SYNOPSIS

Sickle Cell Anemia among the Pregnant women and its complications among the Neonates: a Prospective Cohort Study in Shahdol district of Madhya Pradesh.

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Title: Sickle Cell Anemia among the pregnant women and its complications among the neonates: a Cross-Sectional Study in Shahdol dist. of Madhya Pradesh.

Introduction: Sickle cell anemia, a genetic blood disorder which is characterized by abnormally shaped red blood cells, is a widespread global health concern. It affects millions worldwide, with a significant burden observed in sub-Saharan Africa, the Middle East, and the Mediterranean region, where over 300,000 infants are born with the condition annually. In India, sickle cell anemia is prevalent in certain states and tribal communities, notably Madhya Pradesh, Chhattisgarh, Uttar Pradesh, and Gujarat, with prevalence rates reaching up to 30% in some tribal populations. Madhya Pradesh's tribal belt, including districts like Shahdol, Anuppur, and Umaria, grapples with alarmingly high prevalence rates of up to 35%. Pregnant women with SCA face an increased risk of various complications, including vaso-occlusive crises, infections, and pregnancy-related issues such as preeclampsia and preterm labor. These complications not only threaten maternal health but also have profound implications for neonatal outcomes. Neonates born to mothers with SCA are at a higher risk of being born preterm, having low birth weight, and experiencing other health complications, which can contribute to increased morbidity and mortality. Understanding the prevalence of SCA among pregnant women in Shahdol district and its subsequent impact on neonatal health is crucial for developing targeted healthcare strategies and interventions. This study aims to assess the prevalence of SCA among pregnant women in the district and examine the associated neonatal complications, providing essential data to inform public health policies and improve maternal and child health services in the region.

Research Questions: 1. What are the neonatal complications observed in infants born to mothers with sickle cell anemia in Shahdol District?

2. What current interventions or programs are in place to address sickle cell anemia in Shahdol District?

Objectives: 1. To determine the impact of Sickle Cell Anemia complications (low birth weight, still birth) on neonates among the pregnant women of Shahdol District of Madhya Pradesh.

2. To identify potential interventions or strategies that could be implemented to reduce the prevalence of sickle cell anemia and its impact on maternal and neonatal mortality in Shahdol district.

Hypothesis: Neonates born to mothers with sickle cell anemia in Shahdol district have a higher incidence of health complications compared to neonates born to mothers without the disease.

Null Hypothesis: There is no significant difference in the incidence of health complications between neonates born to mothers with sickle cell anemia and those born to mothers without the disease in Shahdol district.

Literature Review:

S.No.	Summary	Reference
1.	The progress in managing SCD during pregnancy, emphasizing the need for comprehensive care to address the heightened risks for both mothers and fetuses. It underscores the importance of effective management strategies, including preconception care and prenatal screening, while recognizing global disparities in healthcare access. (1)	1. Jain D, Atmapoojya P, Colah R, Lodha P. Sickle Cell Disease and Pregnancy. Mediterr J Hematol Infect Dis. 2019 Jul 1;11(1):e2019040.
2.	The study describes the significant burden of sickle cell disease (SCD) among children in Brazil, particularly in the state of Minas Gerais, where the	2. Fernandes APPC, Januário JN, Cangussu CB, Macedo DL de, Viana MB. Mortality of children with sickle cell disease: a population study. J Pediatr (Rio J). 2010 Aug;86:279–84.

	prevalence is notable. The findings reveal a high mortality rate, especially within the first two years of life, with infection being the leading cause of death followed by acute splenic sequestration. The study emphasizes the need for improved healthcare infrastructure, enhanced medical training, and targeted educational campaigns to mitigate the impact of SCD and reduce mortality rates among affected children.(2)	
3.	This study underscores the importance of supporting women with sickle cell disease who wish to become pregnant. Despite comparable rates of non-sickle-related complications to African-American women without sickle cell disease, maternal and fetal outcomes remain favorable, with a high percentage of live births. However, the risk of small for gestational age infants is elevated, particularly among women with the SS genotype, highlighting the importance of proactive management and identification of risk factors such as preeclampsia and acute anemic events.(3)	3. Smith JA, Espeland M, Bellevue R, Bonds D, Brown AK, Koshy M. Pregnancy in sickle cell disease: Experience of the cooperative study of sickle cell disease. Obstetrics & Gynecology. 1996 Feb 1;87(2):199–204.

4.	Sickle cell disease presents a complex array of clinical manifestations, necessitating tailored preventive measures based on factors such as genotype and age. Public health strategies, including newborn screening, genetic counseling, and preventive therapies like penicillin prophylaxis, have significantly impacted outcomes in affected populations. (4)	4. Olney RS. Preventing morbidity and mortality from sickle cell disease:: A public health perspective. American Journal of Preventive Medicine. 1999 Feb 1;16(2):116–21.
5.	The study establishes a sickle cell disease (SCD) infant cohort through newborn screening in central India. Tracking these infants for 3-4 years reveals early SCD manifestations and highlights the crucial role of early diagnosis, comprehensive care, and parental education in reducing morbidity and mortality. It emphasizes the necessity for accessible tertiary care centers and underscores the variability in SCD phenotypes among Indian patients. Overall, the study provides valuable insights into SCD's natural history, informing future research and clinical practices in the region.(5)	5. Upadhye DS, Jain DL, Trivedi YL, Nadkarni AH, Ghosh K, Colah RB. Neonatal Screening and the Clinical Outcome in Children with Sickle Cell Disease in Central India. PLOS ONE. 2016 Jan 19;11(1):e0147081.
6.	This study highlights the crucial role of vigilant management in sickle cell disease (SCD)	6. Vijay C, Teena S, Fernandes N. Maternal and Neonatal Outcomes with Sickle Cell Disease (SCD) in a Tertiary Health Care Hospital in a South Indian

	pregnancies, emphasizing minimal risks with proper care. Antenatal screening and rigorous fetal surveillance are vital, with cesarean sections often preferred for obstetric complications. Packed red cell transfusions are pivotal, and despite frequent low birth weight, infants typically thrive with NICU support. The findings pave the way for tailored SCD management in India, urging dedicated maternal and child health initiatives moving forward.(6)	Population 1 MedDocs Publishers. 2022 Dec 25;
7.	This study highlights the heightened risk of adverse pregnancy outcomes among women with sickle cell disease (SCD), especially prevalent in tribal communities in Gujarat due to high rates of anemia. Urgent improvements in management strategies are needed to address these challenges, emphasizing the importance of advocating for better care for pregnant women with SCD and anemia to enhance maternal health in tribal regions.(7)	7. Desai G, Anand A, Shah P, Shah S, Dave K, Bhatt H, et al. Sickle cell disease and pregnancy outcomes: a study of the community-based hospital in a tribal block of Gujarat, India. J Health Popul Nutr. 2017 Jan 21;36(1):3.
8.	Sickle cell disease (SCD) presents a substantial health challenge in India, particularly among tribal populations. Tailored	8. Colah RB, Mehta P, Mukherjee MB. Newborn Screening for Sickle Cell Disease: Indian Experience. International Journal of Neonatal Screening. 2018 Dec;4(4):31.

	management strategies are essential due to regional variations in clinical manifestations. Pilot newborn screening programs highlight the need for early intervention, but scaling up and sustaining such efforts are vital. The recent establishment of national guidelines for a Hemoglobinopathy Program signifies progress toward improved SCD management nationwide.(8)	
9.	Sickle cell disease presents significant challenges in pregnancy, especially in high-prevalence areas like central India. Maternal complications, like vaso-occlusive crises and anemia, lead to increased preterm births and cesarean deliveries. Fetal complications, including growth restriction and low APGAR scores, require NICU admissions. Enhanced antenatal care and hematologic support are vital for reducing maternal risks. Further extensive research is essential to enhance outcomes for both mothers and infants affected by sickle cell disease.(9)	9. Acharya N, Kriplani A, Hariharan C. Study of perinatal outcome in pregnancy with sickle cell disease.
10.	The study highlights the significant impact of sickle cell disease (SCD) on	10. Rajauria S, Atreja CB, Mujalda A, Mujalda J, Yadav S, Kundal RK. The Effect of Sickle Cell Hemoglobinopathy

	pregnancy outcomes, especially in regions like India. It emphasizes higher risks of obstetric complications such as anemia, preterm delivery, and stillbirth among pregnant women with SCD. Maternal morbidity and mortality are notably higher in SCD cases, underscoring the urgent need for improved antenatal and perinatal care. Early detection and comprehensive management strategies are crucial to mitigate adverse effects on maternal and fetal health, improving overall pregnancy outcomes in affected populations.(10)	on Pregnancy, Labor, Puerperium, and Fetal Outcome: A Retrospective Cohort Study From a Single Centre. Cureus [Internet]. 2023 Jan 28 [cited 2024 Apr 25]; Available from: https://www.cureus.com/articles/132286-the-effect-of-sickle-cell-hemoglobinopathy-on-pregnancy-labor-puerperium-and-fetal-outcome-a-retrospective-cohort-study-from-a-single-centre
11.	Pregnancy in women with sickle cell disease poses significant risks, demanding proactive screening in public health sectors, especially among scheduled tribes. Improved preconception counseling, antenatal care, complication management, and timely referrals are vital for better outcomes. This study emphasizes the urgent need for comprehensive strategies to address these challenges and enhance care for pregnant women with sickle cell disease, aiming	11. Modi RS, Patel SS, Modi DA, Talesara H. Fetomaternal outcome in sickle cell disease in a tertiary care centre. Int J Reprod Contracept Obstet Gynecol. 2021 Jan 28;10(2):619.

	to reduce adverse outcomes.(11)	
12.	Sickle cell disorders pose a significant genetic and public health challenge in India, especially in regions like Madhya Pradesh. This study underscores the reproductive losses linked to carrier couples, emphasizing the need for genetic counseling and interventions like carrier detection and prenatal diagnosis. Such measures are crucial for preventing affected births and improving health outcomes, benefiting both affected families and the broader global health community. Addressing these challenges is vital for reducing morbidity and mortality associated with sickle cell disorders and ensuring the well-being of future generations.(12)	12. Balgir RS. Population and Public Health Implications of Child Health and Reproductive Outcomes Among Carrier Couples of Sickle Cell Disorders in Madhya Pradesh, Central India. Int J MCH AIDS. 2014;2(2):229–35.
13.	Sickle cell disease poses substantial health risks globally, particularly in high-prevalence regions like India. Newborn screening initiatives, proven effective elsewhere, offer early detection and care, as evidenced by this study in rural south Gujarat. Despite successes, challenges persist in ensuring comprehensive follow-up, underscoring	13. Italia Y, Krishnamurti L, Mehta V, Raicha B, Italia K, Mehta P, et al. Feasibility of a Newborn Screening and Follow-up Programme for Sickle Cell Disease among South Gujarat (India) Tribal Populations. J Med Screen. 2015 Mar 1;22(1):1–7.

	the necessity for integrated healthcare systems to tackle SCD effectively in resource-limited settings.(13)	
14.	Sickle Cell Disease (SCD) is a major global health concern, notably in high-prevalence regions like India. Despite screening efforts, challenges remain in standardizing methods and ensuring comprehensive care. SCD prevalence varies among tribal groups in Gujarat, underscoring the necessity for tailored interventions and continued research. Establishing registries, investigating genetic factors, and understanding morbidity profiles are essential steps for enhancing SCD management and outcomes in India.(14)	14. Saxena D, Yasobant S, Golechha M. Situational Analysis of Sickle Cell Disease in Gujarat, India. Indian Journal of Community Medicine. 2017 Dec;42(4):218.
15	This study provides a deep insight into SCD and its detection, notably through neonatal HPLC screening. It emphasizes early diagnosis through simple blood tests and highlights the prevalence of SCD across diverse populations, stressing the necessity of targeted screening. The efficacy of HPLC in identifying carriers is emphasized, alongside the importance of integrating family studies, especially	15. Hanmante RD, Chopade SW, Dhumure KS, Shere S, Bindu RS. Neonatal Screening for Sickle Cell Disorders. 2011;1(3).

	in communities with high consanguinity rates. Early detection and intervention are pivotal in reducing SCD-related morbidity and mortality, underscoring the need for comprehensive screening approaches.(15)	
16.	The study emphasizes the significant impact of sickle cell disorders on reproductive outcomes and neonatal/infant mortality rates in Madhya Pradesh, India. It highlights heightened reproductive wastage, including abortions, stillbirths, and neonatal deaths, among sickle cell carrier couples compared to normal controls. The trend of increased defective offspring in affected families underscores the need for genetic counseling and intervention. Addressing hereditary factors alongside non-genetic variables is crucial to mitigate the burden of sickle cell disorders and reduce mortality rates. Prevention, early detection, and education efforts are essential to combat these genetic challenges and improve reproductive health outcomes.(16)	16. Balgir RS. Hematological-genetics, Reproductive Health and Family Welfare in Madhya Pradesh, India. Clin Res Hematol [Internet]. 2019 [cited 2024 Apr 26];2(2). Available from: https://asclepiusopen.com/clinical-research-in-hematology/volume-2-issue-2/4.pdf
17.	This study highlights the significant impact of sickle	17. Manjula A A, Tresa M. COMPLICATIONS AND OUTCOMES

	cell anaemia (SCA) on pregnancy outcomes in Kerala, India, with notable risks including sickle cell crisis and obstetric complications. While no significant differences were found between SCA cases and controls in outcomes, further evaluation of complications is warranted. Early and comprehensive management by a multidisciplinary team may aid in mitigating risks associated with SCA in pregnancy, potentially improving outcomes for affected individuals.(17)	OF PREGNANCY IN WOMEN WITH SICKLE CELL ANAEMIA- A STUDY CONDUCTED IN A TERTIARY CARE CENTRE IN NORTH KERALA. jemds. 2017 Aug 10;6(64):4634–9.
18.	Sickle cell disease (SCD) is a global monogenic disorder, first described in the early 20th century. India, with its significant tribal populations, faces a substantial SCD burden, necessitating targeted screening efforts. Recent initiatives like newborn screening programs are crucial for early identification. Co-inheritance with β-thalassemia complicates the disease profile. Challenges in delivering healthcare to tribal populations persist, but innovative models show promise. Understanding maternal and perinatal	18. Colah RB, Mukherjee MB, Martin S, Ghosh K. Sickle cell disease in tribal populations in India. Indian Journal of Medical Research. 2015 May;141(5):509.

	outcomes remains a research focus, with prenatal diagnosis offering important options. Integration of genetic services into primary healthcare is vital, with initiatives by organizations like ICMR and NRHM facilitating equitable access to care.(18)	
19.	Sickle cell disease (SCD) is a global monogenic disorder caused by a β-globin gene mutation, resulting in abnormal hemoglobin (HbS) production. Its pathophysiology involves HbS polymerization, leading to distorted red blood cells and vaso-occlusive events. In India, regions like Madhya Pradesh, Maharashtra, and Odisha have a high SCD burden, especially among tribal populations. Newborn screening programs are vital for early detection, while integrating genetic services into primary healthcare is crucial for quality care. Comprehensive prevention and management strategies are needed to improve health outcomes and life expectancy for affected individuals.(19)	19. Tiwari M, Pandey A, Agrwal A, Dubey GP. PREVENTION OF SICKLE CELL DISEASE AS MAJOR HEALTH BURDEN OF TRIBAL POPULATION OF MADHYA PRADESH. 2015 Jan 1;
20	Pregnancy in women with sickle cell disease (SCD)	20. Mehendale MA, Doshi B, Nayak AH, Bhosale AA, Mulik S. Pregnancy in a

	carries high risks due to complications like anemia and exacerbated physiological changes. Despite improved management with interventions such as prophylactic transfusions, maternal and fetal complications persist. A multidisciplinary approach with experienced hematologists and obstetricians is crucial for better outcomes. Preconception counseling and thorough prenatal care are vital for mitigating risks and improving pregnancy outcomes in SCD patients.(20)	Sickle Cell Disease Patient: A Nightmare! Journal of South Asian Federation of Obstetrics and Gynaecology. 2021 Mar 23;12(5):323–5.

Material and Methods:

- Study Design: Cross - Sectional Study design
- Setting:
    - Healthcare Facilities: District Hospitals, community health centers (CHCs), and primary health centers (PHCs) in Shahdol district could be included in the study setting. These facilities provide maternal and neonatal care services and maintain records of pregnancies, deliveries, and related outcomes.
    - Anganwadi centers: These community-based centers, which are part of the Integrated Child Development Services (ICDS) program in India, could serve as a study setting. Anganwadi workers maintain records of pregnant women, newborns, and children in their respective areas, making them potential sources of data for the study.
- Study population: The study population includes-
    - Pregnant mothers with Sickle Cell Anemia (SCA): This would be the primary group of interest. These individuals would have been

diagnosed with sickle cell anemia through medical records, diagnostic tests, or medical history.
    - Neonates: Newborn babies born to mothers with SCA are included in the study population. These neonates would be monitored for any kind of complications.
- Study duration: The time duration for the study is 3 months whereby the data will be collected and analysed with the help of data available from the public health facilities or community health centers.
- Sample size- With the help of data from RCH- ANMOL dated from 01/04/2022- 31/03/2024 we could identify 43,774 registered pregnant women out of which 74 are sickle cell anemia positive from five health blocks namely Beohari, Burhar, Jaisinghnagar, Pali 1 and Sohagpur. Out of these 74 positive cases, 25 cases are randomly selected as the sample size.
- Data collection technique – This includes both primary and secondary data. Primary data is through quantitative method.
  Quantitative method include- Survey Questionnaire: conducting surveys at the community level i.e., from mothers who have sickle cell anemia.
- Data Analysis plan:
    - Data Cleaning and Preparation: Clean the dataset, checking for missing or erroneous data. Prepare variables of interest, such as sickle cell anemia status, maternal mortality, neonatal mortality, demographic characteristics, and other relevant variables.
    - Descriptive Analysis- Describe the demographic characteristics of the study population, including age, gender, socioeconomic status, and geographical distribution. Calculate the prevalence of sickle cell anemia in the study population.
    - Outcome Assessment: Identify the prevalence of sickle cell anemia cases among the pregnant women within the study population. Assess its association with the complications among the neonates.
    - Statistical Analysis: Conduct statistical tests to determine the prevalence of sickle cell anemia and its association with complications. Use appropriate statistical methods, such as chi-square tests, t-tests, or logistic regression, depending on the nature of the data and research questions.
    - Interpretation and Reporting: Interpret the findings in the context of existing literature and clinical relevance. Discuss the implications of the results for healthcare policy, clinical practice, and future research. Prepare a comprehensive report or manuscript summarizing the study methods, results, and conclusions.

Ethical Considerations: Ethical considerations are paramount in conducting any research involving human subjects, particularly in a study focusing on a sensitive topic such as sickle cell anemia and its impact on maternal and neonatal mortality rates. Here are some key ethical considerations for the study:

- Informed Consent: Ensuring that the participants or their legal guardians provide informed consent before their inclusion in the study. This includes providing clear information about the study objectives, procedures, risks, benefits, and the voluntary nature of participation.
  Consider the cultural and linguistic background of participants in Shahdol District, Madhya Pradesh, and provide information in a manner that is understandable and culturally appropriate.
- Confidentiality and Privacy: Safeguarding the confidentiality of participants' personal and medical information. Ensure that data are anonymized and stored securely to prevent unauthorized access. Avoid the disclosure of identifying information in any publications or presentations to protect the privacy of participants.
- Respect for Autonomy: Respecting the autonomy and decision-making capacity of participants, particularly pregnant women with sickle cell anemia. Provide opportunities for participants to ask questions and withdraw from the study at any time without consequences.

Implications of Research: The implications of the research on the prevalence of sickle cell anemia affecting maternal and neonatal mortality rates in Shahdol District, Madhya Pradesh, could be significant in several areas:

- Public Health Interventions: The findings can inform the development and implementation of targeted public health interventions aimed at reducing maternal and neonatal mortality rates among individuals with sickle cell anemia. Strategies may include early detection and management of sickle cell disease in pregnant women, prenatal screening programs, genetic

counseling services, and access to specialized care during pregnancy and childbirth.

- Health Education and Awareness: The research findings can raise awareness about the impact of sickle cell anemia on maternal and neonatal health outcomes among healthcare providers, community members, and policymakers. Health education initiatives may focus on promoting early detection, encouraging preconception counseling, educating pregnant women about the risks of sickle cell disease, and empowering communities to support individuals with sickle cell anemia.
- Capacity Building: The study may highlight the need for capacity building initiatives to strengthen healthcare infrastructure, enhance the skills and knowledge of healthcare providers, and improve access to essential resources for managing sickle cell anemia in resource-limited settings like Shahdol District. Training programs for healthcare professionals, community health workers, and other stakeholders can help build local capacity for the prevention, diagnosis, and management of sickle cell disease.
- Research Priorities: The research findings may identify gaps in knowledge and areas for further research, guiding future investigations into the epidemiology, pathophysiology, and clinical management of sickle cell anemia in pregnancy. Future research efforts may focus on evaluating the effectiveness of interventions, exploring genetic factors influencing disease severity, investigating the impact of socio-economic determinants on health outcomes, and assessing long-term health outcomes for mothers and infants affected by sickle cell disease.