

*Full Length Research Paper*

# **Risk factors for metabolic syndrome in adult patients with sickle cell anemia in Jazan region, Kingdom of Saudi Arabia**

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Hematological anemia is a characteristic of the hereditary condition known as sickle cell disease. According to several studies, adults with sickle cell disease may exhibit metabolic syndrome symptoms such as hyperglycemia, hypertension, and dyslipidemia. This study's objective was intended to assess the steady-state risk variables for the metabolic syndrome in adults with sickle cell anemia in the Jazan region. A case-control research with 35 adult sickle cell disease patients and 35 healthy controls was carried out. The National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATPIII) was used to diagnose metabolic syndrome after the data were examined to determine fasting plasma glucose, lipid profile, and uric acid. Mean, standard deviation (SD), and p-value were used to express the data. In order to establish statistical significance, a value of 0.05 was employed. Fasting triglyceride levels was comparable between patient and control groups (P-value = 0.54), high density lipoprotein cholesterol (HDL-C) was significantly low in case group compared to control group (P-value = 0.03) and uric acid level was significantly different in patient and control groups (P-value = 0.55). There was significant decrease in HDL-C and FPG among SCD patients compared to control group while no significant difference in fasting triglyceride and uric acid between patients and control groups.

**Key words:** Sickle cell disease, metabolic syndrome, NCEP-ATPIII.

## **INTRODUCTION**

Sickle cell disease (SCD), also known as sickle cell anemia (SCA), is a hereditary hematologic illness that results from substitution of valine for glutamic acid as the sixth amino acid (Akinyanju and Olujuhunbe, 2009).

The pathophysiology of sickle cell anemia is caused by

the presence of aberrant hemoglobin (Hb-s), which has the ability to polymerize in its deoxygenated form. This polymerization leads to sickle red blood cells' (sickle cells') distortion (Maciaszek et al., 2011).

SCD is considered as the world's most prevalent and

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**Table 1.** Risk factor of metabolic syndrome and its level according to NCEP-ATPIII

Risk factor	Defining level
Waist circumference	Man > 120 cm
	Women > 90 cm
Blood pressure	Systolic > 130 mm Hg
	Diastolic > 85 mm Hg
HDL	<40 mg/dl
Triglycerides	>115 mg/dl
Fasting plasma glucose	>110 mg/dl

widespread hemoglobinopathy. In Saudi Arabia, the reported sickle cell trait prevalence ranges from 2 to 27% and up to 2.6% of people have SCD (Clark et al., 2011). Chronic sickle cell anemia is defined by a trio of symptoms that can lead to a variety of biological complications. These biological complications are frequently combined under the umbrella term metabolic syndrome, which is characterized by abnormalities such as type 2 diabetes, dyslipidemia, hypertension, and hyperuricemia (Mohandas and Chasis, 1993).

The metabolic syndrome is a collection of illnesses that increases a person's chance of developing heart disease, vascular and neurological problems, insulin resistance, and diabetes mellitus (Gibson and Ellory, 2002).

The National Cholesterol Education Program claims that if a patient exhibits any three of the following, metabolic syndrome he/she is classified as such by the Adult Treatment Panel III (NCEP-ATP III) (Table 1). Due to high prevalence of SCD and its relation with metabolic syndrome, this study aimed to assess the risk variables for the metabolic syndrome in adult Saudis with sickle cell anemia and also to assess dyslipidemia, hyperglycemia, and hyperuricemia and examine the NCEP-ATPIII criteria for the metabolic syndrome in sickle cell patients and the control group.

## LITERATURE REVIEW

SCD is a kind of hemolytic anemia characterized by sickled red blood cells (RBCs), which are removed from circulation and destroyed at accelerated rates, causing illness. The sickled RBCs have a more significant clinical impact because they obstruct blood vessels, resulting in tissue ischemia and infarction. The presence of aberrant sickle cell hemoglobin (Hb S), which when deoxygenated becomes highly intractable and clumps with other hemoglobin particles inside the RBC, is the underlying abnormality in the RBC of SCA. Long chains that are formed from these aggregates mutilate and sickle RBCs, making them difficult to transport through vessels. Additionally, the deformed RBCs will typically cling to the endothelium, degrading vascular, occlusive ischemia,

increasing the likelihood of myocardial infarction (Perutz, 1978). The sign and symptoms of SCD normally begin to show up about five months of age. They are unique to each individual and develop through time. The warning signs and symptoms are: sickle cells quickly disintegrate and pass away, leaving too few red blood cells behind. Red blood cells typically last 120 days or so before needing to be replaced. The lack of red blood cells caused by sickle cells normally disappears within 10 to 20 days (anemia). Fatigue results from the body not receiving enough oxygen if there are not enough red blood cells. Painful episodes: agony crises, or recurrent episodes of agony, are a common signs of sickle cell anemia. Sickle-shaped red blood cells obstruct the flow of blood to the chest, abdomen, and joints, causing pain. Bones can also experience pain. The duration and intensity of the pain might range from a few hours to several weeks. Only a few pain crises occur for some people each year. Others experience 12 or more pain crises a year. A hospital stay is necessary for a serious pain crisis. With sickle cell anemia, some teenagers and adults may experience chronic pain, which can be brought on by ulcers, bone and joint degeneration, and other conditions. Red blood cells with a sickle shape that impede blood flow to the hands and feet are the source of the swelling in the hands and feet. Infections on a regular basis: sickle cells can harm the spleen, making it more prone to infections. Infants and kids with sickle cell anemia frequently receive immunizations and antibiotics from their doctors to fend against potentially fatal diseases like pneumonia. Puberty or delayed growth: red blood cells give the body the oxygen and nutrition it needs to thrive. Lack of healthy red blood cells can prevent teens from going through puberty and slow down growth in babies and children. Vision issues: sickle cells can clog the tiny blood arteries that supply the eyes. This can harm the retina, the area of the eye responsible for processing visual pictures, and cause vision issues (Brozovic et al., 1987).

Metabolic Syndrome (MetS) is the grouping of cardiovascular risk factors that result from insulin resistance and include central obesity, hyperglycemia, dyslipidemia, and hypertension. Metabolic syndrome is linked to the development and prognosis of CVD and can precede overt diabetes (Adachi and Asakura, 1979).

The medical term for a condition in which a person has diabetes, hypertension, and obesity is metabolic syndrome. Obesity, diabetes, and high blood pressure can all harm the blood vessels on their own, but having all three together is especially risky (Dover, 1994).

If you have three or more of the following, your metabolic syndrome may be diagnosed: being extremely overweight or having excess belly fat. High blood triglyceride levels (fat in the blood) and low HDL (the "good" cholesterol) levels can cause atherosclerosis, in which fatty compounds like cholesterol clog arteries. Persistently high blood pressure of at least 140/90 mmHg and insulin resistance, which is the inability to regulate

**Table 2.** Background of HbSS disease and control group.

Background	Sickle patient (n= 35)	Control group (n=35)	Total (n=70)	P-value
	mean±SD	mean±SD		
Age (year)	24.06±6.06	21.83±1.84	23±4.39	0.06
Gender	13 (43.3)	11 (36.7)	24 (40)	0.33

blood sugar levels (Zorca et al., 2010).

## MATERIALS AND METHODS

The study was conducted in Jazan area in the period of 2021 to 2022. The population was Saudi patients with sickle cell anemia as test group and healthy volunteers as control test. The study was conducted as a cross sectional study (case control study), the total number of samples were 100,50 samples for patients with sickle cell disease, and 50 samples for healthy people matched for age and gender. Sample was taken from patient who have sickle cell disease and on fasting for at least 8 h. The ready data was collected from report of patients from some hospitals in Jazan area. All thirty-five case groups were already diagnosed as SCD which is documented by complete blood count (CBC) and Hb electrophoresis (presence of HbSS), other thirty-five groups or control group were checked for free of SCD and matched with age and gender. Well-known SCD patients are chosen as inclusion criteria, but any Stickler patients with a cardiac condition, whether congenital or acquired, or who were pregnant or suffering from a kidney condition were disqualified from the study. Statistical Package for Social Sciences (SPSS) was used to analyze and show the data. T-test was applied to determine statistical significance at a value of 0.05.

## RESULTS

Thirty-five sickle cell anemia (HbSS) patients and 35 controls were included in this study: population with and without sickle cell anemia disease were used for determination of metabolic syndrome.

The background of both sickle cell anemia patients and the control group is shown in Table 2. There was no discernible difference in age between the patients and the control groups (P-value = 0.06); also gender showed no significant difference between the two groups (P-value = 0.33).

The levels of fasting lipid profiles in the control and sickle cell patient groups are shown in Table 3. When compared with the control group, the patients' fasting cholesterol level was substantially higher (P-value = 0.18). Between the patient and control groups, there were no discernible variations in fasting triglyceride levels (P = 0.54). When compared with the control group, in-patient group's HDL-C and LDL-C levels were both considerably lower (P values of 0.01 and 0.02, respectively).

Table 4 demonstrates fasting plasma glucose (FPG) to be lower in patients as compared to the control (89.4±13.67 in patient group versus 91.4±16.88 in control group) with P-value of 0.03.

Table 5 demonstrates serum uric acid to be higher in patients as compared to the control group (P-value = 0.55).

Table 6 lists the NCEP-ATPIII's (National Cholesterol Education Program-Adult Treatment Panel III) criteria for the metabolic syndrome. There are no data available for systolic blood pressure, diastolic blood pressure, body mass index (BMI) or waist circumference. 0.2% of male and 3.2% of female SCD patients have triglyceride levels above 150 mg/dl. 92.3% of male and 94.4% of female SCD patients have HDL-C levels below 40 mg/dl. 6.6% of male and 1.3% of female SCD patients have fasting plasma glucose levels above 110 mg/dl.

## DISCUSSION

Kingdom Saudi Arabia is one of the most common countries with sickle cell disease (SCD), and since some studies have looked into how the metabolic syndrome develops in this population of patients, this study was conducted to find out the prevalence of this condition.

In the present study, triglyceride levels were not considerably low in the patient group as compared to the control group, and fasting cholesterol levels were not significantly higher in the patient group as compared to the control group (P-value=0.18). However, LDL levels were significantly lower in the patient group when compared with the control group.

Dyslipidemia, defined as TG ≥150 mg/dl or HDL 40 mg/dl (for men) or mg/dl (for women), is one of the criteria for the diagnosis of metabolic syndrome. The mean HDL level was 37.41 w, which is high enough to be considered a risk factor for metabolic syndrome. Only 7.7% of males and 5.6% of females had HDL levels below 40 mg/dl, while the TG level was 88.03 mg/dl.

The effect of SCA on patients' lipid profiles has recently been the subject of studies. In this study, fasting high density lipoprotein levels were significantly lower in the patient group than in the control group, and fasting blood cholesterol levels were not significantly higher in the patient group.

Some research have claimed that secondary gout is a complication of SCA, however in the present study's investigation, we discovered that there was no statistically significant difference between the patient group and the control group in terms of the mean serum uric acid level.

High fasting plasma glucose is one of the criteria used

**Table 3.** Fasting lipid profile in Sickler patient and control group.

Parameter	HbSS patient (n= 35)	Control group (n= 35)	Total (n=70)	P-value
	mean±SD	mean±SD		
Cholesterol	113.3±43.85	99.34±28.96	105.56±36.40	0.18
Triglyceride	82.8±3.96	91.27±6.23	88.03±5.29	0.54
HDL-C	31.2±8.12	43.61±1.95	37.41±1.69	0.01
LDL-C	65.47±4.05	33.32±2.24	49.12±3.50	0.02

**Table 4.** Fasting plasma glucose (FPG) in Sickler patient and control group.

Parameter	HbSS patient (n= 35)	Control group (n= 35)	Total (n= 70)	P-value
	mean±SD	mean±SD		
FPG	89.4±13.67	91.4±16.88	90.4±15.27	0.03

**Table 5.** Serum uric acid among patient and control group.

Parameter	HbSS patient (n= 35)	Control (n= 35)	Total (n= 70)	P-value
	mean±SD	mean±SD		
Uric acid	6.0±3.6	5.5±2.9	5.75±3.25	0.55

**Table 6.** Criteria of metabolic syndrome among Sickler and control group.

Parameter	Male (16)	Female (19)
<b>Control group</b>		
TG (mg/dl)	0.1	7.3
HDL-C (mg/dl)	9.3	13.6
FPG (mg/dl)	14.4	18.3
<b>Patient group</b>		
TG (mg/dl)	0.2	3.2
HDL-C (mg/dl)	92.3	94.4
FPG (mg/dl)	6.6	1.3

to diagnose metabolic syndrome, but in the present study, it was found that only 6.6% of male patients and 1.7% of female patients had FPG levels higher than 110 mg/dl.

## Conclusions

No significant differences were found in the levels of cholesterol, triglycerides, FPG, or uric acid, however, there was a substantial decline in HDL-C in comparison to controls, among SCA patient.

## Recommendation

The reduction of mortality and morbidity is reflected in the

focus on metabolic syndrome development in SCA patients, which may give fresh insight for therapeutic methods.

## CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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