Prevalence & Etiology of Microcytosis in Sickle Cell Anemia Patients
Dr. Talal Al-Harbi¹, Mohammed Al-Matrafi² & Abdulmalik Ismail³

¹Consultant Pediatric Hematologist, King Abdullah Specialist Children Hospital
Riyadh, Saudi Arabia
²³Medical Intern, King Saud bin Abdulaziz University for Health Sciences
Riyadh, Saudi Arabia.

Abstract:
Background: Sickle cell disease, a common condition in Saudi Arabia, can have many complications & devastating outcomes. Some conditions can co-exist with this disease that can add more problems to the patient’s health. In this study we will be looking for the presence of some of these conditions. The prevalence of microcytosis & some of its causes like iron deficiency anemia will also be explored.

Methods: This is a retrospective cross-sectional study that was done in King Abdullah Specialist Children Hospital, Riyadh, Saudi Arabia in which 76 aged were included.

Results: 32 out of 76 had microcytosis with sickle cell disease. No patients had microcytosis due to iron deficiency anemia. 28 (36.8%) patients had high iron values.

Conclusion: Microcytosis can be found in a good number of sickle cell anemia patients. We have found the prevalence to be in 32 (42.1%) of our patients. Iron deficiency was not present in our sample but on the contrary we’ve iron overload in 28 (36.8%) of our patients.

Keywords: sickle cell Disease, microcytosis, Saudi Arabia

Introduction:
Sickle cell disease (SCD) is a group of autosomal recessive disorders that causes the formation of an abnormal hemoglobin S that can cause serious complications and mortality [1]. This abnormal Hgb S, when deoxygenated, polymerizes and becomes insoluble affecting the red blood cell’s flexibility causing the red blood cell to become rigid and takes up the sickle shape [1]. These changes in the cells can affect the lifespan of RBCs, their oxygen capacity and their ability to travel in the microcirculation [2]. These abnormal RBCs can obstruct microcirculation or large blood vessels because of their impaired shape and flexibility. This in turn can interrupt healthy blood flow to organs and results in infarcts in various organs, causing severe pain from vaso-occlusive events resulting in “hand-foot” syndrome (painful dactylitis caused by infarcts of the small bones) which is usually the first presentation of the disease and may lead to digits of varying lengths [2]. Other conditions that might happen in the vaso-occlusive crisis include infarcts in the bones, lungs, spleen, spinal cord, avascular necrosis of the joints, and strokes (which are the most serious vaso-occlusive event) [2]. Another condition that happens with patients of sickle cell disease is the visceral sequestration crisis, which is the sickling and pooling of the blood within organs and may lead to the most feared complication, which is the acute chest syndrome [2]. This sequestration can cause a severe exacerbation of anemia in the event of sequestration in the spleen that may lead to splenectomy in the future if it recurs [2]. Also, hemolytic anemia occurs in these patients with the presence of other events like the aplastic crisis and the hemolytic crisis. In both these events there is rapid decline of hemoglobin and abdominal pain usually accompanies this condition [2]. Also, ulcers may appear in the lower limb as a result of local blood stasis and ischemia. Proliferative retinopathy and priapism are other clinical manifestations in this disease [2]. In addition, chronic liver damage may happen with the repeated micro infarcts. The kidney also can be affected resulting in infarcts in the medulla with papillary necrosis [2]. This in turn will cause failure to concentrate urine resulting in dehydration that will lead to another crisis happening since it is one of the most important precipitators of these events [2].Also, pulmonary hypertension is common in these patients and is a major risk of mortality [2].

Genetic defects in hemoglobin are the most common of all genetic disorders and sickle cell disease is one of them [1, 2]. This disorder can
be found in many regions throughout the world. In the US, SCD affects about 72,000 people and 2 million are carriers [3]. In Africa, SCD affects nearly 200,000 newborns yearly [4]. In Saudi Arabia, there aren’t sufficient studies on the prevalence of SCD but many physicians believe that the magnitude of the disease is underestimated [5]. In a regional experience with newborn screening for SCD in the Eastern province for a period of 9 years, the prevalence of sickle cell trait was about 21% and for SCD was 2.6% [5, 6, 7]. According to the Saudi Premarital Screening Program, the prevalence of SCD gene in adult population is 4.2% for sickle cell trait and 0.26% for SCD in comparison to the Eastern Province, which has a prevalence of 17% for sickle cell trait and 1.2% for SCD making it the highest region in terms of prevalence the entire Kingdom.

SCD cannot be the only underlying problem for some patients. Other types of disorders can be associated with SCD like iron deficiency anemia. But there are no studies done to see how many patients are affected by these diseases and the link between their associations and the clinical impact on the course of SCD in our community. Studying the etiology of microcytosis in SCD patients will help in understanding its clinical impact on the disease in this specific community. Also, studying the prevalence of iron deficiency anemia in these patients has never been done before in the NGHA community. The aim of this study is to see how much of an impact microcytosis will do on SCD patients.

Objectives:

- **Aim of the Study:**
  - To determine the prevalence and etiology of microcytosis in sickle cell anemia patients in King Abdulaziz medical city.

- **Specific Objectives:**
  - To determine the prevalence of microcytic anemia in sickle cell disease patients.

- **Secondary Objectives:**
  - To determine the prevalence of iron deficiency anemia in sickle cell disease patients

Methods:

This is a retrospective cross sectional study done in King Abdullah Specialist Children Hospital (KASCH) that has reviewed sickle cell anemia patient charts. The prevalences of microcytosis, iron deficiency were the main aspects that have been reviewed.

- **Study Area/Setting:**
  - This study has been conducted in King Abdullah Specialist Children Hospital in the pediatric hematology/oncology division which is part of the Oncology department.
  - It currently has five medical divisions: Adult Hematology, Adult Medical Oncology, Gynecology Oncology, Pediatric Hematology/Oncology, and Palliative Care. A division of Radiation Oncology is soon to be established, as part of the planned comprehensive cancer center.
  - It offers the Saudi Arabian National Guard communities with comprehensive cancer care services, ranging from prevention and screening, diagnosis and state-of-the-art therapeutic interventions. For those patients with advanced disease, the department offers palliative care and end-of-life services, to enable the highest achievable possible quality of life for themselves and their family members. The department also supports current best-practice models for patient-centered care & multidisciplinary care.

- **Study Subjects:**
  - This study includes all pediatric sickle cell anemia patients aged 1-18, males and females, admitted in the hospital in the time period from 2010 till 2014.

- **Study Design:**
  - The study done is a retrospective cross sectional study in which patient charts have been reviewed. This is the most suitable study design to assess the prevalence of microcytosis in the sickle cell anemia population.

- **Sample Size:**
  - We wanted to see how much the prevalence of microcytosis was by measuring the MCVs of the patients having sickle cell anemia. The exact number of the population in NGHA is not known. So, we have taken all of the patients that were available in the time period we have chosen for the study. The total number we got was 76 patients.

- **Sampling Technique:**
  - since the number is small and limited. We’ve taken all the patients available in our time period.

- **Data Collection Methods, Instrument Used, Measurements:**
We’ve collected the data by reviewing the charts of patients with sickle cell disease that were selected for the study. A data sheet tool has been used for collecting the values. Then all the data has been coded then transferred to SPSS & analyzed. The data chosen from these charts was MCV average values, Ferritin (average, Min & Max) values.

Data Management and Analysis Plan:
In this study we’ve used a univariate descriptive analysis to see the frequencies of having an MCV < 75 fL (Microcytosis) in all patients with sickle cell disease. Having low ferritin average levels. Having abnormal min & max values of ferritin. All of these calculations have been done using SPSS.

Results:

Chart 1.

Second, for the ferritin studies only for 54 patients out of the total number of 76 patients, we have found that the average in 26 (34.2%) was normal while in 28 (36.6%) the average was high & no patients had low average values. For the min values, we’ve found that 36 (47.6%) had normal min values while 18 (23.7%) had high min values & no patients with low values. For the max values we have found that 18 (23.7%) had normal max ferritin values while 36 (47.7%) had high max values. Also, no patients had low max ferritin values. The missing values in all the mentioned above tests were 22 (28.9%). See charts 2, 3, 4.
Third, to see if the Microcytosis was caused by iron deficiency we’ve compared the MCV results of the Microcytic (having low MCV) patients and their average Ferritin values. We have got a total of 32 patients with Microcytosis but only 21 patients have had complete data. Out of these 21 we have found that 13 (40.6%) had normal average values while 8 (25.0%) had high average values. See chart 5.

**Discussion:**
As we mentioned above in the results, 32 out of 76 have microcytosis with sickle cell disease. Surprisingly there wasn’t a single patient in our study that had iron deficiency, so we could confidently say that our patients don’t have microcytosis caused by iron deficiency. Also, only 25 patients from the total of 32 microcytic patients had complete data. 25 patients have an unknown cause of microcytosis after reviewing all their labs & finding their results to be normal. In another 5 patients, the cause couldn’t be determined because of incomplete or missing data. In addition an interesting finding has been found in this population in which there is an iron overload a large number of patient. We’ve found that 28 (36.8%) patients had high iron values. Some of these patients had values reaching 8000 and even 9000 & that is more than 25 times the upper limit of the normal ferritin values. Since most of our patients in this study are admitted with a painful crisis, there is a possibility of an over transfusion
trend in treating these patients in the sitting of a crisis that needs to be reviewed.

**Conclusion:**
Microcytosis can be found in a good number of sickle cell anemia patients. We have found the prevalence to be in 32 (42.1%) of our patients. Iron deficiency was not present in our sample but on the contrary we’ve iron overload in 28 (36.8%) of our patients. Finally, treatments with blood transfusions should be reviewed to avoid iron overload.

**Ethical approval and conflict of interest:**
This article has been approved by KAIMRC ethical committee. There is no conflict of interest.

**References:**