovered a statistical significant difference in the mean HbF levels in patients (5.16±4.04) compared to controls (1.04±0.44) [12]. Another study in Western Nigeria discovered a similar trend among children [11]. In this study, there was a significant increase in the mean HbF levels for both severe and non-severe groups compared to the control p=0.05. The non-severe group had the highest value; (7.12 %), followed by the severe group (5.30±2.3) then the control group (0.32±0.1). This higher HbF level in the non-severe group, could probably be the reason for the fewer number of crises per year compared to their counterpart in the severe group with 5.30% having higher number of crises per year. The control group had the least HbF level of 0.32%. The control group is made up of apparently healthy Hb genotype AA individuals.

This work confirms the study [13] which stated that in Sickle cell patients, HbF concentration vary from 0.1% to 30% with an average of about 8%. In this work, a significant increase in the HbF levels of both severe and non-sever groups were discovered although the values were a bit lower than the value given as the average in the work done by Ofori-aqua and his colleagues [13].

There was no significant correlation between HbF and any of the haematological parameters in both severe and non-severe SCA patients (Table 2). This finding contradicts a previous study in 2017 that stated that Haemoglobin F correlated positively with all the haematological parameters [11]. Franco *et al* in their work in 2006 found out that patients with high haemoglobin F level also had high haemoglobin concentration[14]. There was no positive correlation between haemoglobin F and Hb concentration in the various groups in this study. This could have been due to variations in the haemoglobin F levels in the various groups. Some patients have devastating disease manifestations with HbF levels near 20% [13]. In this study, it was discovered that some sickle cell individuals that had three or more number of crisis in a year had very high haemoglobin levels and some with one or no crisis had very low foetal haemoglobin levels.

For instance, we encountered such cases as a 34year old male homozygous sickle cell participant who had not had crisis in the past five (5) years and had not been under any form of medication, yet his foetal haemoglobin level was 0.8%. The 34 years old man in this study falls under the non-severe

group by reason of no crisis for the past five years, but his foetal haemoglobin level mimics that of the severe group (0.8%). Since foetal haemoglobin is a major prognostic factor for the clinical complication found in sickle cell anaemia [13], one should have expected a positive correlation between foetal haemoglobin and other haematological parameters in the two groups studied. Genetic studies have been published in their numbers, in a bid to explain the phenotypic variability in sickle cell anaemia, yet very little have been achieved in this regard [15].]. Environmental factors have also been implicated as a cause of this variability[16].

5. Conclusion

Foetal haemoglobin level increased in all sickle cell patients but showed higher level in those having less number of crisis per year compared to those having more number of crisis per year. Foetal haemoglobin level did not correlate significantly with any of the haematological parameters in the two groups studied. This means that Foetal haemoglobin, though known as the major prognostic factor for clinical complications found in sickle cell anaemia, has some limitations in this respect. This study recommends that further studies should look into the aspect of environmental factors contributing to this variability.

Ethical Consideration and Informed Consent

Ethical approval was obtained from the Research unit of the FCT Abuja, with protocol approval number: FHREC/2015/01/27/19-05-15 and the pa tients gave their consent before sampling in accordance with the declarations of Helsinki.

CONSENT

In accordance with international or university standard, patient's written consent was obtained and preserved by the authors.

ETHICAL APPROVAL

A written approval of the Ethics committee was collected and preserved by the authors in accordance with international and University standard.

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