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# Awareness of Retinopathy among Sickle Cell Patients

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***Authors' contribution***

*This work was carried out in collaboration between all authors. Authors SA and YA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SAM and HAG and MA managed the analyses of the study. Author AA managed the literature searches. All authors read and approved the final manuscript*.

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## ABSTRACT

**Background:** Sickle cell disease (SCD) is a haemoglobinopathy that is inherited in an autosomal recessive pattern. Retinopathy is a complication of SCD, which varies from mild peripheral retinopathy to severe proliferative retinopathy that can cause loss of vision.
**Methods:** A cross-sectional study was conducted from June 2020 to January 2021 aiming to determine the knowledge of retinopathy among patients with sickle cell disease using a validated self-administered questionnaire.
**Result:** A total of 166 respondents completed the questionnaire. Females constituted the majority of participants (62.7%). The age group 31–40 years consitituted 28.3% and were associated with higher knowledge scores. The average knowledge score was also significantly higher in respondents from the Eastern region (B = 1.82, P < 0.05) compared to respondents from Riyadh. The main reason for not having an eye check was the perceived lack of importance of visits among 56.8%.

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**Conclusion:** Sickle cell disease patients are prone to complications such as retinopathy which can be detected by frequent follow-up. Almost half of the studied sample showed above average knowledge of retinopathies related to sickle cell disease.

*Keywords: Sickle cell disease; genetic condition; hematology retinopathy; haemoglobinopathy.*

## 1. INTRODUCTION

Sickle cell disease (SCD) is the most prevalent type of haemoglobinopathy around the world [1]. It arises from mutations within the normal β-globin gene and is inherited in an autosomal recessive pattern [2] According to World Health Organization (WHO), hemoglobinopathies are prevalent in more than 5 percent of the world population [3] SCD is mostly prevalent in sub-Saharan Africa, India, Saudi Arabia and Mediterranean countries [4] In Saudi Arabia, the prevalence of the sickle cell gene in the adult population was measured to be 4.2% for sickle cell trait and 0.26% for SCD, with the highest incidence recorded in the Eastern Province (around 17% for sickle-cell trait and around 1% for SCD) [5]. The high frequency and prevalence of sickle cell anemia (SCA) in Saudi Arabia is linked to consanguineous marriage, which accounts for more than 50% of marriages, with 40-50% being first cousin marriages [1].

SCD can present with neurologic, ophthalmic, renal and gastrointestinal manifestations, and can affect growth and development [6] It is also associated with hemolytic conditions [7-8]. These complications, including hemolytic anemia, infections and cerebrovascular accidents, impact patients both physically and mentally [9-10] In states of diminished oxygen pressure, polymerization occurs leading to a transition in the structure of red blood cells which are liable to painful attacks of small vessel occlusions, eventually injuring different organs [11]. These complications may occur even to sickle cell trait patients with single gene mutations in extremely low oxygen situations [12].

Retinal vaso-occlusions tend to occur mostly in younger individuals, starting at the periphery of the retina, leading to hypoperfused regions that may become ischemic. In some cases, retinal neovascularization occurs in these regions [13] SCD retinopathy can be characterized as non-proliferative and proliferative. The presentation can range from moderate vascular occlusion on the periphery, to devastating proliferative sickle cell retinopathy (PSR) with loss of vision [14-17] The appearance of salmon patches, iridescent spots, and dark sunbursts is characteristic of nonproliferative sickle retinopathy (NPSR) [18] The major cause of vision deterioration in patients with sickle cell disease is proliferative sickle retinopathy (PSR) which is characterized by neovascularization [18]

SCD patients have a lower average life span and multiple recurring, disabling and costly illnesses. The growing prevalence of sickle cell disease places strain on modern healthcare systems [19] Early periodic ophthalmologic screening is important to avoid and treat retinopathy in patients with sickle cell anemia before the condition worsens [2].

## 2. METHODS AND MATERIALS

This was a cross-sectional study to assess the awareness of retinopathy among sickle cell disease patients using a validated self-administered questionnaire. In collaboration with the Security Forces Hospital, SCD clinic data were used to contact eligible patients to explain the purposes of the study. Individuals of both genders who were above 16 years old and diagnosed with SCD were invited to participate. Those below 16 years old were excluded. The questionnaire, which was self-administered in Arabic, was distributed and collected through Research Electronic Data Capture (REDCap) electronic data capture tools between August 2020 to January 2021.

The questionnaire was modeled after the survey tool developed by Alshehri et al. after gaining consent from the authors, with three additional questions added [20]. The questionnaire consisted of 31 questions separated into three sections. The first section included eleven questions about participant demographic data. The second section included eleven multiple-choice questions that assessed their knowledge regarding sickle cell disease and its effect on vision. The final section included six questions that assessed respondents' attitudes towards SCD-associated retinopathy and whether they had knowledge of the importance of regular eye screening. Respondents were also asked to assess the impact of the COVID-19 pandemic on

their follow-up routine. The knowledge score was calculated for each respondent by summing the answers to the eleven questions related to knowledge. Respondents were awarded one point for each answer of "yes". A maximum score of eleven was possible.

## 2.1 Statistical Analysis

Counts and percentages were used to summarize the distribution of categorical variables. The mean ± standard deviation were used to summarize the knowledge score. Linear regression was used to assess factors associated with the total knowledge score. Backward stepwise elimination using the Akaike information criterion (AIC) was used to eliminate non-significant variables. Hypothesis testing was performed at 5% level of significance. All analyses were performed using R version 3.6.3.

## 3. RESULTS

The survey was attempted by 184 respondents. However, only 166 respondents completed the questionnaire. Respondents aged 18–21 years old represented 39.8% of the study sample, while respondents aged 22–30 and 31–40 years represented 28.9% and 28.3%, respectively. Males and females represented 37.3% and 62.7% of the study sample, respectively Table 1.

Respondents whose highest level of education was high school represented 33.7% of the study sample, while 42.8% had a bachelor's degree. Respondents from the Southern region constituted 41.9% of the study population. The age at diagnosis was less than 21 years in 151 participants (96.7%), and more than 20 years in the remaining 3.31%. A family history of SCD was reported by 77.8%. Approximately half of the respondents did not have a family member diagnosed with both SCD and an eye disease (49.7%). More than half of the respondents (64.2%) did not use medical contact lenses or glasses. Only 4.64% of the respondents had a history of ophthalmologic surgery.

The majority of respondents understood that SCD is a genetic disorder (96%). More than half of respondents (58.3%) knew that SCD could affect the eyes, and one-third reported that they did not know. One-third of the sample identified SCD patients to be at a higher risk of eye trauma than others, and 39.1% knew that SCD could cause eye pain and redness. While 21.2% believed that SCD-associated retinopathy is curable, only 11.3% reported that SCD could cause permanent blindness. Less than one-quarter of the participants (21.2%) recognized that retinal injury was the cause of blindness in SCD patients. Half of the study sample reported that yearly ophthalmologic exams are needed in SCD patients, and more than half understood that regular screening was the best way to prevent permanent blindness. Only 9.93% knew that laser could be used to treat SCD associated retinopathy. At least 50% of respondents reported they did not know the answer to each question. Sources of information included family (22.6%), internet (29.2%), physicians (40.6%), and other healthcare practitioners (7.55%).

Overall, 45.7% of the respondents were advised by at least an ophthalmologist/optometrist or a hematologist to check their eyesight in relation to SCD. Approximately one-third of the respondents were advised to check their eyesight by an ophthalmologist (33.8%) or a hematologist (39.3%). Only 36.4% of respondents had an ophthalmologist evaluation for SCD-related diseases (n = 55). During the past 12 months, one-third of participants had an eye exam (33.1%). Of these, 40 (80%) reported using eye drops or having eye imaging. The main reasons for not having an ophthalmic exam were the perceived lack of importance of visits (56.8%), financial expenses (10.5%), transportation (6.32%), and others (26.3%).

The majority of respondents reported fewer hematology clinic visits due to the COVID-19 pandemic, while 21.3% reported that the pandemic had no effect on their check-ups.

The average knowledge score was 4.18 ± 2.48. Only eight participants answered more than 8 questions correctly, while 17.9% answered o nly one question correctly.

Respondents aged 31–40 years had significantly higher knowledge scores than respondents aged 22–30 years ($B = 1.15$, $P < 0.05$). The average knowledge score was significantly higher in respondents from the Eastern Provence ($B = 1.82$, $P < 0.05$) and the Western region ($B = 1.21$, $P < 0.05$) compared to respondents from Riyadh. Knowledge scores were significantly lower in males than females ($B = -1.61$, $P < 0.05$). Lower knowledge scores were also associated with unwareness of family history of SCD ($B = -2.12$, $P < 0.05$).

**Table 1.Demographic characteristics**

| | [ALL] | N |
|---|---|---|
| | N=166 | |
| Age: | | 151 |
| 18 - 21 | 66 (39.8%) | |
| 22 - 30 | 48 (28.9%) | |
| 31 - 40 | 47 (28.3%) | |
| 41+ | 5 (3.01%) | |
| gender: | | 151 |
| Female | 104 (62.7%) | |
| Male | 62 (37.3%) | |
| Education: | | 151 |
| Illiterate | 3 (1.81%) | |
| Primary school | 14 (8.43%) | |
| Middle school | 17 (10.2%) | |
| High school | 56 (33.7%) | |
| Bachelor | 71 (42.8%) | |
| Post-graduate | 5 (3.01%) | |
| Region: | | 151 |
| East | 15 (9.68%) | |
| Riyadh | 44 (28.4%) | |
| South | 65 (41.9%) | |
| West | 31 (20.0%) | |
| Age at diagnosis: | | 151 |
| < 21 | 146 (96.7%) | |
| > 20 | 5 (3.31%) | |
| Yearly frequency of sickle cell crisis: | | 151 |
| None | 13 (8.61%) | |
| One | 15 (9.93%) | |
| Two | 24 (15.9%) | |
| Three | 30 (19.9%) | |
| > 3 | 69 (45.7%) | |
| Do you have a family member with SCD that suffers from eye diseases or sees an ophthalmologist? | | 151 |
| No | 75 (49.7%) | |
| I do not know | 12 (7.95%) | |
| Yes | 64 (42.4%) | |
| Do you wear eyeglasses or medical contact lenses? | | 151 |
| No | 97 (64.2%) | |
| Yes | 54 (35.8%) | |
| Have you had any eye operation? | | 151 |
| No | 144 (95.4%) | |
| Yes | 7 (4.64%) | |

## 4. DISCUSSION

Sickle cell disease is a relatively common genetic condition in Saudi Arabia, notably linked to consanguinous marriage. Although awareness of the risk of congenital and hereditary defects associated with consanguinity has increased, it is still practiced in keeping with cultural norms. The Saudi Premarital Screening Program reported the prevalence of the sickle cell phenotype and disease in the adult population to be 4.2% and 0.26%, respectively, with a rising incidence recorded in the Eastern Region [21].

In Saudi Arabia, there is no screening program for sickle cell disease retinopathy. In Canada, PSR eye screening has been recommended for HbSC at 9 years of age and for HbSS at 13 years of age [22]. In Jamaica, the recommended age of screening is 12 years [23].

Our study was comparable to a Jamaican study which included 100 participants [24]. In a study conducted in the Eastern Province, 59.1% of the respondents were 31-40 years old and 62.7% were female [20].

In the present study, 58.3% of participants were aware that SCD can affect the eye, while in the Eastern Province study, only 38.6% of the population were aware of SCD ocular complications [20]. Most participants

**Table 2. Knowledge regarding SCD associated retinopathy**

| | [ALL] N=151 | N |
|---|---|---|
| Cause of SCD: | | 151 |
| Allergic | 2 (1.32%) | |
| Food-related | 4 (2.65%) | |
| Genetic disorder | 145 (96.0%) | |
| Can SCD affect the eye: | | 151 |
| No | 12 (7.95%) | |
| I do not know | 51 (33.8%) | |
| Yes | 88 (58.3%) | |
| Source of information (If yes): | | 106 |
| Family member | 24 (22.6%) | |
| Internet | 31 (29.2%) | |
| Other Health care provider | 8 (7.55%) | |
| Physician | 43 (40.6%) | |
| SCD can cause permanent blindness: | | 151 |
| No | 20 (13.2%) | |
| I do not know | 114 (75.5%) | |
| Yes | 17 (11.3%) | |
| SCD patients can avoid permanent blindness: | | 151 |
| No | 5 (3.31%) | |
| I do not know | 112 (74.2%) | |
| Yes | 34 (22.5%) | |
| SCD associated retinopathy is curable: | | 151 |
| No | 11 (7.28%) | |
| I do not know | 108 (71.5%) | |
| Yes | 32 (21.2%) | |
| The required frequency of ophthalmology visits for SCD patients: | | 151 |
| Every year | 74 (49.0%) | |
| Every two years | 9 (5.96%) | |
| Every five years | 4 (2.65%) | |
| Every ten years | 1 (0.66%) | |
| I do not know | 63 (41.7%) | |
| Treatment of sickle cell disease-associated retinopathy: | | 151 |
| Eye drops | 15 (9.93%) | |
| Glasses | 40 (26.5%) | |
| I do not know | 75 (49.7%) | |
| Laser | 15 (9.93%) | |
| Surgery | 6 (3.97%) | |
| SCD patients are at a higher risk of eye trauma than others: | | 151 |
| No | 11 (7.28%) | |
| I do not know | 88 (58.3%) | |
| Yes | 52 (34.4%) | |
| SCD can cause eye pain and redness: | | 151 |
| No | 25 (16.6%) | |
| I do not know | 67 (44.4%) | |
| Yes | 59 (39.1%) | |
| Cause of blindness in SCD patients: | | 151 |
| Retinal injury | 32 (21.2%) | |
| Increased intraocular pressure | 13 (8.61%) | |
| Optic nerve injury | 9 (5.96%) | |
| Cataract | 2 (1.32%) | |
| I do not know | 95 (62.9%) | |
| Best way to prevent blindness in SCD patients: | | 151 |
| Regular screening | 83 (55.0%) | |
| Healthy nutrition | 22 (14.6%) | |
| The use of medical glasses | 9 (5.96%) | |
| I do not know | 37 (24.5%) | |

**Table 3. Attitude towards regular screening in SCD patients**

| | [ALL] N=151 | N |
|---|---|---|
| Advised by an ophthalmologist or optometrist to check eyesight because of SCD: | | 151 |
| No | 100 (66.2%) | |
| Yes | 51 (33.8%) | |
| Advised by a hematologist to check eyesight because of SCD: | | 150 |
| No | 91 (60.7%) | |
| Yes | 59 (39.3%) | |
| Eye check by an ophthalmologist to see if SCD has affected eyesight: | | 151 |
| No | 96 (63.6%) | |
| Yes | 55 (36.4%) | |
| Reason for not having an eye check: | | 95 |
| Financial status | 10 (10.5%) | |
| No need to visit without visual problems | 54 (56.8%) | |
| Other | 25 (26.3%) | |
| Transportation | 6 (6.32%) | |
| Eye check by an ophthalmologist during the past 12 months: | | 151 |
| No | 101 (66.9%) | |
| Yes | 50 (33.1%) | |
| Eyes drops before examination or eye imaging: | | 50 |
| No | 10 (20.0%) | |
| Yes | 40 (80.0%) | |
| Did COVID-19 pandemic affect your appointments in hematology clinics? | | 150 |
| A negative effect (fewer visits) | 95 (63.3%) | |
| No effect | 32 (21.3%) | |
| A positive effect (remote appointments and constant follow-up) | 23 (15.3%) | |

of our study were able to respond correctly to questions about SCD-related eye disease, in contrast to the Jamaican study [24]. The total awareness scores of participants from the Eastern and Western regions were considerably greater compared to respondents from Riyadh, which corroborates previous research [20] Our study also found that the knowledge level of SCD ocular complications was higher with increasing age and education levels. Al-Azri supported the hypothesis of a positive association between SCD awareness and patient education level [25]. Almost 89% of our sample were unaware that SCD can cause irreversible ocular injury, which is consistent with previous work [20,24].

Although 45.7% of respondents were recommended by an ophthalmologist/optometrist or a hematologist for an eye evaluation, 36.4% never had their eyes examined. Similarly, only 25% had regular eye examinations in a prior study [24]. It is recommended to strictly adhere to a yearly ophthalmic assessment in adults with SCD and a biennial evaluation of children to avoid ocular complications. Participants in our study reported the main reason for not having a regular eye exam was the precieved lack of importance of these visits (56.8%). The association between increased incidence and prevalence of ocular manifestations with increased age has been documented in various studies. [26,27]

When asked about the impact of the COVID-19 pandemic, 63.3% of our sample reported that it negatively affected their hematology clinic visits. This finding is consistent with an international study [28].

The primary limitation of this study was a small sample size. The final sample was around 39% of the calculated sample size due to the limited number of patients in the collaborative institution. This limitation precluded generalizing results on Riyadh city targeted population. Moreover, since Riyadh is the capital city of Saudi Arabia, patients from other cities seek medical care in its tertiary and specialized hospitals. This poses another limitation, as the studied sample are not all citizens of Riyadh.

## 5. CONCLUSION

Patient awareness of the nature and possible complications of their disease is important in preventing disease progression. Sickle cell disease patients are prone to many complications which can be avoided and early

managed by frequent physician follow-ups. Almost half of our sample showed above average knowledge of retinopathies related to SCD. This study has offered a better understanding of factors leading to variations in patient awareness, emphasizing the importance of patient education by treating physicians and recommending regular ophthalmic exams.

## CONSENT AND ETHICAL APPROVAL

The approval to conduct this study was obtained on June 4, 2020 from the Institutional Review Board (IRB) of Princess Nourah bint Abdulrahman University and on September 20, 2020 from the IRB of Security Forces Hospital in Riyadh, Saudi Arabia.

We contant our target by their phone numbers, after gaining their verbal consent, the elements of the questionnaire were obtaind.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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