

# PREVALENCE OF PULMONARY HYPERTENSION IN SICKLE CELL ANEMIA PATIENT IN KSA

## Abstract

**Introduction:** Pulmonary hypertension (PH) is a relatively common and severe complication of SCI and an independent risk factor for mortality. Sickle cell disease is considered one of the most common diseases in the Kingdom of Saudi Arabia. When a healthy disease related to cardiovascular health is highlighted, sickle cell anemia may be the most common and related disease in high pulmonary pressure. In this study, we aimed **in this study** to determine prevalence of PHTN in SCA patient, and associated risk factors with it.

**Methodology:** This is an analytical cross-sectional study conducted in kingdom of Saudi Arabia (General population, SCA patient and CVD patient), from 29/7/2020 till 15/11/2020. The study was depending on online self-reported questionnaire that included assessing the demographic factors as gender, nationality besides, disease-related information: SCA patient, CVD patient and DM patient.

**Results:** we received 794 responses to our questionnaire where 93.5 % of them were Saudi Arabian. The prevalence of sickle cell anemia is 8.8 %. Male represented 29.8 % of patients while female represented 52.2 % of patients. In SCA patients, the prevalence of PHTN was 31.8 %. Moreover, it was found that having cardiac disease is considered a risk factor for developing PHTN where 37.7 % of patients having cardiac disease had PHTN compared with 6.2 % of health patients (OD: 9.16, 95 % CI: 5.5479 to 15.13, P=0.000) while diabetes mellitus increase risk for developing PHTN by more than seven fold (OD: 7.6, 95 % CI; 4.7175 to 12.4, P=0.000) and disorder of nervous system by 12 folds (OD: 12.7; 95 % CI: 7.6658 to 21.09, P=0.000).

**Conclusion:** we had found that the prevalence of SCA among Saudi Arabia is 8.8 % with a higher prevalence in female than male. Moreover, the prevalence of PHTN in SCA patients was high about 31.8 % which is much higher than its prevalence in normal individuals. Moreover, it was found that having cardiac disease is considered a risk factor for developing PHTN besides, having diabetic condition and disorder of nervous system which increased risk for developing PHTN in SCA by nine, seven and 12-fold respectively.

## Introduction:

Sickle cell anemia (SCA) is one of the most common monogenic medical conditions in the world with a prevalence of 1 % to 4 % of newborns in sub-Saharan Africa [1] and one individual per 600 ones in United states [2]. It is a type of autosomal recessive mendelian diseases that could happened after a single point mutation in beta  $\beta$ -globin gene [3] at position 6. Sickle cell disease (SCD) is characterized by recurrent episodes of vaso-occlusion, ischemia-reperfusion injury, and chronic hemolysis [4]. Pulmonary hypertension (PH) is a relatively common and severe complication of SCD and an independent risk factor for mortality [5,6].

Pulmonary hypertension is a type of high blood pressure that affects the arteries in your lungs and the right side of your heart. PHTN is defined as a resting mean pulmonary artery pressure (mPAP)  $\geq 25$  mm Hg. According to WHO, PHTN is classified in to 5 group including precapillary, postcapillary, or both pre and postcapillary PH [7]. The first subgroup (Precapillary) is defined as a mPAP of  $\geq 25$  mm Hg with a mean pulmonary artery wedge pressure (PAWP) or left ventricular end diastolic pressure (LVEDP) of  $\leq 15$  mm Hg plus increased pulmonary vascular resistance (PVR) [8]. Patients with sickle cell disease may have a lower baseline PVR due to anemia; thus, increased PVR is defined as  $\geq 160 \text{ dyn}\cdot\text{s}\cdot\text{cm}^{-5}$  or  $\geq 2$  Wood units [9].

Sickle cell disease is considered one of the most common diseases in the Kingdom of Saudi Arabia. When a healthy disease related to cardiovascular health is highlighted, sickle cell anemia may be the most common and related disease in high pulmonary pressure, especially since this is one of the most prominent complications. Associated with this disease. This research would help in addition to other research in terms of knowing the extent of sickle cell anemia today and the prevalence of pulmonary hypertension associated with this disease. Therefore, we aimed in this study to determine prevalence of PHTN in SCA patient, and associated risk factors with it.

## Methodology:

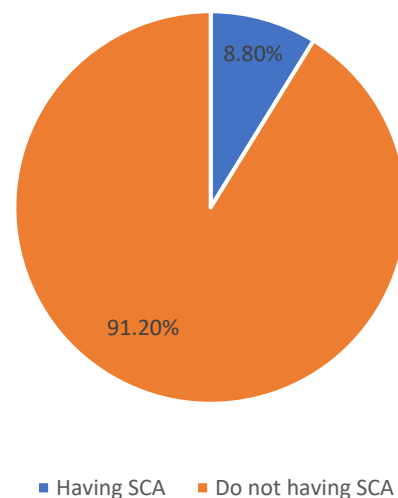
This is an analytical cross-sectional study conducted in kingdom of Saudi Arabia (General population, SCA patient and CVD patient), from 29/7/2020 till 15/11/2020. Sample size will be calculated using OpenEpi for sample size calculation for cross sectional where the inclusion criteria was SCA patient and CVD patient. The study was depending on online self-reported questionnaire that included assessing the demographic factors as gender, nationality besides, disease-related information: SCA patient , CVD patient and DM patient.

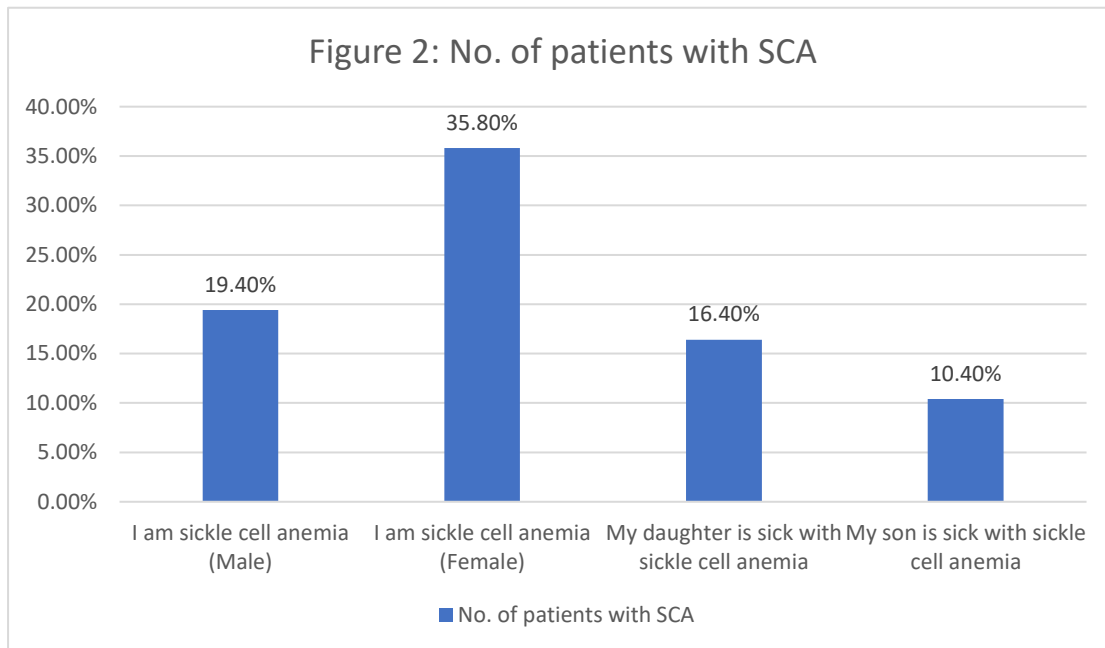
Data was entered and analyzed using SPSS version 25. Descriptive statistics was performed and categorical data was displayed as frequencies and percentages while measures of central tendencies and measures and dispersion was used to summarize continuous variables. Univariate and multivariate analysis was performed to investigate association between exposure factors and associated disease. statistical significance is set at a P value of 0.05 or less. Administrative approval was sought from the unit of biomedical ethics research committee, king Abdulaziz university. An informed consent was sought from the participants.

## Results:

In this study, we received 794 responses to our questionnaire where 93.5 % of them were Saudi Arabian. The prevalence of sickle cell anemia is 8.8 % (Figure 1) where were male represented 29.8 % of patients (19.4 % as reported by patients and 10.4 % as reported by parents) and female represented 52.2 % of patients (35.8 % as reported by patients and 16.4 % as reported by parents). Moreover, 1.5 % of total sample indicated that all of their family suffered from sickle cell anemia (Figure 2).

Figure 1: No. of participants





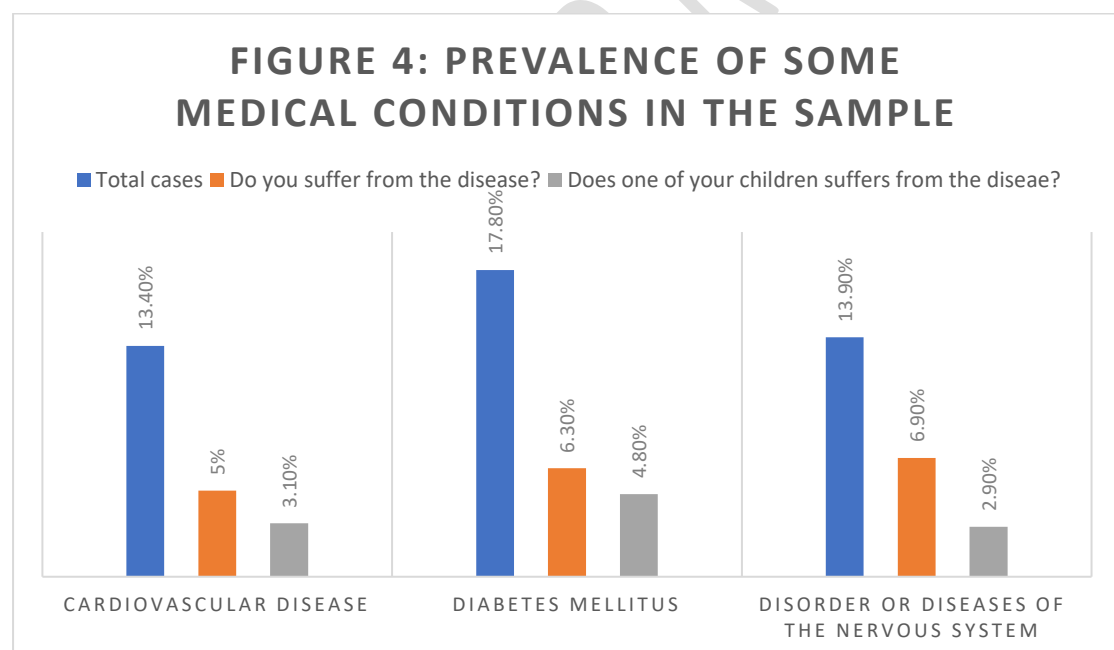
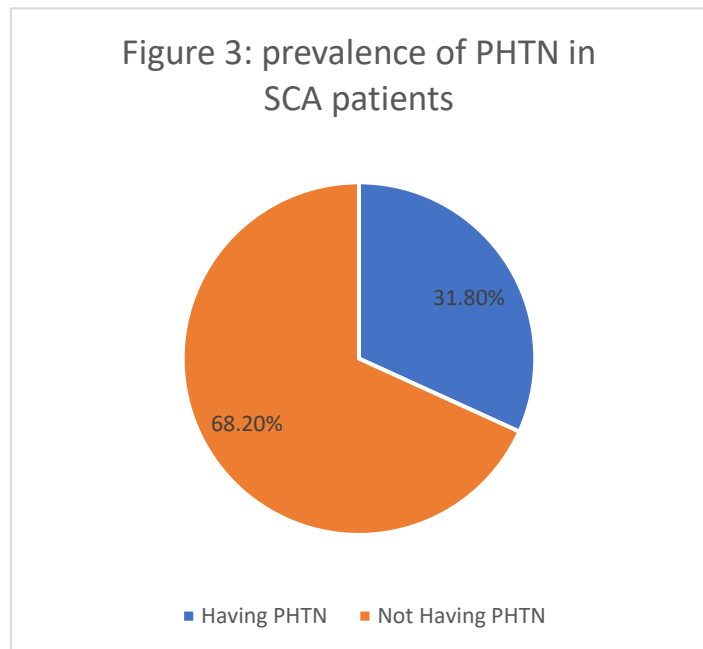
The prevalence of PHTN in total sample was 10.5 % where 3.8 % of participants reported that they had PHTN while 1.8 % indicated that their children had PHTN and 7.2 % indicated that they had other family members with PHTN (Table 1).

Table 1: Prevalence of PHTN in the sample		Frequency	Percent
Having PHTN among total sample	No	701	89.5
	Yes	82	10.5
Does any of your children have high pulmonary blood pressure?	No	713	91.1
	Yes	14	1.8
	Other	56	7.2
Do you have high pulmonary blood pressure?	No	753	96.2
	Yes	30	3.8

In SCA patients, the prevalence of PHTN was 31.8 % (Figure 3), however this prevalence is much higher than the prevalence of PHTN in normal population which was 8.5 % where the risk of PHTN was higher by five time in patients with SCA than normal patients (OR: 5.0186, 95 % CI: 2.8081 to 8.96, P=0.000).

Moreover, 13.4 % of the sample reported that they were, their

children or other family members had cardiovascular disease, 17.8 % reported about diabetes mellitus and 13.9 % of disorder of nervous system (Figure 4).



Moreover, it was found that having cardiac disease is considered a risk factor for developing PHTN where 37.7 % of patients having cardiac disease had PHTN compared with 6.2 % of health patients (OD: 9.16, 95 % CI: 5.5479 to 15.13, P=0.000). Furthermore, having diabetic condition and disorder of nervous system are other risk factors where diabetes mellitus increase risk for developing PHTN by more

than seven fold (OD: 7.6, 95 % CI; 4.7175 to 12.4, P=0.000) while disorder of nervous system by 12 folds (OD: 12.7; 95 % CI: 7.6658 to 21.09, P=0.000) (Table 2).

Table 2: Relation between some medical conditions and having PHTN		Having PHTN				
		No		Yes		P-Value
Having cardiac disease	No	635	93.8%	42	6.2%	0.000*
	Yes	66	62.3%	40	37.7%	
Having diabetic condition	No	605	94.2%	37	5.8%	0.000*
	Yes	96	68.1%	45	31.9%	
Having disorder or diseases of the nervous system	No	637	94.7%	36	5.3%	0.000*
	Yes	64	58.2%	46	41.8%	

## Discussion:

In the current study, we aimed in this study to determine prevalence of PHTN in SCA patient, and associated risk factors with it among 794 participants who had completed the questionnaire. In this study, the prevalence of SCA was 8.8 %. This prevalence is higher than reported by the Saudi Premarital Screening Program which estimated that the prevalence of sickle cell gene is only 4.2 % [10]. Other studies conducted in Saudi Arabia found that SCA represented 20 % of all patients' admissions for anemia during one month [11] and study conducted in Makkah where patients with SCA represented the largest portion of patients' admissions among anemic patients with a prevalence of 38.38 % [12]. While in rural hospital in central India, the prevalence of SCA among all hemoglobin disorders was 5.7 % [13]. Moreover, in this study, we had found the prevalence of SCI was higher in female than male (52.2 % of patients were female vs 29.8 % of males). This is in opposite to the results of other studies including study of Hazzazi who reported that 49.1 % of the SCI patients were male and 50.9 % were female [11], and study of M. Alkot who found that males represented 54.5 % of SCA patients [14].

In this study, we had found the prevalence of PHTN in SCA patients was 31.8 % which was higher than prevalence in healthy individuals (8.3 %) with increased risk

for developing PHTN in SCA patients by five folds. This prevalence is higher than reported in other studies including the study of D. Adedoyin who found that only 3.6% of these patients with sickle cell disease had evidence of pulmonary hypertension [15], and the study conducted in Northern Nigeria where the prevalence in 2008 was 25% [16].

Moreover, it was found that having cardiac disease is considered a risk factor for developing PHTN besides, having diabetic condition and disorder of nervous system which increase risk for developing PHTN in SCA by nine, seven and 12 fold respectively. This is similar to many epidemiologic studies which had shown that diabetic patients are at increased risk for developing pulmonary hypertension (PH) independent of coronary artery disease, congestive heart failure, hypertension, or smoking [17].

This study had some unavoidable limitations including depending on questionnaire to collect medical data about previous event in participants life which may lead to some memory bias or wrong report of their medical conditions. On the other hand, this up to our knowledge is the first study to assess the prevalence of PHTN among Saudi Arabian patients with SCA.

In conclusion, we had found that the prevalence of SCA among Saudi Arabia is 8.8 % with a higher prevalence in female than male. Moreover, the prevalence of PHTN in SCA patients was high about 31.8 % which is much higher than its prevalence in normal individuals. Moreover, it was found that having cardiac disease is considered a risk factor for developing PHTN besides, having diabetic condition and disorder of nervous system which increased risk for developing PHTN in SCA by nine, seven and 12 fold respectively.

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