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Original Article

Pathology Section

Antenatal Screening for Haemoglobinopathies and Maternal Outcomes at a Rural Healthcare Facility in Piparia, Gujarat, India: A Prospective Cohort Study

MIHIR KUMAR BHALODIA[1], NIDHI BHALODIA[2]

ABSTRACT

Introduction: Haemoglobinopathies are inherited genetic blood disorders caused by defects in the structure or production of haemoglobin. World Health Organisation (WHO) estimates that approximately 5% of the world's population carries a gene for a haemoglobin disorder. Each year, over nine million carrier women become pregnant, leading to more than 332,000 affected pregnancies or births worldwide, mostly in low- and middle-income countries. In India, it is estimated that over 10,000 children are born annually with thalassaemia or Sickle Cell Disease (SCD). Thus, early detection through systematic antenatal screening is crucial to identify carriers, enables risk assessment for the foetus, and guides appropriate genetic counselling for prevention of severe haemoglobin disorders.

Aim: To evaluate prevalence of haemoglobinopathies in antenatal women and identify their association with maternal complications.

Materials and Methods: This prospective cohort study was conducted in the Department of Pathology at a rural tertiary healthcare facility in Piparia, Gujarat, India, from January 2024 to June 2025. A consecutive sampling technique was used, and all antenatal women attending the Department of Obstetrics and Gynaecology during the study period who met eligibility criteria and provided written informed consent were enrolled. Universal antenatal screening was performed for all enrolled participants, and a total of 1,770 antenatal women were included in the study. Participants were followed prospectively from enrollment until delivery. Maternal outcomes were assessed using hospital medical records and obstetric case files, and relevant obstetric and delivery outcomes were documented using standardised clinical records.

All participants underwent routine antenatal laboratory investigations, including Complete Blood Count (CBC). Blood samples were further analysed using the sickling test and haemoglobin analysis on a Bio-Rad Variant II High-Performance Liquid Chromatography (HPLC) analyser (Bio-Rad Laboratories, Hercules, California, USA) for the detection and characterisation of haemoglobinopathies.

Results: In the present study, a total of 1,770 antenatal women were screened for haemoglobinopathies, and 210 were found to have a haemoglobinopathy, resulting in a prevalence of 11.86%. Of the 210 women diagnosed with a haemoglobinopathy, Sickle Cell Trait (SCT) was the most common, found in 176 participants (83.8%). The occurrence of preterm delivery, preeclampsia, and postpartum haemorrhage was significantly higher among women with haemoglobinopathies than among those without haemoglobinopathies. Women with haemoglobinopathies had a 3.35-fold higher risk of preterm delivery {Relative Risk (RR)=3.35; 95% Confidence Interval (CI): 2.74-4.10; p<0.00001}, a 2.22-fold higher risk of preeclampsia (RR=2.22; 95% CI: 1.76-2.80; p<0.00001), and a 2.80-fold higher risk of postpartum haemorrhage (RR=2.80; 95% CI: 1.93-4.07; p<0.00001) compared to women without haemoglobinopathies.

Conclusion: The present study found an association between haemoglobinopathies and adverse maternal outcomes, including preeclampsia, preterm delivery, and postpartum haemorrhage. These findings highlight the importance of routine antenatal screening, early diagnosis, appropriate genetic counselling, and multidisciplinary obstetric care for pregnant women with haemoglobinopathies. Strengthening screening programs and integrating them into public health planning is essential.

Keywords: Maternal complications, Postpartum haemorrhage, Preeclampsia, Preterm delivery, Sickle cell trait

INTRODUCTION

Haemoglobinopathies are inherited genetic blood disorders caused by defects in the structure or production of haemoglobin. The most common forms are thalassaemia and Sickle Cell Disease (SCD) [1,2].

Globally, haemoglobinopathies represent a major public health problem. Approximately 5% of the world's population is estimated to carry a potentially pathological haemoglobin variant, and about 7% of pregnant women are carriers of haemoglobin disorders. More than 330,000 infants are estimated to be born annually with serious haemoglobin disorders, while approximately 1.1% of couples worldwide are at risk of having a child affected by a severe haemoglobinopathy [2]. These disorders are particularly prevalent in South Asia, the Mediterranean region, the Middle East, and sub-Saharan Africa [1,2].

In India, haemoglobinopathies constitute an important public health concern because of the country's large and genetically diverse population. The prevalence of haemoglobin variants varies considerably according to geographical region, ethnicity and community. Sickle cell disease is particularly prevalent among several tribal and other high-risk populations in central and western India [3,4]. β-thalassaemia trait also shows substantial regional and ethnic variation, with higher frequencies reported in several communities across the country [5,6]. Studies from different Indian regions have demonstrated considerable variation in the prevalence of sickle cell disease and other haemoglobinopathies, emphasising the importance of population-specific screening strategies [7,8].

Thalassaemia is broadly classified into α- and β-thalassaemia according to the affected globin chain. The clinical spectrum ranges

from asymptomatic carrier states to severe anaemia requiring regular blood transfusion and lifelong medical care [9]. Sickle cell disease, in contrast, results from the production of haemoglobin S and is characterized by chronic haemolytic anaemia and recurrent vaso-occlusive complications. The clinical manifestations may include painful crises, acute chest syndrome and progressive end-organ damage [10]. Sickle cell trait, in which HbS is inherited with normal HbA, is generally asymptomatic, although rare complications may occur under specific physiological or environmental conditions [11].

Improved medical care and advances in the management of haemoglobinopathies have enabled more women with these disorders to survive to reproductive age and undertake pregnancy [12]. Pregnancy, however, imposes substantial physiological demands that may exacerbate pre-existing anaemia and disease-related complications. Maternal haemoglobin concentration is an important determinant of pregnancy outcome, and severe maternal anaemia has been associated with adverse maternal and foetal outcomes [13]. Women with sickle cell disease are at increased risk of several pregnancy-related complications, including pre-eclampsia, preterm birth, foetal growth restriction, stillbirth and maternal morbidity [14,15].

Pregnancy in women with homozygous sickle cell disease is associated with particularly adverse maternal and perinatal outcomes. A systematic review and meta-analysis of 21 observational studies reported that women with HbSS had a significantly higher risk of maternal mortality (RR=5.98; 95% CI: 1.94-18.44), pre-eclampsia (RR=2.43; 95% CI: 1.75-3.39), preterm delivery (RR=2.21; 95% CI: 1.47-3.31), stillbirth (RR=3.94; 95% CI: 2.60–5.96), and small-for-gestational-age infants (RR=3.72; 95% CI: 2.32–5.98) compared with women without sickle cell disease [16]. These findings highlight the importance of early recognition and appropriate antenatal management of women with haemoglobinopathies.

Although haemoglobinopathies themselves are inherited disorders and cannot be prevented by screening, early identification of carriers through antenatal screening is essential. Screening facilitates identification of at-risk couples, partner testing, genetic counselling, assessment of foetal risk and informed reproductive decision-making, including appropriate prenatal diagnostic options [17,18]. Antenatal screening is therefore particularly important in populations with a high prevalence of haemoglobin variants.

High-Performance Liquid Chromatography (HPLC) has become an important laboratory technique for the detection and quantification of haemoglobin fractions and several common haemoglobin variants. It offers advantages including rapid analysis, reproducibility and simultaneous quantification of different haemoglobin fractions [19]. Studies from India have demonstrated the utility of HPLC in detecting haemoglobin variants and haemoglobinopathies in large populations [20,21]. However, because certain haemoglobin variants may show overlapping retention times or co-elution, HPLC findings may occasionally require correlation with clinical findings and, where indicated, additional electrophoretic or molecular investigations.

Despite these benefits, consistent antenatal screening practices are not yet uniformly implemented across India. Moreover, information on the prevalence and diversity of these conditions in specific vulnerable groups, such as pregnant women, remains scarce [10]. This study was conducted to help bridge this critical knowledge gap.

The present study aimed to determine the prevalence of haemoglobinopathies among antenatal women; to identify the patterns of haemoglobinopathies detected and to assess the association between haemoglobinopathies and maternal complications.

MATERIALS AND METHODS

The present prospective cohort study was conducted in the Department of Pathology at a rural tertiary healthcare facility in Piparia, Gujarat, India, from January 2024 to June 2025. The study was started after obtaining approval by the Institutional Review Board vide letter no. SVIEC/ON/MEDI/SRP/22061. A consecutive sampling technique was used, and all antenatal women attending the Department of Obstetrics and Gynaecology during the study period who met eligibility criteria and provided written informed consent were enrolled. Universal antenatal screening was performed for all enrolled participants, and a total of 1,770 antenatal women were included in the study. Participants were followed prospectively from enrollment until delivery. Maternal outcomes were assessed using hospital medical records and obstetric case files, and relevant obstetric and delivery outcomes were documented using standardised clinical records.

Sample size calculation: The sample size calculation was done using the expected effect size by OpenEpi, version 3 for the present cohort study.

Two-sided significance level (1-alpha): 95

Power (1-beta, % chance of detecting): 80

Ratio of sample size, unexposed/exposed: 8

Percent of unexposed with outcome: 9

Percent of exposed with outcome: 17

Relative Risk (RR): 2

Risk/prevalence ratio: 1.8

Risk/prevalence difference: 7.5

Sample size exposed: 173

Sample size non exposed: 1378

The present study included 1,770 antenatal women (210 with haemoglobinopathies and 1,560 without haemoglobinopathies), which exceeded the required sample size and provided adequate statistical power to assess the association between haemoglobinopathies and adverse maternal outcomes.

Inclusion criteria: All pregnant women aged <40 years who attended the antenatal clinic during the study period were included, regardless of gestational age. Both primigravida and multigravida women, with singleton or multiple pregnancies, were included. Women attending either their first or follow-up antenatal visits were included. In addition, all referred antenatal patients presenting to the tertiary care centre during the study period were included.

Exclusion criteria: All participants with incomplete clinical or laboratory data, as well as those who declined to provide informed consent, were excluded from the study. Additionally, individuals with a documented history of blood transfusion within the preceding three months were excluded, as transfusion may interfere with the interpretation of HPLC results. Certain rare variants of haemoglobinopathies like Haemoglobin D (HbD), Haemoglobin Q (HbQ), Haemoglobin Lepore (Hb Lepore), and Haemoglobin E (HbE) are excluded. Alpha-thalassaemia cases were also excluded because they require molecular confirmation.

Definitions

Anaemia in pregnancy: Pregnant women were considered anaemic if their haemoglobin concentration was less than 11.0 g/dL, in accordance with the WHO criteria. Anaemia was further categorised based on haemoglobin levels as mild (10.0-10.9 g/dL), moderate (7.0-9.9 g/dL), and severe (<7.0 g/dL) [21].

Preterm delivery: Preterm delivery was defined as the birth of a live infant occurring before 37 completed weeks of gestation, regardless of the mode of delivery [22].

Preeclampsia: Preeclampsia is a multisystem progressive disorder characterised by the new onset of hypertension and proteinuria or the new onset of hypertension plus significant end-organ dysfunction with or without proteinuria, typically presenting after 20 weeks of gestation or postpartum. During pregnancy, hypertension

is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg [23].

Oligohydramnios: Oligohydramnios was diagnosed on obstetric ultrasonography when the Amniotic Fluid Index (AFI) was 5 cm or less, or the single deepest vertical pocket measured less than 2 cm [24].

Postpartum haemorrhage: Postpartum haemorrhage was defined as blood loss of at least 500 mL following vaginal delivery or at least 1000 mL after caesarean section within the first 24 hours after childbirth [25].

Maternal sepsis: Maternal sepsis was defined as a severe, life-threatening condition caused by organ dysfunction resulting from infection occurring during pregnancy, labour, childbirth, abortion, or the postpartum period [26].

Study Procedure

The study population included women attending the Antenatal Outpatient Department (ANC OPD) and the labour ward. A total of 1,770 pregnant women who met the predefined inclusion and exclusion criteria were enrolled. After obtaining informed consent, approximately 5 mL of venous blood was drawn into Ethylenediaminetetraacetic Acid (EDTA) vacutainers.

All participants underwent routine antenatal laboratory investigations, including CBC. CBC was performed only as part of the routine antenatal evaluation and was not included in the primary study analysis.

Sickling tests were done using a freshly prepared 2% sodium metabisulfite solution as the reducing agent. The sealed smears were incubated and examined approximately two hours after preparation, and again at 12 hours to detect sickled red blood cells. Only positive sickling tests were confirmed by HPLC. For HPLC analysis, about 2 mL of venous blood collected in EDTA tubes was processed with the Bio-Rad Variant II analyser (Bio-Rad Laboratories, Hercules, California, USA).

The analyser was calibrated according to the manufacturer's recommendations before analysis. Internal quality control was performed using the manufacturer's control materials before routine sample analysis, and the laboratory participated in an external quality assurance programme to ensure the accuracy and reliability of test results. The HPLC diagnosis criteria is shown in [Table/Fig-1].

Parameters	Normal	Borderline/trait	Suggestive of disease
HbA2	2.0 - 3.5%	3.5 - 4.0%	>4.0% β-thalassaemia Trait
HbS	Absent (0%)	35 - 45 % Sickle Cell Trait (SCT)	>50 - 90% Sickle cell disease
HbE	Absent (0%)	25 - 35% HbE Trait	>70 - 97% HbE homozygous
HbD	Absent (0%)	40 - 48% HbD Trait	>60 - 90% HbD homozygous
Hb Lepore trait	Absent (0%)	10-18% Hb Lepore trait	-
HbQ	Normal	20 % Hb Q	-

[Table/Fig-1]: HPLC diagnosis criteria.

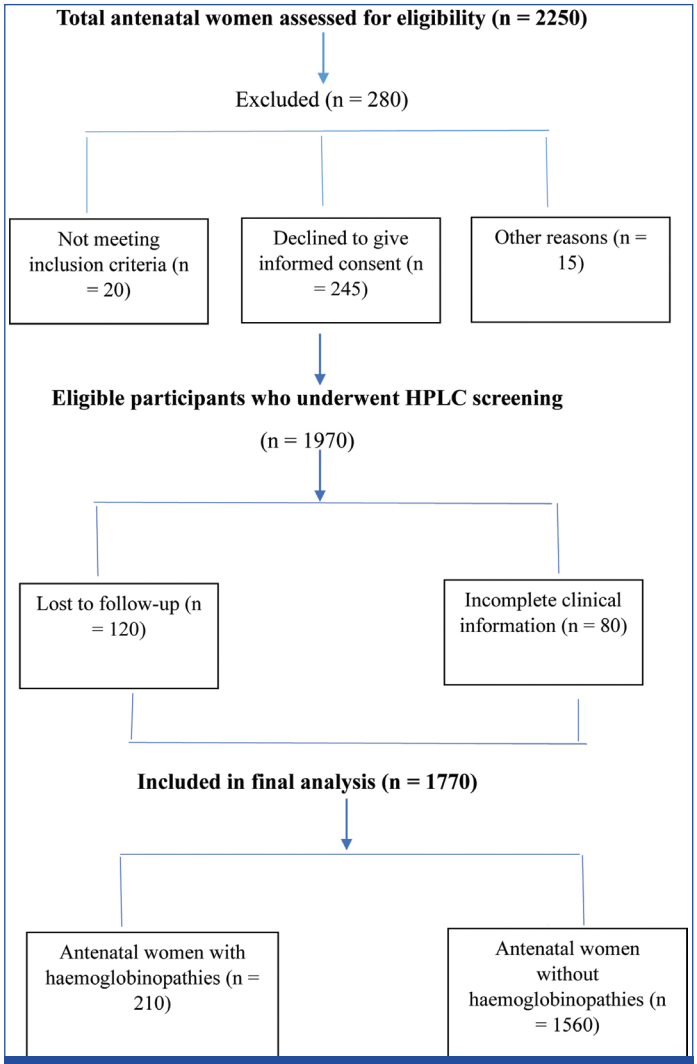
Data collection: Following enrollment, participants were prospectively followed through routine antenatal visits until delivery by the treating obstetricians as part of standard antenatal care. Maternal outcomes were obtained from antenatal records, inpatient case files, labour room registers, and delivery records. Obstetric complications, including preterm delivery, preeclampsia, maternal sepsis, oligohydramnios, and postpartum haemorrhage, as well as gestational age, were documented from the medical records and entered into a predesigned case record form by the investigators for statistical analysis. Maternal postpartum complications were recorded during the hospital stay until discharge.

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel 2019 and analysed using the Statistical Package for the Social Sciences (SPSS) version 22.0. Continuous variables were presented as mean±Standard Deviation (SD), while categorical variables were summarised as frequencies and percentages. Comparisons between categorical variables were performed using the Chi-square test. A 95% Confidence Interval (CI) was used, and p-value of <0.05 was considered statistically significant. The association between haemoglobinopathy status and maternal outcomes was evaluated using RRs with corresponding 95% CIs.

RESULTS

A total of 2,250 antenatal women were assessed for eligibility during the study period. Of these, 280 women were excluded because they did not meet the predefined inclusion criteria. The remaining 1,970 eligible participants underwent HPLC screening for the detection of haemoglobinopathies. Following screening, 200 women were further excluded due to incomplete clinical or laboratory records, loss to follow-up before completion of evaluation, or insufficient data for analysis. Consequently, 1,770 antenatal women with complete demographic, clinical, and laboratory information were included in the final analysis [Table/Fig-2].



[Table/Fig-2]: Flow diagram of participant selection.

In the present study, 1770 antenatal women were screened for haemoglobinopathies. Among them, 210 women were diagnosed with a haemoglobinopathy, resulting in a prevalence rate of 11.86% (95% CI: 10.35%-13.37%) in the study population.

The age distribution of antenatal women with and without haemoglobinopathy is presented in [Table/Fig-3]. Among women diagnosed with haemoglobinopathy (n=210), the majority belonged

to the 20-30 years age group (137, 65.2%), followed by those aged<20 years (45, 21.4%) and >30 years (28, 13.3%). In the non haemoglobinopathy group (n=1560), 950 (60.8%) women were aged 20-30 years, 535 (34.3%) were <20 years, and 75 (4.8%) were >30 years. The mean age of women with haemoglobinopathy was higher compared to those without haemoglobinopathy (24.73±5.36 years vs 22.91±4.78 years). A statistically significant difference was observed in the age distribution between the two groups (χ^2=33.036, p<0.0001), with a higher proportion of women aged >30 years among those with haemoglobinopathy.

Age (years)	With haemoglobinopathies (n=210)	Without haemoglobinopathies (n=1560)	Value
Less than 20	45 (21.4%)	535 (34.3%)	χ^2=33.036 p<0.0001
20-30	137 (65.2%)	950 (60.8%)	
More than 30	28 (13.3%)	75 (4.8%)	
Mean age±SD (years)	24.73±5.36	22.91±4.78	

[Table/Fig-3]: Age-wise distribution of antenatal women.

The 44.8% of women with haemoglobinopathies attended their first antenatal visit at ≤12 weeks of gestation, 24.8% between 13-20 weeks, 22.9% between 21-28 weeks, and 7.6% after 28 weeks as shown in [Table/Fig-4]. In comparison, among women without haemoglobinopathies, 39.2% attended their first antenatal visit at ≤12 weeks, 39.6% between 13-20 weeks, 17.2% between 21-28 weeks, and 4.0% after 28 weeks. The distribution of gestational age at antenatal booking differed significantly between the two groups (χ^2 = 21.13, p<0.0001), indicating a significant association between haemoglobinopathy status and the timing of the first antenatal visit.

Gestational age at booking	With haemoglobinopathies (n=210)	Without haemoglobinopathies (n=1560)	Value
≤12 weeks	94 (44.8%)	612 (39.2%)	χ^2=21.13 p<0.0001
13-20 weeks	52 (24.8%)	618 (39.6%)	
21-28 weeks	48 (22.9%)	268 (17.2%)	
>28 weeks	16 (7.6%)	62 (4.0%)	

[Table/Fig-4]: Gestational age at booking.

A significant difference in the distribution of parity between women with and without haemoglobinopathies (χ^2=9.05, p=0.029) as shown in [Table/Fig-5]. Among women with haemoglobinopathies, 39.0% had parity 1, 42.4% had parity 2, 12.8% had parity 3, and 5.7% had parity greater than 3, compared with 47.6%, 32.2%, 14.6%, and 5.6%, respectively, among women without haemoglobinopathies.

Parity	With haemoglobinopathies (n=210)	Without haemoglobinopathies (n=1560)	Value
1	82 (39.0%)	742 (47.6%)	χ^2=9.05 p=0.029
2	89 (42.4%)	502 (32.2%)	
3	27 (12.8%)	228 (14.6%)	
>3	12 (5.7%)	88 (5.6%)	

[Table/Fig-5]: Comparison of parity between women with haemoglobinopathies and women without haemoglobinopathies.

In the analysis, the normal haemoglobin group served as the baseline reference category against which different categories were compared. The severity of anaemia was significantly higher among women with haemoglobinopathies compared to those without haemoglobinopathies (χ^2=163.37, p<0.0001). Only 11.4% (24/210) of women with haemoglobinopathies had normal haemoglobin levels, compared to 58.3% (910/1560) in the non haemoglobinopathy group. Mild anaemia was observed in 25.2% and 33.0% of women with and without haemoglobinopathies, respectively, with women having haemoglobinopathies showing a fourfold higher RR (RR=4.00; 95% CI: 2.50-6.41). Moderate anaemia was the most common category among women with haemoglobinopathies, affecting 54.2% (114/210), compared with only 8.2% (128/1560) of women without haemoglobinopathies, corresponding to a markedly increased risk (RR=34.63; 95% CI: 22.10-54.25). Severe anaemia was also substantially more frequent in the haemoglobinopathy group (9.0% vs. 0.45%), with a RR of 28.45 (95% CI: 17.06-47.43). These findings demonstrate a strong association between haemoglobinopathies and increased severity of maternal anaemia [Table/Fig-6].

Variables	With haemo-globinopathies (n=210)	Without haemo-globinopathies (n=1560)	Relative Risk (RR) (95% CI)	Value
Normal	24 (11.4%)	910 (58.3%)	1.00	χ^2=163.37 p<0.0001
Mild anaemia	53 (25.2%)	515 (33.0%)	4.00 (2.50-6.41)	
Moderate anaemia	114 (54.2%)	128 (8.2%)	34.63 (22.10-54.25)	
Severe anaemia	19 (9.0%)	7 (0.45%)	28.45 (17.06-47.43)	

[Table/Fig-6]: Proportion of anaemia among antenatal patients.

Out of the 210 individuals screened for haemoglobinopathies, SCT was the most common, found in 176 participants (83.8%). Sickle Cell Disease (SCD) was identified in 13 participants (6.19%), while β-thalassaemia trait was present in 21 participants (10%). These results emphasise the dominance of SCT in the study group, with lower rates of β-thalassaemia trait and SCD [Table/Fig-7].

Haemoglobinopathies	n (%)
Sickle Cell Trait (SCT)	176 (83.8%)
Sickle Cell Disease (SCD)	13 (6.19%)
β-thalassaemia Trait	21 (10%)

[Table/Fig-7]: Distribution of haemoglobinopathies based on HPLC testing (n=210).

Women with haemoglobinopathy had a significantly higher incidence of several adverse maternal complications than those without haemoglobinopathy. Preterm delivery occurred in 97 (46.1%) women with haemoglobinopathy versus 215 (13.8%) without, corresponding to a 3.35-fold increased risk (RR=3.35, 95% CI: 2.74-4.10; χ^2=133.88, p<0.00001). Similarly, the risk of preeclampsia was significantly higher among women with haemoglobinopathy (33.3% vs. 15.0%; RR=2.22, 95% CI: 1.76-2.80; χ^2=43.73, p<0.00001). Postpartum haemorrhage was also more frequent in the haemoglobinopathy group (15.2% vs. 5.4%), with a nearly threefold increased risk (RR=2.80, 95% CI: 1.93-4.07; χ^2=28.73, p<0.00001). In contrast, maternal sepsis occurred less frequently among women with haemoglobinopathy than among those without (11.4% vs. 19.8%), indicating a significantly lower risk (RR=0.57, 95% CI: 0.39-0.83; χ^2=8.61, p=0.003). Although oligohydramnios was more common in women with haemoglobinopathy (6.6% vs. 4.1%), the difference was not statistically significant (RR=1.63, 95% CI: 0.93-2.85; χ^2=2.88, p=0.09) [Table/Fig-8].

DISCUSSION

In the present study, 1,770 antenatal patients were screened for haemoglobinopathies, and 210 were found to have a haemoglobinopathies, resulting in a prevalence rate of 11.86% within the study population. This prevalence is higher than the 9.24% reported by Bandita P et al., [20] and the 6.79% observed in the study by Bharkha et al., [7]. The increased rate in the present study may be due to regional, ethnic, and demographic differences, especially variations in the proportions of tribal and non tribal populations across India. As the study was conducted in a tertiary care centre, it likely received referrals from a wide geographic area, including high-risk or previously screened populations, which may have contributed to a higher prevalence rate. The hospital is a rural-based tertiary care centre; therefore, antenatal mothers with

Complication	With haemoglobinopathies (n=210)	Without haemoglobinopathies (n=1560)	p-value	Relative Risk (RR) (95% CI)
Preterm delivery	97 (46.1%)	215 (13.8%)	$\chi2 = 133.88$ *p<0.00001	3.35 (2.74-4.10)
Preeclampsia	70 (33.3%)	234 (15%)	$\chi2 = 43.73$ *p<0.00001	2.22 (1.76-2.80)
Maternal sepsis	24 (11.4%)	310 (19.8%)	$\chi2 = 8.61$ p-value 0.003	0.57 (0.39-0.83)
Oligohydramnios	14 (6.6%)	64 (4.1%)	$\chi2 = 2.88$ p-value 0.09	1.63 (0.93-2.85)
Postpartum Haemorrhage	32 (15.2%)	85 (5.4%)	$\chi2 = 28.73$ *p<0.00001	2.80 (1.93-4.07)

[Table/Fig-8]: Comparison of complications among antenatal women.
Test applied Chi-square test; *Indicate statistically significance at p≤0.05

a history of anaemia, previous adverse pregnancy outcomes, or suspected haemoglobin disorders are often referred from nearby villages for specialised screening and evaluation.

In a study conducted by Balgir RS in Central India, a prevalence rate of 12.26% was reported. Such variations may be attributed to the use of more sensitive and advanced diagnostic techniques, such as capillary electrophoresis, which enable improved detection of mild or silent variants, thereby resulting in a higher observed prevalence rate [18].

A markedly higher proportion of individuals with haemoglobinopathies were found to be anaemic (88.5%) than those without haemoglobinopathies (41.6%). A study conducted in Gujarat by Ahuja TV et al., reported that among 570 antenatal women, 514 (90.25%) were anaemic [16]. Of these anaemic cases, 480 (84.21%) had Iron Deficiency Anaemia (IDA), 27 (4.73%) had megaloblastic anaemia, and 7 (1.27%) exhibited dimorphic anaemia.

In the present study, out of 210 antenatal women, SCT was the most common, found in 176 participants (83.8%). These results emphasise the dominance of SCT in the study population, with lower rates of thalassaemia trait and SCD.

Compared to other studies, significant differences in the distribution of haemoglobinopathies are observed across various regions and populations. Priyadarsini B et al., [20] reported a much lower prevalence of SCT (38.64%) and a higher rate of thalassaemia trait (34.09%) and SCD (15.9%), along with Hb E thalassaemia (2.27%). Similarly, Balgir RS observed relatively low frequencies of haemoglobinopathies, with SCT at 7.45%, SCD at 1.68%, and thalassaemia trait at 2.89%, along with minor variants such as Hb E trait (0.24%) [18].

The occurrence of preterm delivery, preeclampsia, and postpartum haemorrhage was significantly higher among women with haemoglobinopathies than among those without haemoglobinopathies. Women with haemoglobinopathies had a 3.35-fold higher risk of preterm delivery (RR=3.35; 95% CI: 2.74–4.10; p<0.00001), a 2.22-fold higher risk of preeclampsia (RR=2.22; 95% CI: 1.76–2.80; p<0.00001), and a 2.80-fold higher risk of postpartum haemorrhage (RR=2.80; 95% CI: 1.93–4.07; p<0.00001) compared to women without haemoglobinopathies.

In the present study, maternal sepsis was less common among those with haemoglobinopathies 24 (11.4%) than among those without 310 (19.8%), and the difference was statistically significant (χ^2=8.61, p=0.003). Women with known haemoglobinopathies were classified as high-risk pregnancies and therefore received more intensive antenatal surveillance, prompt treatment of infections, and closer intrapartum and postpartum monitoring. These measures may reduce progression of localised infections to clinically significant maternal sepsis. Additionally, differences in baseline maternal characteristics, obstetric interventions, other co-morbidities, referral patterns, or residual confounding between the two groups may have influenced the observed association.

Studies from other regions, such as those by Dipal et al., [17], Pathak V et al., [8], Harwani B [7], and Ahuja T et al., [27], also reported lower proportions of SCT compared to the present study, with frequencies ranging from 1.5% to 4.03%. These studies, however, documented a wider spectrum of rare variants, including Hb D Punjab, Hb Q India, Hb J Paris-I, Hb O Indonesia, and heterozygous combinations of Hb S and Hb D or Thalassemia [Table/Fig-9] [7,8,17,18,20,27].

Name of author	% Prevalence of haemoglobinopathies	Most common age group	Distribution of haemoglobinopathies			
			Sickle Cell Trait (SCT)	Sickle Cell Disease (SCD)	β-thalassaemia trait	Other variants
Present study (n=1770)	11.86%	20-30 years	83.8%	6.19%	10%	-----
Harwani B et al., 2025 [7] (n=560)	6.79%	--	2.32%	0.54%	3.57%	HbD-0.18% HbS and HbD-0.18%
Pathak V et al., 2024 [8] (n=226)	15%	21-30 years	3.1%	0.4%	11.5%	Heterozygous for sickle cell and thalassaemia - 0.9%
Balgir RS 2015 [18] (n=416)	12.26%	---	7.45%	1.68%	2.89%	Hb E trait -0.24%
Bandita P et al., 2022 [20] (n=476)	9.24%	below 25 years of age	38.64 %	15.9 %	34.09%	Hb E Thal -2.27%
Bhukhanvala DS et al., 2013 [17] (n=3009)	5.74%	---	1.5 %	---	3.38 %	Hb D Punjab trait-0.36 % Hb E trait-0.23 % Hb D Iran trait -2 cases Hb Q India trait-2 cases Hb J Paris-I 3 cases Hb O Indonesia trait-1 case
Ahuja TV et al., 2024 [27] (n=700)	9.75%	Mean age-26.9±3.65 years	4.03%	---	5.08%	Hb D Punjab-0.52% Hb Q India -0.17%

[Table/Fig-9]: Comparison among various studies [7,8,17,18,20,27].

The observed differences in the distribution of haemoglobinopathies among various studies may be attributed to genetic heterogeneity, regional and ethnic diversity, as well as differing sample sizes and screening methodologies.

The higher rate of adverse obstetric outcomes in women with haemoglobinopathies may be attributed to underlying pathophysiological mechanisms. Chronic anaemia leads to reduced oxygen-carrying capacity, resulting in maternal and placental hypoxia and impaired placental development [21,26]. In sickling disorders, abnormal erythrocytes contribute to vaso-occlusion, endothelial dysfunction, oxidative stress, and inflammation, thereby reducing uteroplacental perfusion and increasing the risk of complications such as preterm birth and preeclampsia [28].

Additionally, chronic haemolysis releases free haemoglobin, which reduces nitric oxide bioavailability, promoting vasoconstriction and vascular injury. Severe and persistent anaemia may also impair uterine contractility and reduce physiological reserve during labour, increasing the risk of postpartum haemorrhage [25,29]. In contrast, no significant difference in oligohydramnios was observed, suggesting that amniotic fluid volume may be influenced more by other obstetric and foetal factors than by maternal haemoglobinopathy alone.

In the study by Bandita P et al., the incidence of preterm delivery (χ^2=47.63 p<0.0001), Oligohydramnios (χ^2=36.051, p<0.0001) and antepartum haemorrhage (χ^2=14.179, p<0.0016) was found to be significantly higher among individuals with haemoglobinopathy compared to those without the disorder [20]. Furthermore, the occurrence of various types of sepsis, including asymptomatic bacteriuria (13.64%), puerperal sepsis (6.82%), urinary tract infection (11.36%), and pneumonia (4.54%), was notably greater among antenatal women with haemoglobinopathy than in those without, where the incidences were 4.63%, 8.33%, 4.63%, and 0.46%, respectively.

Contrary to the present study findings, Serjeant GR et al., reported that postpartum haemorrhage does not appear to be more common in women with haemoglobinopathies [28].

Villers MS et al., and Al Jama FE et al., reported a significant association between sickle cell disorder and both Intrauterine Growth Restriction (IUGR) and low birth weight [29,15]. Similarly, Bandita P et al., observed that the incidence of foetal growth restriction and low birth weight among women with haemoglobinopathy was 39.39% and 54.55%, respectively, compared to 7.54% and 17.10% in the control group without haemoglobinopathy [20]. These differences were statistically significant (p<0.0001).

Limitation(s)

The present study has several limitations. Because this single-centre study was conducted at a tertiary care referral hospital, the findings may be affected by referral bias and may not be generalisable to the broader antenatal population. In addition, the analysis was based on unadjusted comparisons, and potential confounders such as socioeconomic status, nutritional status, body mass index, severity of anaemia, access to antenatal care, co-existing medical conditions, and obstetric interventions were not evaluated. Neonatal outcomes and long-term maternal follow-up were not assessed. Although HPLC is a reliable screening and diagnostic tool for the detection of common haemoglobin variants, certain uncommon or complex variants require confirmatory testing by haemoglobin electrophoresis and molecular genetic analysis for definitive characterisation. In addition, α-thalassaemia cannot be reliably diagnosed by HPLC alone, as conventional HPLC primarily estimates the relative proportions of haemoglobin fractions (HbA, HbA_2, and HbF) rather than directly assessing α-globin chain deficiency. These confirmatory investigations were not performed in the present study. As this was an observational study conducted in routine clinical practice, the treating obstetricians were aware of the participants' haemoglobinopathy status at the time of clinical management. Consequently, the assessment and documentation of obstetric outcomes were not blinded, introducing the possibility of observer bias. Although outcome data were extracted from routinely maintained hospital records using a standardised case record form, the potential for observer bias cannot be completely excluded.

CONCLUSION(S)

The present study found an association between haemoglobinopathies and adverse maternal outcomes, including preeclampsia, preterm delivery, and postpartum haemorrhage. These findings highlight the importance of routine antenatal screening, early diagnosis, appropriate genetic counselling, and multidisciplinary obstetric care for pregnant women with haemoglobinopathies. Strengthening screening programs and integrating them into public health planning is essential.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Pathology, SBKSMI and RC, Sumandeep Vidyapeeth Deemed to be University, Vadodara, Gujarat, India.
2. Associate Professor, Department of Microbiology, SBKSMI and RC, Sumandeep Vidyapeeth, Deemed to be University, Vadodara, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Mihir Kumar Bhalodia,
Associate Professor, Department of Pathology, SBKSMI and RC, Sumandeep Vidyapeeth Deemed to be University, Vadodara-391760, Gujarat, India.
E-mail: dr.mihirbhalodia@gmail.com

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