

To Cite:

Maqbul MS, Sarhan RN, Elshahti AK, Albalbisi GM, Alzahrani SS, Binghafrah MS. A study on the prevalence of pediatric sickle cell intricacy amongst the urban population in the Makkah region of Kingdom of Saudi Arabia. *Medical Science* 2022; 26: ms509e2602. doi: <https://doi.org/10.54905/disssi/v26i130/ms509e2602>

Authors' Affiliation:

¹Department of Microbiology and Immunology, IBN Sina National College for Medical Studies, Al Mahjar Street 31906, Jeddah 21418, Kingdom of Saudi Arabia

²Department of Medicine, IBN Sina National College for Medical Studies, Al Mahjar Street 31906, Jeddah 21418, Kingdom of Saudi Arabia

***Corresponding author**

Department of Microbiology and Immunology, IBN Sina National College for Medical Studies, Al Mahjar Street 31906, Jeddah 21418, KSA

Email: muazzamsheriffm@gmail.com

Peer-Review History

Received: 15 November 2022

Reviewed & Revised: 17/November/2022 to 29/November/2022

Accepted: 30 November 2022

Published: 02 December 2022

Peer-review Method

External peer-review was done through double-blind method.

URL: <https://www.discoveryjournals.org/medicalscience>



This work is licensed under a Creative Commons Attribution 4.0 International License.

A study on the prevalence of pediatric sickle cell intricacy amongst the urban population in the Makkah region of Kingdom of Saudi Arabia

Muazzam Sheriff Maqbul^{1*}, Rayan Nasser Sarhan², Assalah Khalid Elshahti², Ghadi Mohammed Albalbisi², Saleh Sadan Alzahrani², Muath Salem Binghafrah²

ABSTRACT

The Sickle Cell Disease (SCD) time honored among the interrelated couples because of the mutation of gene ensuing with inside the alteration of pink blood cells to a sickle form inflicting animated phenomenon ensuing in extreme intricacies many of the people which posses a brilliant have an effect on their each mental and health situations destructing the everyday existence of the individual. This moves sectional purpose take a look at changed into a try to examine the intricacies of SCD in many of the pediatric city populace of Makkah vicinity with inside the Kingdom of Saudi Arabia. The pattern length changed into envisioned the usage of the G strength calculator and the received responses from the goal populace of a thousand volunteers changed into analyzed with the aid of using the Microsoft Excel and IBM SPSS Statistics for Windows model 23 changed into used for test ing (IBM SPSS, IBM Corp., Armonk, N.Y., USA) with the aid of using representing the P-values (<005) in probabilities to decide the significance. The outcomes had been pleasant in align with the take a look at the goal. This take a look at recommends that the network surroundings encounter a whole lot of entanglements because of SCD however those oughts to be as it should be controlled with the essential measures with the aid of using clinical and nursing group of workers supervised with the aid of using applicable public business enterprise authorities.

Keywords: Sickle Cell Disease (SCD), Pediatric Urban population, Makkah region, Complications of Sickle Cell Disease (SCD), Intricacies.

1. INTRODUCTION

Sickle cell disease (SCD) is associated with mutations in the gene encoding the hemoglobin-globin chain (Hosani et al., 2005). SCD is a blood disease. It requires regular hospitalization and imposes a large financial burden on the

healthcare system. The disease affects and causes many organs in the human body. In this disease, hemoglobin mutations in the gene give rise to sickle cells and sickle hemoglobin (HBS) (Brandow et al., 2020). These irregularly shaped blood cells are so viscous that they clog various blood vessels and block or slow down circulation to the body's organs damage may occur. SCD is found almost everywhere, but is most common in the Mediterranean and Middle East (Laurence et al., 2006). Many Arab countries have reported varying degrees of prevalence of SCD (Hosani et al., 2005). The majority were from Qatar and Oman (3.9% and 3.8% respectively) about 1.9% in the United Arab Emirates. The prevalence of SCD varies by region, with the highest in the eastern region (0.17%) and the lowest in the southern region and Al Madinah (0.01%). Despite the fact that the mutations are the same in SCD patients clinically, it ranges from a benign, mostly asymptomatic condition (Lubega et al., 2018). In Saudi Arabia, there are two major clinical phenotypes of SCD. Moreover, painful crises and vascular disorders occur later in life.

Patients with SCD suffer from chronic hemolytic anemia, which can lead to lifethreatening complications (Brousseau et al., 2010). It is usually due to acute sickle cell phenomenon and microvascular occlusion of blood cells, causing pain and organ damage, especially if attacks occur frequently. In most cases, severe SCD complications require hospitalization, burdening both the healthcare system and families (Dabari et al., 2015). In these cases, painful crises and infections are reasons for hospitalization (Payne et al., 2017). Additionally, hospitalizations may be for blood transfusions related to anemia. Newborn screening is the most effective preventive measure for SCD complications (Autti et al., 2005). These programs allow vaccination to be implemented as quickly as possible. Annual screening with transcranial doppler ultrasound is recommended in addition to hydroxyurea. This is due to mutations in the gene encoding the β -globin chain of hemoglobin (Chou et al., 2015; Levenson et al., 2008). The disease affects many organs in the human body, resulting in morbidity and mortality. These patients live on lower incomes than other patients. In this disease, mutations in the hemoglobin gene result in sickle cells and sickle hemoglobin (HBS). Because they are so viscous, they lodge in various blood vessels and impede or slow circulation to various organs (Dampier et al., 2017). Reduced circulation causes organ damage.

SCD is found almost everywhere, but is more common in the Mediterranean and Middle East. Many Arab countries report varying levels of his SCD prevalence. The prevalence in Qatar and Oman was (3.9% and 3.8%, respectively). Nevertheless, conversion rates for SCD patients are similar, around 1.9% in the UAE (United Arab Emirates). The situation in the UK is unique as SCD is a common health problem among local children.SCD varied by state, with the highest in the eastern region (0.17%) and the lowest in the southern region and Al Madinah (0.01%). It can progress clinically from a severe, potentially fatal condition to a benign, largely asymptomatic condition (Nobrega et al., 2018). Difficult emergencies and vascular complications develop later (Faulstich et al., 1986).

Crosssectional studies have been conducted to identify potential short and long-term complications of SCD in children (Almeida et al., 2001). This study assess community understanding of sensitization, its effects on more general conditions and populations, particularly those hospitalized or hospitalized and whether these complications are life threatening (Muazzam et al., 2022). This cross-sectional study combines qualitative and quantitative research techniques. Data were analyzed using Microsoft Excel and SPSS. Values were expressed as percentages. IBM SPSS Statistics for Windows version 23 (IBM SPSS, IBM Corp., Armonk, NY, USA) was used for test ing a Pearson's esteem test revealed a true relationship (Maqbul et al., 2021). Data were considered basic if the P-value was less than 0.05. The complexity of the examples provided by the participants was lifted and processed with excellent cross-sectional analysis techniques.

2. MATERIALS AND METHODS

The necessary information on the complexities among the urban pediatric population in the Makkah territory was gathered from online survey questionnaires written in both Arabic and English using a crosssectional retrospective study design. The obtained information was categorized using a number of criteria, including (a) sociodemographic information, (b) complexity, (c) the administration of medical procedures, (d) hereditary problems with prevention measures of awareness and (e) the child's health well-being SCD. The study was conducted under the title "A study on the prevalence of pediatric sickle cell intricacy amongst the urban population in the Makkah Region of KSA" was sanctioned by IBN Sina National College Research Review Board Institutional Human Ethics Committee with ethical approval IRRB-02-01112022along with the protocol identification number 004MP14102022. This study was conducted from July 1, 2022 to October 31, 2022, with a total of 1000 participating volunteers.

The sample size for this study was calculated using the G-Power statistical analyzer and a variety of different equations to determine the minimum number of subjects required to enroll in a study in order to have sufficient statistical power to detect a treatment effect. Before the study began, it was determined that a sufficient number of topics should be included to provide statistical power to detect a difference and avoid type II error. Variables such as baseline incidence, population variance and

treatment effect size determined statistical power. A 5% alpha cut-off to calculate in medical literature (0.05) with a cut-off of 20% for beta is used in medical literature to calculate. The intended audience was parents of pediatric patients. 1) This study was open to parents of children sickle cell disease. 2) Sickle cell disease hereditary with a family history. The exclusion criteria were as follows: 1) Because the study was limited to children below the age of 16, responses from people over the age of 16 were not considered. 2) Restricted to Makkah region, so responses from other regions were not considered.

The study was coordinated by combining qualitative and quantitative data collection methods. SPSS and Microsoft Excel computed data. The numbers represented the values (percent). For the evaluation, IBM SPSS Statistics for Windows version 23 was used (IBM Corp., Armonk, USA). The Pearson’s esteem test was used to determine true correlations. If the P-values were less than 0.05, the data were considered basic. The complexities faced by the pediatric population were surveyed and processed using a well-designed cross-sectional review technique. The study’s power was set to 80% with and set to 0.05 and 0.2, respectively. The sample (n = 100) was calculated to estimate the required study populace to discover the difference (20%).

To assess the relationship between independent variables and study results, the Chi-square and Pearson statistical analyses were used. Univariate and multivariate regression analyzed by Cox proportional hazard model to identify risk analysis for the pediatric population.

3. RESULT AND DISCUSSION

The sample population for this study was 1000 people, but because we received so many responses, we only had about 1000 people participate in the survey. The collected data were thoroughly tabulated in Table 1 depicts study's explanation, with the appropriate responses categorized and depicted in the form of wellbrewed for descriptive analysis. SPSS and Microsoft Excel computed the data. The numbers represented the values (percent). For the evaluation, IBM SPSS Statistics for Windows version 23 was used (IBM Corp., Armonk, USA). The Pearson’s esteem test was used to calculate true correlations. If the P-values were less than 0.05, the data were considered basic. Table 2 summarizes the calculated P-values.

Table 1 Response rate for the study

Survey Questionnaires	Responserate (%)
Demographic Distribution	
Makkah	23
Jeddah	25
Taif	32
Rabugh	11
Others	09
Age group in years	
0-2	22
2-5	24
5-9	23
9-12	21
12-16	10
Gender -Specific	
Male	28
Female	72
Ethnicity	
Citizen	81
Resident	19
Accent	
Native	91
Non-native	09
Qualification	
Bachelors	47

Masters	18
Elementary	25
Others	10
Do your child have Dactylitis?	
Yes	22
No	56
Not Sure	22
Do your child have enlarged spleen??	
Yes	09
No	77
Not Sure	14
Do your child have chest or back or bone pain?	
Yes	49
No	41
Not Sure	10
Do your child have unequal legs?	
Yes	13
No	59
Not Sure	28
Does your child suffered from an infection previously or Covid-19?	
Yes	38
No	61
Not Sure	01
Do your child have double vision, bleeding in the eyes or vision loss or hematuria?	
Yes	11
No	85
Not Sure	04
Do your child have shortness of breath or ulcers or neurological issues?	
Yes	42
No	55
Not Sure	03
Does your child suffer fatigue or low energy level most of time?	
Yes	47
No	46
Not Sure	07
Does your child take medications?	
Yes	32
No	68
Not Sure	0
Does your child consume more	

fluid intake?	
Yes	55
No	40
Not Sure	05
Does your child Vaccinated?	
Yes	67
No	28
Not Sure	05
Does your child undergo bone marrow transplant?	
Yes	2
No	95
Not Sure	03
Did your child diagnose with SCD?	
Yes	9
No	88
Not Sure	03
Do you have any family members diagnosed with SCD?	
Yes	12
No	43
Not Sure	45
How to prevent SCD?	
Pre-Marital Screening	41
Pre-Marital Genetic Counseling	30
Not Sure	09
How do you rate the general well being of your child's health in the SCD of 1 to 10	
1	01
2	02
3	05
4	04
5	15
6	02
7	15
8	10
9	27
10	19

Socio-Demographic data

This survey was conducted among the urban population of the Makkah region, which includes Makkah, Jeddah, Taif, Rabugh and other territory urban areas. Participants from Makkah were 23%, Jeddah was 25%, Taif was 32%, Rabigh was 11% and other provincial urban regions were 9%. The dispersion of the responses was symbolically represented by the P-esteem obtained by using

the Pearson Chi-Square test , which was 0.06. The cumulative response for the demographic data responses were depicted in the Figure 1.

Table 2 P-Value esteem for the study

SurveyQuestionnaires	P Value Esteem (<)
Demographic Distribution	0.06
Age group in years	0.004
Gender -Specific	0.009
Ethnicity	0.07
Accent	0.812
Qualification	0.007
Do your child have Dactylitis??	0.315
Do your child have enlarged spleen?	0.133
Do your child have chest or back or bone pain?	0.346
Do your child have unequal legs?	0.001
Does your child suffered from an infection previously or Covid-19?	0.202
Do your child have double vision, bleeding in the eyes or vision loss or hematuria?	0.003
Do your child have shortness of breath or ulcers or neurological issues?	0.09
Does your child suffer fatigue or low energy level most of time?	0.07
Does your child take medications?	0.002
Does your child consume more fluid intake?	0.003
Does your child Vaccinated?	0.325
Does your child underwent bone marrow transplant?	0.05
Did your child diagnose with SCD?	0.04
Do you have any family members diagnosed with SCD?	0.518
How to prevent Sickle cell disease?	0.28
How do you rate the general well being of your child's health in the SCD of 1 to 10	0.38

The general bio-data review survey questionnaires were directed based on ethnicity, age-group in years, gender-specific, accent with qualification and were presented as an outline to the volunteers. The Pearson's esteem test revealed that the vast majority of the participants were citizens, with 81% versus 19% residents, a difference of 0.07 P-esteem for the age group 0-2years, 22% of parents participated in the intricate child. 24% were aged 2 and 5, 23% were aged 5 and 9, 21% were aged 9 and 12 and 10% were aged 12 and 16. The achieved significant difference in terms of the P-esteem obtained by using the Pearson's esteem test was 0.004. In terms of gender specific conveyance, approximately 72% were female participants and 28% were male participants, with the Pearson's esteem test yielding a P-esteem of 0.009. There was a significant difference in the P-esteem by using the Pearson Chi-Square test , which was 0.812 in regards to the accent conveyance of the participants, with 91% being native and only 9% being non-native volunteers. The allocation of schooling level revealed that the vast majority of workers (18%) were masters. Bachelors had

47%, elementary had 25% and others had 10%, with the Pearson's esteem test yielding a P-esteem of 0.007. The cumulative response for the socio bio-information responses were depicted in Figure 2.

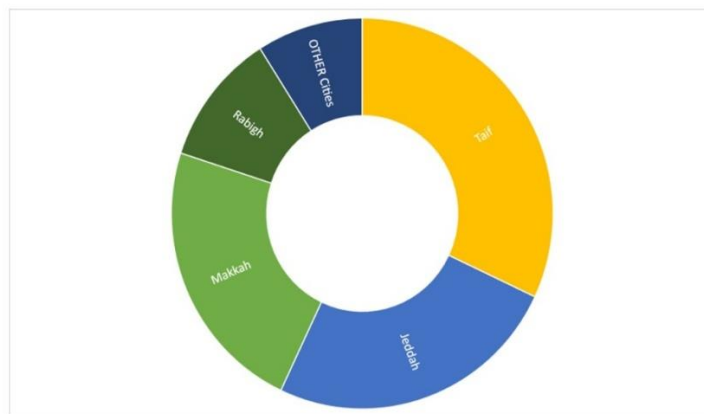


Figure 1 The demographic distribution of the response



Figure 2 The Socio Bio Information.

Intricacies

The arrangement of public based on Yes or No survey questionnaires about the complications caused by sickle cell disease was well drafted and depicted as the outline based on the level of reaction received. The questionnaire "Do your child have Dactylitis?" (Piel et al., 2013) 22% of those who responded volunteers were Yes while addressed No with 56% Not Sure 22% and a massive difference of 0.315 P-esteem obtained by utilizing the Pearson Chi-Square test . The Pearson's esteem test yielded a P-esteem of 0.133 for the poll "Does your child have an enlarged spleen?" (Piel et al., 2013) with 9% responding Yes, 77% responding No and 14% responding No I'm not sure. The response to the poll "Do your child have chest or back or bone pain?" (Perlin et al., 1994) the responses were 49% for Yes, 41% for No and 10% for Not Sure, with a huge difference of 0.346 P-esteem obtained by using the Pearson's esteem test for the poll. The following poll in this category was about "Do your child have unequal legs?" (Osunkwo et al., 2012) the Pearson's esteem test revealed that the response rate for Yes was 13% No was 59% and not sure was 2%, with a difference of 0.001 P-esteem. The following classification survey was conducted. "Does your child suffer from an infection previously or Covid-19?" (Muazzam et al., 2021) the huge difference in P-esteem obtained by using the Pearson's esteem test for the poll was 0.202, with the volunteers answering Yes with 38%, No with 61% and not sure with 1%. The response to the poll " Do your child have double vision, bleeding in the eyes or vision loss or hematuria?" (Piel et al., 2013) the Pearson's esteem test for the poll yielded a significant difference of 0.03 P-esteem with responses of 11% for Yes, 85% for No and 4% for Not Sure. This class's most recent survey was "Do your child have shortness of breath or ulcers or neurological issues?" (Jonassaint et al., 2016) the large difference in P-esteem obtained by using the Pearson's esteem test for the survey was 0.09, with the majority of the participants answering No with 55%, Yes with 42% responses and not sure with 3% respectively. The most recent significant poll in this category was on "Does your child suffer fatigue or low energy level most of time?" (Treadwell et al., 2015) for which a critical 47% answered Yes, 46% No and 7% Unsure, with a huge

difference in P-esteem obtained by using the Pearson’s esteem test for the poll being 0.07. The cumulative responses for the general intricacies’ responses were depicted in Figure 3.

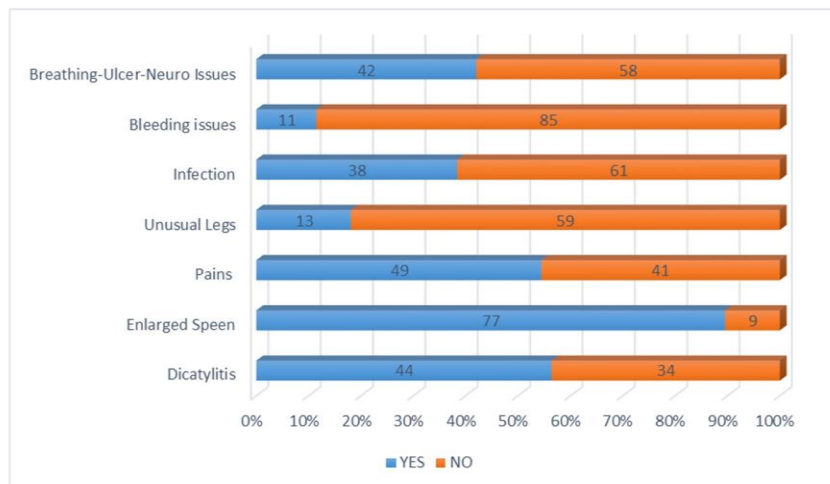


Figure 3 The general intricacies

Administration of Medical procedures

A series of planned survey questionnaires were devised to focus on the class about the administration of medical procedures for the recovery and the outcomes were depicted. The proposed poll to the target population regarding "Does your child take medications?" the response for heart palpitation was 32% Yes, 68% No and there was no response for Not sure, with the P-esteem obtained by using the Pearson’s esteem test being 0.002, indicating a clear significant difference. The following survey was directed in terms of "Does your child consume more fluid intake?" where 55% of those polled responded positively to the a Yes, 40% said yes, 40% said no and 5% said no. The P-esteem obtained by using the Pearson’s esteem test was 0.03 which was a significant difference. The second most recent poll was directed at the target population in terms of "Does your child Vaccinated?" the response for the option Yes was 67%, outperforming other confusions, while the response for the option No was 28%, while the Not sure option received only 5%, with the P-esteem obtained using the Pearson’s esteem test being 0.325, indicating a minor difference. The most recent significant poll in this category was on "Does your child under went bone marrow transplant?" which a critical 2% answered Yes while 95% answered No. The significant difference in P-esteem obtained by using the Pearson’s esteem test for the poll was 0.05. The cumulative response for the medical procedures administered responses were depicted in the Figure 4.

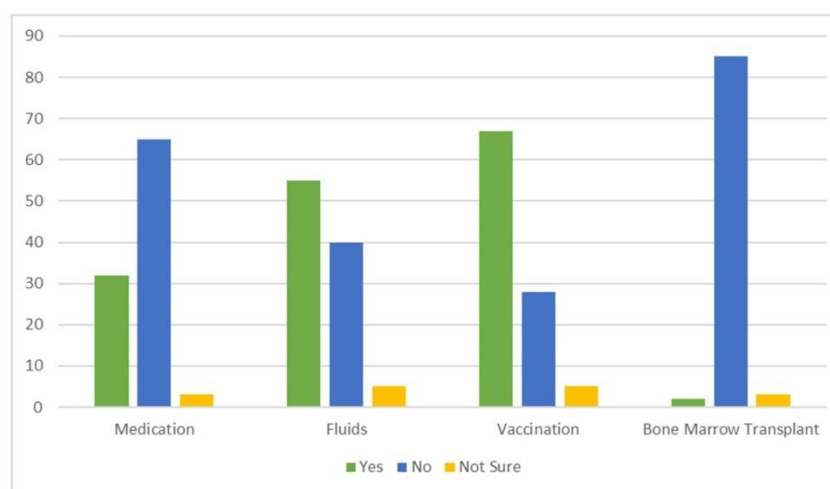


Figure 4 The medical procedures administered

Hereditary issues with Prevention measures of awareness

A series of survey questions were designed to focus on the study of hereditary issues with prevention measures of awareness for sickle cell diseases with original poll was aimed at the target population "Did your child diagnose with SCD" Yes was 98%, outperforming other reactions due to its prominence majority of diseases. Different responses included 88% for No and 3% for Not

sure the P-value of.0.04, which was not a significant difference. The other poll aimed at "Do you have any family members diagnosed with SCD?" for which the reaction was practically indistinguishable from the previous survey questionnaires with minor distinction with reaction for Yes was 12% which outperformed different reactions due to its prevalence related to the majority of the diseases. The option No achieved 43%, while not sure received 45% and the P-esteem was 0.518. The final question in this class of poll was specifically strategized at the end regarding disease prevention and awareness "How to prevent Sickle cell disease?" for which a critical 41% addressed Pre-Marital Screening, 30% addressed Pre-Marital Genetic Counseling and 9% were unsure with a huge difference in P-esteem for the poll being 0.28. The cumulative response for the diagnosis and prevention responses were depicted in the Figure 5.

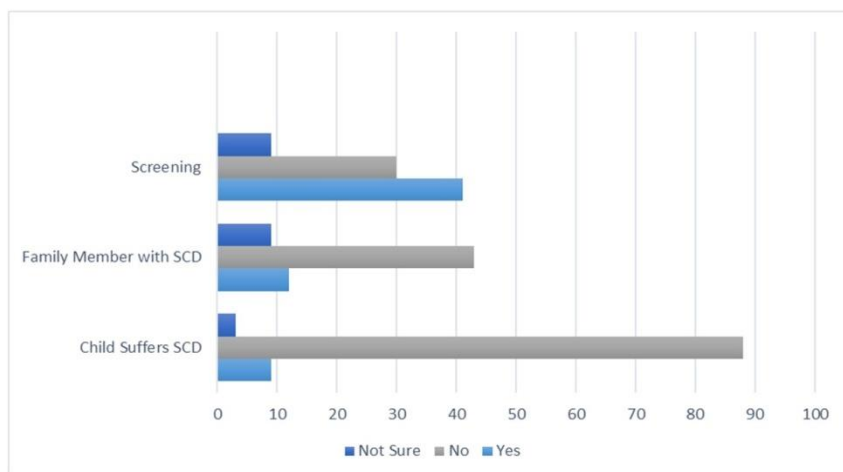


Figure 5 Diagnosis and Prevention

Well-Being SCD of the child’s health

The final questionnaire in this cross-sectional study was designed specifically to investigate the disease on the health of children (Kroenke et al., 2001) and the responses were analyzed on a SCD of 1 to 10, with the results displayed. This question was to raise awareness among the target community about the volunteers' psychological state as their child's health unfolded using a questionnaire "How do you rate the general well being of your child’s health in the SCD of 1 to 10 based on SCD?" (Sil et al., 2016; Smith et al., 2008) the majority of volunteers (19%) felt the impact rate of 10, while the impact rates of 5, 7 and 8 received similar percentage responses of moderate 15, 15 and 10%, respectively. The other effect rate SCD of 1, 2, 3, 4, 6 and 9 received a small percentage of responses, with 1, 2, 5, 4, 2 and 27% respectively. The significant difference in P-value for the questionnaire category was 0.038. The cumulative response for the general well-being of the child’s health based on SCD responses were depicted in the Figure 6.

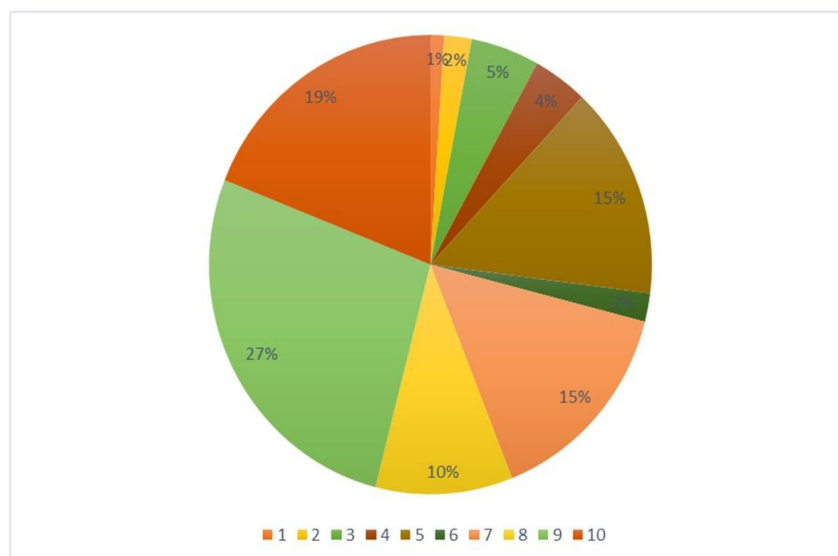


Figure 6 General well-being of the Child’s Health based on Sickle Cell Disease

4. CONCLUSION

This rationale cross-sectional study was architected to find out the intricacies faced due to SCD by the pediatric populace in the Makkah region by surveying 1000 parents with the online survey questionnaires blended with qualitative and quantitative methods. The outcome of this rationale study was excellent and will be a boon to the health authorities to combat the incidence. In this study it was found that only a scared pediatric population was inflicted with SCD. This study will be serving as a sample study for the future elaborated study of the whole nation. The findings of this study have clearly shown that though there were intricacies due to SCD but were well managed by the authorities.

Acknowledgement

The authors are very thankful to the administration of Ibn Sina National College, Al Mahjar 31906, Jeddah and KSA for giving us constant encouragement, support and guidance.

Source of Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Ethical Approval

The study was conducted under the title "A study on the prevalence of pediatric sickle cell intricacy amongst the urban population in the Makkah Region of KSA" was sanctioned by IBN Sina National College Research Review Board Institutional Human Ethics Committee with ethical approval IRRB-02-01112022 along with the protocol identification number 004MP14102022.

Authors' contributions

All authors have made equal contribution to the work and approved it for publication.

Muazzam Sheriff Maqbul: Conception, literature search, design, Supervision and organized the work and final approval.

RayanNasser Sarhan: Conception and design of the work, Revisions and final approval.

Assalah Khalid Elshahti: Writing, Critical review of final draft and final approval.

Ghadimohammed Alalbisi: Investigation, conceptualization, methodology, wrote the original draft of the manuscript.

Saleh Sadan Alzahrani: Conceptualization, methodology, co- wroteand organized the original draft of the manuscript.

MuathSalem Binghafrah: Methodology, writing, reviewing, aligning and editing.

All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

1. Al Hosani H, Salah M, Osman HM, Farag HM, Anvery SM. Incidence of haemoglobinopathies detected through neonatal screening in the United Arab Emirates. *East Mediterr Health J* 2005; 11:300-307.
2. Almeida AM, Henthorn JS, Davies SC. Neonatal screening for haemoglobinopathies: The results of a 10-year program in an English Health Region. *Br J Haematol* 2001; 112:32-35.
3. AuttiRamo I, Makela M, Sintonen H, Koskinen H, Laajalahti L. Expanding screening for rare metabolic disease in the newborn: An analysis of costs, effect and ethical consequences for decision making in Finland. *Acta Paediatr* 2005; 94:1126-1136.
4. Brandow AM, Carroll CP, Creary S, Edwards-Elliott R, Glassberg J, Hurley RW. American Society of Hematology

- 2020 guidelines for sickle cell disease: Management of acute and chronic pain. *Blood Adv* 2020; 4(12):2656–701.
5. Brousseau DC, Panepinto JA, Nimmer M, Hoffmann RG. The number of people with sickle-cell disease in the United States: National and state estimates. *Am J Hematol* 2010; 85(1):77–8.
 6. Chou R, Turner JA, Devine EB, Hansen RN, Sullivan SD, Blazina I. The effectiveness and risks of long-term opioid therapy for chronic pain: A systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med* 2015; 162(4):276–86.
 7. Dampier C, Palermo TM, Darbari DS, Hassell K, Smith W, Zempsky W. AAPT diagnostic criteria for chronic sickle cell disease pain. *J Pain* 2017; 18(5):490–8.
 8. Darbari DS, Hampson JP, Ichesco E, Kadom N, Vezina G, Evangelou I, Clauw DJ, Vi TJG, Harris RE. Frequency of hospitalizations for pain and association with altered brain network connectivity in sickle cell disease. *J Pain* 2015; 16(11):1077–86.
 9. Faulstich ME, Carey MP, Ruggiero L, Enyart P, Gresham F. Assessment of depression in childhood and adolescence: An evaluation of the Center for Epidemiological Studies Depression SCDle for Children (CES-DC). *Am J Psychiatry* 1986; 143(8):1024–7.
 10. Jonassaint CR, Jones VL, Leong S, Frierson GM. A systematic review of the association between depression and health care utilization in children and adults with sickle cell disease. *Br J Haematol* 2016; 174(1):136–47.
 11. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16(9):606–13.
 12. Laurence B, George D, Woods D. Association between elevated depressive symptoms and clinical disease severity in African-American adults with sickle cell disease. *J Natl Med Assoc* 2006; 98(3):365–9.
 13. Levenson JL, McClish DK, Dahman BA, Bovbjerg VE, Penberthy LT. Expression and anxiety in adults with sickle cell disease: The pisces project. *Psychosom Med* 2008; 70(2):192–6.
 14. Lubega FA, DeSilva MS, Munube D, Nkwine R, Tumukunde J, Agaba PK. Low dose ketamine versus morphine for acute severe vaso occlusive pain in children: A randomized controlled trial. *Scand J Pain* 2018; 18(1):19–27.
 15. Maqbul MS, Bajubair AM, Althakafi AM, Alnaggar ARA, Aljumaydi AA, Alsadi AN, Khan SM, Iqbal S, Ikbal AR. A Saudi national population-based awareness and practice of periodic medical check-up. *Asian J Pharm* 2021; 06:15. doi: 10.22377/ajp.v15i3.4154
 16. Maqbul MS, Binhashr HAN, Almana OMM, Algarni JM, AL Zamil MM, Alghamdi, Aljuhani RAS, Fallatah AOS, Alharbi RAG, Khan AA, Iqbal SMS, Dawoud A, Ikbal AR, Mohammed T, Elsaadani MEAE. A study on the prevalence of self-medication among urban population in Makkah region. *J Med Sci* 2022; 02:08. Journal-article Part of ISSN: 2321-7367, Part of ISSN: 2321-7359. doi: 10.54905/disssi/v26i120/ms62e2039
 17. Nobrega R, Sheehy KA, Lippold C, Rice AL, Finkel JC, Quezado ZMN. Patient characteristics affect the response to ketamine and opioids during the treatment of vaso-occlusive episode-related pain in sickle cell disease. *Pediatr Res* 2018; 83(2):445–54.
 18. Osunkwo I, Ziegler TR, Alvarez J, McCracken C, Cherry K, Osunkwo CE. High dose vitamin D therapy for chronic pain in children and adolescents with sickle cell disease: Results of a randomized double blind pilot study. *Br J Haematol* 2012; 159(2):211–5.
 19. Payne AB, Mehal JM, Chapman C, Haberling DL, Richardson LC, Bean CJ. Trends in sickle cell disease-related mortality in the United States, 1979 to 2017. *Ann Emerg Med* 2020; 76(3S):S28–36.
 20. Perlin E, Finke H, Castro O, Rana S, Pittman J, Burt R. Enhancement of pain control with ketorolac tromethamine in patients with sickle cell vaso-occlusive crisis. *Am J Hematol* 1994; 46(1):43–7.
 21. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Dewi M. Global epidemiology of sickle hemoglobin in neonates: A contemporary geostatistical model-based map and population estimates. *Lancet* 2013; 381(9861):142–51.
 22. Sil S, Cohen LL, Dampier C. Psychosocial and functional outcomes in youth with chronic sickle cell pain. *Clin J Pain* 2016; 32(6):527–33.
 23. Smith WR, Penberthy LT, Bovbjerg VE, McClish DK, Roberts JD, Dahman B. Daily assessment of pain in adults with sickle cell disease. *Ann Intern Med* 2008; 148(2):94–101.
 24. Treadwell MJBB, Kaur K, Gildengorin G. Emotional distress, barriers to care and health-related quality of life in sickle cell disease. *J Clin Outcomes Manag* 2015; 22:10.