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Research Article

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C-Reactive Protein Levels in Adults With Sickle Cell Disease Visiting the University College Hospital, Ibadan, Nigeria

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Abstract

Sickle cell anemia is one of the major problem in the society, especially the health-care sector. Millions of people in the world are affected and one of the highest incidence occurred in Nigeria. The situation has been further worsened by the insufficient/ inappropriate genetic counseling and diagnosing procedure for the condition. C-reactive protein is one of the greatest indicators that can prevent patients with sickle cell disease from going into cardiac arrest if its level is determined early. This study aimed at improving knowledge on the significance of C-reactive protein as one of the indicators for a possible cardiac attack on sickle cell patients. 131 persons above 18 years of age were recruited, 95 of which were sickle-celled patients and 36 without sickle-cell used as control. Questionnaires were used to collect demographic information of the participants, while their blood samples were collected into Lithium Heparin bottle (3ml), spunned, and plasma was separated, aliquoted in 2 vials and stored at -80oC. Roche (COBAS 311) was used to analyse for C-reactive protein and data summarized in tables. Mean age was 35.4years ±SD=7.54years which ranges from 19 to 56years for sickle cell subjects, and 36.8years ±SD=9.11years which ranges from 19 to 58years for control. The male to female ratio was approximately 2:1 in control and 2.4:1 in sickle cell subjects. 2(2.1%) sickle cell patients had abnormal C-reactive protein, there is no significant difference in mean C-Reactive protein between Sickle cell patients and non-Sickle cell patients (p=.551) and there is no significant relationship between C-Reactive protein in HBSS and haematological parameters like white blood cell (p=0.622) and platelets (p=0.622). No significant disparity was determined between the sickle cell and non-sickle cell individuals. Hence, further studies are needed to confirm the factor behind the abnormal C-reative protein in the two groups.

Keywords: Sickle Cell Disease (SCD), C-Reactive Protein (CRP), Haematological Parameters, Biomarkers, Myocardial Infarction, Electrophoresis

1. Introduction

According to, sickle cell anemia (SCA) is a major problem in the society, particularly the health-care sector [1]. Millions of people globally are affected and one of the highest incidence occurred in Nigeria. The situation has been further worsened by the insufficient/ inappropriate genetic counseling and diagnosing procedure for the condition.

Patients with sickle cell have a highly diverse clinical results characterized by painful vaso-occlusive crises (VOC), stroke, priapism, pulmonary hypertension, acute chest syndrome (ACS) and complications resulting into chronic injuries to organs. The clinical severity of presentation has been known to rely on factors such as disease haplotype, level of end-organ dysfunction and also the parallel inheritance of α-thalassemia [2].

The signs and complications of the disease arise majorly from the crises (clinical and subclinical). Activation and damage of endothelial cells with activation of adhesion molecules results in inflammation, release of C-reactive protein (CRP) and other inflammatory mediators and resultant enhancement of ischemia. These and other evidences suggest an association between SCD and chronic inflammatory state, where inflammation, oxidative stress and tissue oxidative damage occur, and lead to different disease severity levels and end-organ dysfunction. Exploring the role of CRP in this chronic inflammatory state is very important if we must search for therapeutic targets in this disease [3].

CRP is one of the greatest indicators that can prevent patients with sickle cell disease from going into cardiac arrest if its level is determined early. A CRP test can also be used to measure the risk of developing coronary artery disease, a condition in which the arteries of the heart are narrowed and can lead to a heart attack.

This study therefore aimed to improve knowledge on the

significance of C-Reactive Protein as one of the indicators for a possible cardiac attack on sickle cell patients who are on routine visit to the Haematology Day care Unit of the University College Hospital, Ibadan, Nigeria.

2. Materials and Method

3. Study Location

The study was carried out in the Haematology Day Care Unit, University College Hospital, Ibadan, Nigeria.

4. Study Subjects/Population

After informed consent was obtained, 131 individuals above 18 years of age were recruited. Ninety-Five (95) among them were persons with known sickle cell disease status who had previously been diagnosed to be Haemoglobin S (HbS) by haemoglobin electrophoresis. While the control group comprised of Thirty-Six (36) Haemoglobin A individuals. Their HbA status was confirmed with the aid of haemoglobin electrophoresis. They were students and workers in the study hospital.

5. Inclusion and Exclusion Criteria

Only individuals who consent to participate in the study, were within the age bracket 18-60, confirmed Sickle Cell Disease patients, and HbA controls with no previous history of any chronic ill health were enrolled for the study, while Patients with infection, chronic inflammatory condition other than Sickle Cell Disease, renal disease unrelated to Sickle cell Disease, symptomatic heart disease, rheumatoid arthritis or other autoimmune diseases, hypothyroidism, diabetes mellitus, or steroid therapy were excluded. Also, non-consenting individuals, pregnant sickle cell disease patients, and others who do not meet up with the selection criteria were not enrolled for the study.

6. Sample Collection and Storage

Sample was collected into Lithium Heparin bottle (3ml) and was subsequently spunned. Plasma was separated from the blood, aliquoted in 2 vials and stored at -80oC at the Blood bank, University College Hospital Ibadan. Haemoglobin electrophoresis at pH 8.4–8.6 was done using the cellulose acetate method.

7. Chemistry Analysis

Haemoglobin electrophoresis at pH 8.4–8.6 was done using the cellulose acetate method in order to reconfirm the sickle cell patients and to ascertain the haemoglobin genotype of the healthy individuals . Analysis for C-reactive protein was done using chemistry analyzer Roche (COBAS 311), a part of the Cobas 4000 family, which is a mid-size, robust and easy to use Floor Model Chemistry analyzer.

8. Statistical Analysis

Data analysis was carried out with Statistical Package for Social Sciences (SPSS) version 21.0. The data were summarized in tables, discreet variables expressed as percentages, while continuous variables were expressed as mean and standard deviation. Proportions were compared using the Chi-square (X2) test.

9. Ethical Consideration

A letter for ethical approval was sought and obtained from ethical committee of the Oyo state Hospital Management Board, Ministry of Health, Ibadan. Also, consent from all the participants was obtained before their inclusion into the study.

10. Results

Table 1 showed that the mean age was 35.4years ±SD=7.54years which ranges from 19 to 56years for sickle cell subjects, and 36.8years ±SD=9.11years which ranges from 19 to 58years for control. The male to female ratio was approximately 2:1 in control and 2.4 :1 in sickle cell subjects, where there were 24(66.7%) male and 12(33.3%) female in control, while there were 67(70.0%) male and 28(29.5%) females in sickle cell subjects.

In table 2, there were 93(97.9) with normal CRP level, while 2(2.1%) had abnormal CRP. This implied that there is likelihood of only 2(2.1%) of the Sickle cell patients to develop crises secondary to Myocardial Infarction.

In table 3, sickle cell subjects had a mean CRP±SD of 2.29±1.28 with a range of 0.01-5.10, while the control had a mean CRP±SD of 2.14±1.29 with a range of 0.01-4.30. There is no significant difference in mean C-Reactive protein between Sickle cell patients and non Sickle cell patients (p=.551).

Table 4 showed that there is no significant relationship between C-Reactive protein and haematological parameters like white blood cell (p=0.622) and platelets (0.622) in sickle cell patients.

Variables	Subject (N=95) N(%)	Control(N=36) n (%)
Age (years)		
≤20	2(2.1)	1(2.8)
21-30	22(23.2)	8(22.2)
31-40	50(52.6)	13(36.1)
41-50	19(20.0)	12(33.3)
51-60	2(2.1)	2(5.6)
Mean (SD) range	35.4(7.54) 19-56	36.8(9.11) 19-58
Sex		
Male	67(70.0)	24(66.7)
Female	28(29.5)	12(33.3)

Table 1: Demographic characteristics of participants

Variables	Frequency	Percentage (%)
CRP		
Normal	93	97.9
Abnormal	2	2.1

Table 2: Effect of C-Reactive protein in relation to Sickle cell patients in crises secondary to Myocardial Infarction

Variables	Group	N	Mean	Std. Deviation	95%CI	Range	p-value
CRP	Subject	95	2.29	1.28	2.027-2.55	.01-5.10	.551
	Control	36	2.14	1.29	1.70-2.57	.01-4.30	
	Total	131	2.25	1.28	2.03-2.46	.01-5.10	

Table 3: Chi square on difference in mean of C-Reactive protein in HBSS patients and non-patients

Parameters	Status	CRP		Total	p-value
		Normal N(%)	Abnormal N(%)		
white blood cell	Normal	20(100.0)	0	20	0.622
	Abnormal	73(97.3)	2(2.7)	75	
Platelets	Normal	73(97.3)	2(2.7)	75	0.622
	Abnormal	20(100.0)	0	20	

Table 4: Chi square on relationship between C-Reactive protein in HBSS and haematological parameters

11. Discussions

The mean age was 35.4years ±SD=7.54years which ranges from 19 to 56years for sickle cell subjects, and 36.8years ±SD=9.11years which ranges from 19 to 58years for control. The male to female ratio was approximately 2:1 in control and 2.4 :1 in sickle cell subjects, where there were 24(66.7%) male and 12(33.3%) female in control, while there were 67(70.0%) male and 28(29.5%) females in sickle cell subjects.

There were 2(2.1%) sickle cell patients with abnormal CRP. An important relationship exists between SCD and CRP. Stated that complications of sickle cell disease arise mainly from the crises (clinical and subclinical), exploring the role of CRP in this chronic inflammatory state is therefore very important as we search for therapeutic targets in this disease [4]. Also explained that increase in CRP levels is proportional to inflammatory stimulus [5]. In a study by CRP was confirmed to be a very important biomarker to predict heart failure in patients with acute myocardial infarction [6]. Out of 21(42%) sickle cell patients with positive CRP during their early phase presentation, 17(80.9%) were discovered with vaso-occlusive crisis in the follow up, whereas, among 29 patients with CRP negativity during the early phase, only 4 patients (13.8%) developed vaso-occlusive crisis in the follow up, and all the 4 later became CRP positive [7].

This study showed that there was no significant difference in mean C-Reactive protein between Sickle cell patients and non-Sickle cell patients (p=.551). This disagreed with Manwani and whose finding revealed that CRP is significantly increased in crisis compared with the stable state in HbSS individuals and in HbSS compared with HbAS and HbAA individuals. Also recorded in a similar study in Nigeria that mean CRP level of HbSS was significantly higher than that of HbAA and HbAS individuals [8]. CRP level increased significantly in the asymptomatic steady state HbSS individuals compared to the control group (P = 0.001) [9]. The high CRP level in non-sickle cell individuals recorded in this study may be due to underlying health conditions/ lifestyle of the individuals such as diabetics, high blood pressure, obesity, smoking and lots more.

Findings in this study revealed that there is no significant relationship between C-Reactive protein in HBSS and haematological parameters like white blood cell (p=0.622) and platelets (p=0.622). This is evident that haematological parameters act independently of C-Reactive protein level, hence, white blood cells count and platelets will not influence adults' sickle Cell conditions resulting into crisis. Found a weak positive though, not significant relationship between CRP level and white blood cells as well as platelets count. Found a negative correlation between white blood cell and CRP levels of sickle cell patients (P = 0.73), and opined that negative correlation between CRP and haematological parameters is an indication that the relationship between CRP and disease severity in asymptomatic steady state HbSS individuals is a negative one. However suggested the use of serum concentration of CRP as an indicator of the severity of disease and possible onset of complications in adults with SCD [10].

12. Conclusions

Fewer sickle cell patients had abnormal CRP and it was not significantly different from that of the non-sickle cell individuals. CRP was also not significantly related with haematological parameters, particularly white blood cells and platelets. Further study need to be conducted to determine if the abnormal CRP was due to crisis, disease severity in sickle cell patients, or underlying health conditions in the case of non-sickle cell individuals.

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