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C - reactive Protein Level and WBC Count as Biomarkers for Vaso-Occlusive Crisis among Patients with Sickle Cell Disease

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Abstract **Background:** Sickle cell disease (SCA) was recognized as an inflammatory condition. C-reactive protein (CRP) and white blood cell (WBC) count consider as biomarkers for inflammation. The present study aimed to assess the role of CRP and WBC count in vaso-occlusive crisis compared to a symptomatic steady state in HbSS patients. **Methods:** A total of 100 Sudanese patients with sickle cell anemia (74 were in vaso-occlusive crisis and 26were in steady state condition) attended to Sudan Sickle Cell Anemia Center (SSCAC), North Kordofan State (Sudan) during the period of February to June 2015. CRP level and WBC count were measured for all patients. The mean of CRP level and WBC count in vaso-occlusive crisiswere determined and compared to steady state using independent t-tests. Then the association between WBC count, CRP level, and vaso-occlusive crisis were determined using Pearson's correlation test. **Results:** In a total of 100 sickle cell anemiapatients, the mean of CRP level was found to be significantly higher in patients with Vaso-Occlusive crisis (16.43mg/l±12.35SD) in contrast to the steady state patients (4.56mg/l ± 1.45SD), P value = 0.000. Also the mean of WBC count was raised significantly in vaso-occlusive crisis compared to steady state (19.366 ± 10.6SD) (7.676 ± 2.0SD) respectively, P value = 0.000. CRP level in vaso-occlusive crisis was correlated positively with WBC count Pvalue = 0.000. **Conclusions and recommendations:** Increased CRP level and WBC count may be an early predictor of vaso-occlusive crisis; accordingly measurement of these biomarkers should be done asroutine follow up for patients with sickle cell anemia.

Keywords Sickle cell anemia, Vaso-Occlusive crisis, C-reactive protein, WBC

1. Introduction

Sickle cell anemia (SCA) is characterized by chronic hemolytic anemia related to a point mutation in the beta-globin gene of hemoglobin molecule at the sixth amino acid (Glu6Val) [1]. In Sudan, the presence of SCA already well documented among Kordofan and Darfur region in western Sudan. An extensive literature search was carried out about the prevalence of sickle cell anemia in Sudan, accessing the US National Library of Medicine, the WHO Eastern Mediterranean Region resources, the Catalogue for Transmission Genetics in Arabs and papers and documents published in Sudan, showed that the prevalence of SCA varied in different areas in Sudan with the highest rates reported from Western Sudan where one in every 123 children born in Messeryia tribe in Western Sudan is at risk of having SCA [2]. High frequency and clinical severity of the sickle cell anemia, make it a major public health problem, due to the present of different types of crisis, [3]. Most frequent crisisis the vaso-occlusive crisis (VOC) which accountfor the majority of SCD (Sickle cell disease)-related hospital admissions [4]. The prevalence of vaso-occlusive crisis in Sudan is not well documented, However Bayoumi RA reported that the vaso-occlusive crisiswas presented mainly among Sudanese Young patients [5]. The vaso-occlusive crisis results from the polymerization of deoxy-hemoglobin S as a consequence there is tissue ischemia leading to acute and chronic pain as well as organ damage that can affect any organ in the body, including bones, joints, brain, eyes, liver, kidneys, and lungs [6].

Different major complications of SCD such as acute chest syndrome [7], cerebrovascular disease [8], kidney failure [9] and early deaths [10] lead to variability in biomarkers. These biomarkers have important roles in the management of SCD, including early diagnosis of complications, detection of

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chronic organ damage, identification of individuals at risk of a severe clinical course, and monitoring response to treatment. Additionally, biomarkers could help to identify and unravel pathophysiological processes [11].

Vaso-occlusive crisis Activate and damagesthe endothelial cells lead to inflammation; As a result inflammatory biomarkers and subsequent enhancement of ischemia are release [12].

Production of C-reactive protein (CRP) is a part of a nonspecific acute phase response to inflammation and tissue necrosis [13]. Elevated levels of CRP, as a general biomarker of inflammation, have been previously reported in patients with SCD [14, 15]. High levels in the steady state have been correlated with increased frequency of acute pain (P. value 0.001) in children with SCD was reported by Krishnan S, et al [16]. Most studies find that levels of CRP increase during vaso-occlusion and may be of value in anticipating the development of acute chest syndrome [17].

White blood cell (WBC) count was also be considered as a biomarker of inflammation [18]. As the frequency of vaso-occlusive episodes was a marker of poorer survival in patients with sickle cell anemia [19], the study of the biomarkers may helps in prevention of vaso-occlusive crisis. Overall, the present study hypothesized that sickle cell Sudanese patients with higher CRP and WBC count would have an increased risk for vaso-occlusive crisis. The present study aimed to assess the role of CRP level and WBC count invaso-occlusive crisis compared to a symptomatic steady state in HbSS patients.

2. Material and Methods

The study included 100 Sudanese patients (58% males, 42% females) with sickle cell anemia their age ranged (8 month-15 years old). A total of 74% of them in vaso-occlusive crisis (painful episode), while 26% on a symptomatic steady state condition [Steady state condition was defined as no manifest crisis for at least4 weeks after the last episode, 3 or more months after the lastblood transfusion and no febrile episode for at least 2 weeks] [15]. All patients were attended to Sudan sickle cell anemia center (SSCAC), Northern Kordofan State, Western Sudan, during February and June 2015.

The study had been approved from the ethical committee of Sudan Sickle Cell Anemia Center, El-Obied - Sudan, in addition to a written informed consent was obtained from all patients or their parents/caregiver before sample collection. Patients whom refuse singing informed consent were excluded from the study.

Demographic and clinical data have been collected in structured questionnaire from each patient. A total of 3 ml of venous blood was collected in EDTA anticoagulated tube from each patient, for determination of WBC count using automated hematology analyzer SYSMEX KX-21N®.Then, the blood was centrifuged at 4000 rpm for 10 minutes to obtain plasma for determination of CRP level using commercial kits (ichroma™CRP) using ichroma instrument.

Data were analyzed using SPSS software computer program version 21. Mean of the CRP level and WBC countamong vaso-occlusive crisis and steady state patients were determined using independent t-test. The correlation of CRP level in vaso-occlusive crisis, steady state condition and WBC count was determined using Pearson's correlation test. Curve estimation test was used to determined the correlation between CRP level and WBC count in vaso- occlusive crisis. P-value was considered of significance difference at value of 0.05 and 95% confidance degree.

3. Result

When Independent t-test have been applied, the data showed significant raised in the mean of C. reactive protein in vaso-occlusive crisis patients compared to patients in a symptomatic steady state [(16.43mg/l±12.35) and (4.56mg/l ± 1.45) respectively], Pvalue=0.000.

Also the test showed significant raised in the mean of WBC count in vaso-occlusive crisis patients compared to patients in a symptomatic steady state [(19.366 ± 10.645SD) and (7.676 ± 2.019SD) respectively], P value = 0.000.

Pearson correlation test showed that the CRP level in vaso-occlusive crisis was correlated positively with WBC count (P value=0.000). The curve showed that the regression between CRP level and WBC count in vaso-occlusive crisis was linear regression, R=.385 [Figure 1].

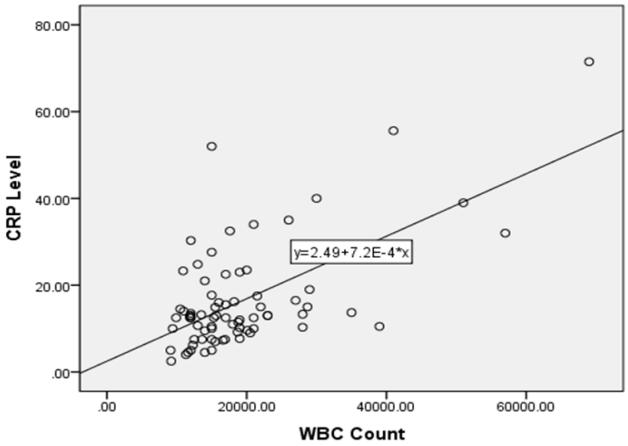

Figure 1. Scatter plots between CRP and TWBCs among Vaso-occlusive crisis group

4. Discussion

Sickle cell anemia (SCA), the most common inheritable disease, leading to a public health problem due to the occurrence of complications which mainly arise from the crisis, especially vaso-occlusive crisis [20].

In this study, we found that CRP level was higher in Vaso-occlusive crisis patients than in Steady state patients and this result is in agreement with Okocha Cet. Al [21]. The mean of white blood cell count (WBC) in this study was

elevated in vaso-occlusive crisis patients compared with patients in steady state, our finding agreed with previous study which showed that, there was strong association between WBC count and the presence of vaso-occlusive crisis [16].

Also there is a significant positive correlation between CRP level and WBC count in vaso-occlusive crisis patients which was not agreed with the findings of Okocha, C et al [21]. The present study showed that CRP level and WBC count stayed in a linear regression models during vaso-occlusive crisis and that was in accordance with previous study [21].

In fact most of the patients with sickle cell anemia are develop one of the complications specially the vaso-occlusive crisis which is the most frequent, and if not diagnosed early they may develop organ damage and die in early age. So, the early prediction of vaso-occlusive crisis by the detection of the CRP level and WBC count which might be beneficial in disease management.

5. Conclusions and Recommendations

The importance of reducing the complication of sickle cell anemia emphasizes the needs for further research with a view to vaso-occlusive crisis (VOC) to reduce SCA morbidity.In conclusion, the present study findings showed a strong association between the inflammatory biomarkers CRP and WBC count with VOC events in SCA patients. Our finding indicates that elevated WBC count could be predictors of vaso-occlusive crisis and accordingly, the determination of CRP level and WBC count may have a clinical impact in the prevention and management of vaso-occlusive crisis in Sudanese patients with Sickle cell anemia.

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