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Research Article

Prevalence of Incidental Haemoglobin Variants in Asymptomatic Individuals - A Hospital Based Study

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ABSTRACT

Introduction: Hemoglobin variants are inherited hemoglobinopathies that often remain clinically silent and are detected incidentally during routine hematological investigations. Early identification of such variants is essential for appropriate counseling and prevention of long-term complications, particularly in regions with a high prevalence of hemoglobin disorders.
Aims: To determine the prevalence of incidental hemoglobin variants among asymptomatic individuals and to analyze their hematological and anemia profiles.
Materials and Methods: This retrospective study was conducted at SevenHills Hospital, Marol, Andheri East, Mumbai, India, over a period of one year. A total of 4,139 cases were analyzed, comprising 2,093 males and 2,046 females. Complete blood count parameters and hemoglobin variant analysis were reviewed. Cases showing hemoglobin variants were further evaluated for anemia severity and genotype-specific hematological patterns.
Results: Out of 4,139 individuals screened, 45 cases (1.09%) were identified with hemoglobin variants, while 4,094 cases (98.91%) had normal hemoglobin patterns. Among the variant-positive cases, 23 (51.11%) were males and 22 (48.89%) were females. Severe anemia was observed in 37.78%, moderate anemia in 33.33%, mild anemia in 20.0%, and normal hemoglobin levels in 8.89% of cases. The SS and SF genotypes were predominantly associated with severe anemia, whereas the SC genotype was commonly associated with milder anemia or normal hemoglobin levels. A statistically significant association was observed between hemoglobin genotype and anemia severity in both genders.

Keywords*: Hemoglobin variants; Asymptomatic individuals; Anemia; Hemoglobinopathies; Screening; Complete blood count.*

INTRODUCTION

More than 1,000 human hemoglobin variations with single amino acid changes have been identified, resulting in physiological consequences of various severity[1]. HbS is the most prevalent pathogenic hemoglobin mutation worldwide, arising from substitutional alteration.[2]. Other common types of hemoglobin are HbC, HbD, and HbE. HbS is the most prevalent kind of pathological hemoglobin in Africa, while HbD is more common in Indian communities and HbE is more common in Southeast Asian cultures[3]. People with thalassemia, a disease that affects the production of alpha- or beta-globin chains of hemoglobin, may have higher amounts of HbA_2 fractions and fetal hemoglobin (HbF). HbS and HbE can also be present at the same time as beta thalassemia. In the Mediterranean region, the occurrence of mixed sickle and beta thalassemia characteristics is most prevalent.

The sickle hemoglobin mutation is a structural variation of normal adult hemoglobin A caused by a single-point mutation that replaces the amino acid glutamic acid with valine at position six of the β-globin chain[4]. Carriers or heterozygous (AS) persons inherit one HbS allele and one HbA allele and are normally asymptomatic, whereas homozygous (SS) individuals receive HbS alleles from both parents and have sickle cell anemia, characterized by acute and chronic problems. The homozygous sickle hemoglobin variation (HbSS) is known as sickle cell anemia (SCA) because it causes hemolysis. It is the most prevalent hereditary genetic illness in the world and the most severe type of sickle cell disease (SCD). People with the HbSS and HbSβ° genotypes have the most severe symptoms of SCD [5].

Most of the children who are affected are thought to die within the first few years of life if they don't get the right therapy, which is sometimes hard to get in low-income, high-burden countries. Sickle cell disease is a genetic blood ailment that causes red blood cells to be defective. This leads to a high rate of illness and death. HbSS, HbSC, HbSD, HbSE, and HbSβ°/β thalassemia are all common types of SCD. About 275,000 of the 330,000 newborns born each year with significant hemoglobinopathies have SCD, making it the most common hemoglobinopathy in the world [6]. In sub-Saharan Africa, some 240,000 children with SCD are born each year. These numbers back up the UN General Assembly's decision to call SCD a serious global public health issue because it causes a lot of illness and death and has a big effect on the economy[7].

Only about 10% of people with sickle cell disease (SCD) live in developed countries. People with homozygous sickle hemoglobin mutation (HbSS) who live in wealthy nations are expected to live for about 39 years[8]. There is a lack of information about how common sickle cell disease is in the Volta area of Ghana. The objective of this study was to ascertain the prevalence of sickle cell disease among patients at Ho Teaching Hospital and to evaluate the hemoglobin variations among the participants.

MATERIALS AND METHODS

Study Design: This was a retrospective observational study conducted to evaluate the prevalence of incidental hemoglobin variants among asymptomatic individuals.

Place of Study: The study was carried out at SevenHills Hospital, Marol, Andheri East, Mumbai, India.

Period of Study: The study was conducted over a period of one year.

Study Variables: The study variables included demographic parameters such as age and gender, hematological parameters obtained from complete blood count (CBC) including hemoglobin concentration, red blood cell indices, and platelet count, as well as hemoglobin variant status. In cases identified with hemoglobin variants, the type of hemoglobin genotype and severity of anemia were also analyzed.

Sample Size:A total of 4,139 cases were included in the study, comprising 2,093 males and 2,046 females. Among these, 45 cases were identified with hemoglobin variants and were further evaluated for detailed hematological analysis.

Inclusion Criteria

- Asymptomatic individuals who underwent routine hematological investigations during the study period
- Availability of complete blood count and hemoglobin variant analysis records
- Patients of either gender included in the hospital database during the study period

Exclusion Criteria

- Patients with incomplete or missing hematological data
- Individuals with known hemoglobinopathies diagnosed prior to the study period
- Patients with acute or chronic illnesses that could significantly affect hematological parameters
- Individuals with a history of recent blood transfusion

Statistical Analysis:

Data were entered and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. The prevalence of refractive errors was calculated, and associations with screen time and other risk factors were assessed using chi-square tests for categorical variables and independent t-tests or ANOVA for continuous variables. Correlation between screen time and severity of refractive errors was evaluated using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant.

RESULT

Table 1: Demographic Characteristics of Study Participants (N = 4139)

Gender	Number	Percentage (%)
Male	**2093**	**50.56**
Female	**2046**	**49.44**
Total	**4139**	**100**

Table 2: Distribution of Hemoglobin Variants among Study Participants

Parameter	Number	Percentage (%)
Normal hemoglobin	**4094**	**98.91**
Hemoglobin variants	**45**	**1.09**
Total	**4139**	**100**

Table 3: Gender Distribution among Participants with Hemoglobin Variants (n = 45)

Gender	Number	Percentage (%)
Male	**23**	**51.11**
Female	**22**	**48.89**
Total	**45**	**100**

Table 4: Anemia Status among Participants with Hemoglobin Variants (n = 45)

Anemia Severity	Number	Percentage (%)
Severe anemia	**17**	**37.78**
Moderate anemia	**15**	**33.33**
Mild anemia	**9**	**20**
Normal	**4**	**8.89**
Total	**45**	**100**

Table 5. Gender-Based Classification of Anemia Stratified by Hemoglobin Genotype among Hemoglobin-Variant–Positive Patients (n = 45)

Male Patients

Hb Genotype	Total n (%)	Severe n (%)	Moderate n (%)	Mild n (%)	Normal n (%)	*P* value
SC	23 (46.94)	2 (8.70)	6 (26.09)	8 (34.78)	7 (30.43)	**0.006**
SS	19 (38.78)	12 (63.16)	3 (15.79)	3 (15.79)	1 (5.26)	
SF	7 (14.29)	5 (71.43)	1 (14.29)	0 (0.00)	1 (14.29)	

Female Patients

Hb Genotype	Total n (%)	Severe n (%)	Moderate n (%)	Mild n (%)	Normal n (%)	*P* value
SC	24 (38.10)	3 (12.50)	7 (29.17)	9 (37.50)	5 (20.83)	**0.004**
SS	29 (46.03)	18 (62.07)	7 (24.14)	1 (3.45)	3 (10.34)	
SF	10 (15.87)	5 (50.00)	3 (30.00)	2 (20.00)	0 (0.00)	

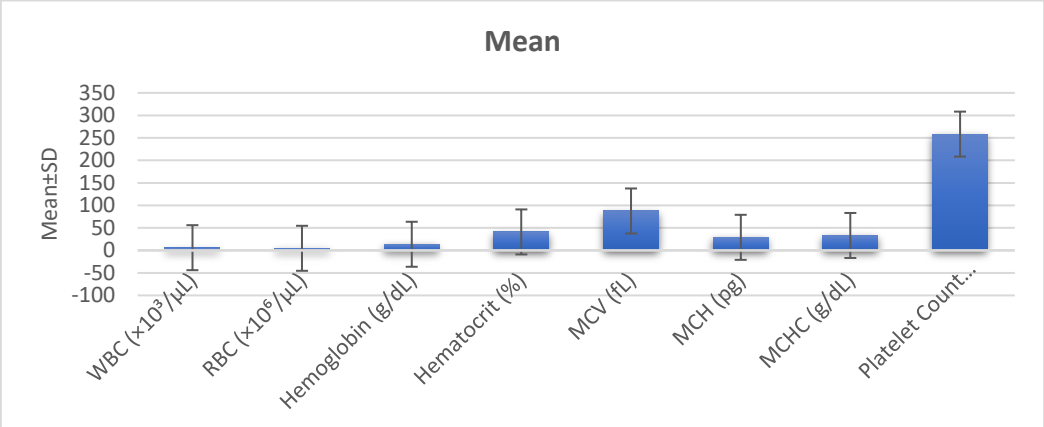

Figure 1: Mean Hematological Indices of Study Participants (n = 45)

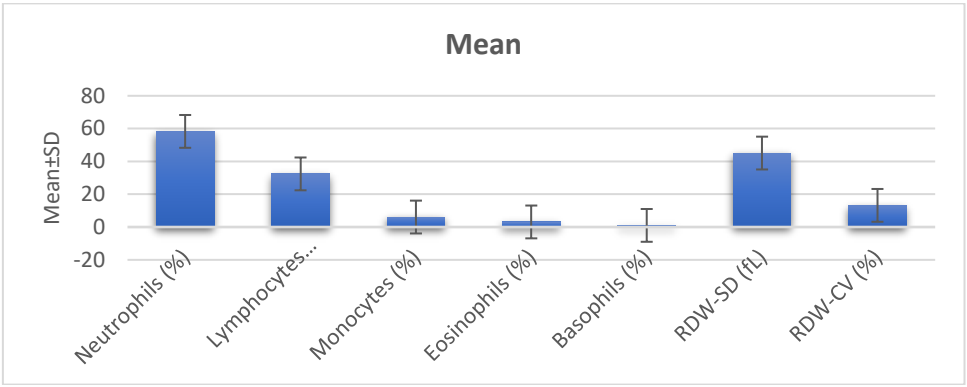

Figure 2: Mean Differential Leukocyte Count and RDW Parameters (n = 45)

Out of a total of 4,139 individuals screened in the present study, normal hemoglobin patterns were observed in 4,094 participants (98.91%), while hemoglobin variants were detected incidentally in 45 participants (1.09%), This finding highlights a low prevalence of hemoglobin variants among the general asymptomatic population screened in this study. Among the 45 participants identified with hemoglobin variants, 23 were males (51.11%) and 22 were females (48.89%). The gender distribution was nearly equal, indicating no marked gender predominance in the occurrence of incidental hemoglobin variants within the study population.

Assessment of anemia severity among participants with hemoglobin variants revealed varying degrees of anemia. Severe anemia was observed in 17 participants (37.78%), followed by moderate anemia in 15 participants (33.33%) and mild anemia in 9 participants (20.0%). Notably, 4 participants (8.89%) exhibited normal hemoglobin levels despite the presence of hemoglobin variants.

These findings suggest that although hemoglobin variants were detected incidentally, a substantial proportion of affected individuals exhibited moderate to severe anemia, while a small subset remained hematologically normal, emphasizing the variable clinical expression of hemoglobin variants.

Gender-based analysis of anemia severity stratified by hemoglobin genotype among hemoglobin-variant–positive patients (n = 45) demonstrated a significant association between genotype and anemia severity in both males and females. Among male patients, the SC genotype constituted 23 (46.94%) cases, with the majority presenting with mild anemia (34.78%) or moderate anemia (26.09%), while severe anemia was observed in 8.70% of cases and 30.43% remained hematologically normal. In contrast, males with the SS genotype (38.78%) predominantly exhibited severe anemia (63.16%), followed by moderate and mild anemia (15.79% each), with only 5.26% showing normal hemoglobin levels. The SF genotype (14.29%) among males was largely associated with severe anemia (71.43%), indicating a more severe hematological impact. The association between hemoglobin genotype and anemia severity in males was found to be statistically significant ($p = 0.006$).

Among female patients, the SS genotype was the most prevalent (46.03%) and was predominantly associated with severe anemia (62.07%), followed by moderate anemia (24.14%). Females with the SC genotype (38.10%) most commonly presented with mild anemia (37.50%) and moderate anemia (29.17%), while 12.50% had severe anemia and 20.83% maintained normal hemoglobin levels. The SF genotype (15.87%) in females showed a mixed pattern, with 50.00% exhibiting severe anemia and 30.00% moderate anemia. The association between hemoglobin genotype and anemia severity among females was also statistically significant ($p = 0.004$).

Overall, the findings indicate that the SS and SF genotypes are strongly associated with severe anemia in both genders, whereas the SC genotype is more frequently associated with milder forms of anemia or normal hemoglobin levels, underscoring the genotype-specific and gender-influenced hematological variability among individuals with hemoglobin variants.

Analysis of complete blood count parameters (Table 1) revealed that the mean total leukocyte count (WBC) was 6.05 ± 0.42 $\times 10^3/\mu L$, which lies within the normal reference range, indicating the absence of underlying infection or inflammatory conditions in the study population. The mean red blood cell (RBC) count was 4.72 ± 0.23 $\times 10^6/\mu L$, while the mean hemoglobin concentration was 13.65 ± 0.51 g/dL, suggesting that the majority of participants were non-anemic despite the presence of incidental haemoglobin variants.

The mean hematocrit (HCT) value was 41.10 ± 1.60%, consistent with adequate red cell mass. Red cell indices demonstrated a mean corpuscular volume (MCV) of 87.6 ± 1.1 fL, mean corpuscular hemoglobin (MCH) of 29.1 ± 0.2 pg, and mean corpuscular hemoglobin concentration (MCHC) of 33.2 ± 0.3 g/dL, indicating a predominantly normocytic normochromic blood picture among the study participants.
The mean platelet count was 258.4 ± 18.6 $\times 10^3/\mu L$, which was within normal physiological limits, with no evidence of thrombocytopenia or thrombocytosis.

Evaluation of differential leukocyte count and red cell distribution width parameters showed that the mean neutrophil percentage was 58.3 ± 2.1%, followed by lymphocytes at 32.4 ± 2.0%, monocytes at 6.1 ± 0.7%, eosinophils at 3.1 ± 0.5%, and basophils at 1.0 ± 0.2%. These findings reflect a normal leukocyte differential pattern, further supporting the asymptomatic status of the study population.

The mean RDW-SD was 45.1 ± 1.2 fL, and the mean RDW-CV was 13.2 ± 0.3%, indicating minimal variation in red cell size and a largely homogeneous erythrocyte population. This suggests that incidental haemoglobin variants in these individuals did not result in significant anisocytosis.

DISCUSSION

Prevalence of Incidental Hemoglobin Variants

In the present study, screening of 4,139 asymptomatic individuals revealed that 4,094 (98.91%) had normal hemoglobin patterns, while 45 individuals (1.09%) were incidentally detected to have hemoglobin variants. This low prevalence indicates that hemoglobin variants are relatively uncommon in the general asymptomatic population; however, their incidental identification underscores the importance of large-scale hematological screening. The finding of a 1.09% prevalence suggests that a small but clinically relevant proportion of individuals may harbor hemoglobin variants without overt symptoms.The high prevalence of HbAS found in this study suggests that without health policy regulations that include extensive health education, there is a significant likelihood of a growing population of individuals with sickle cell disease in the near future, as inheriting one copy of an abnormal hemoglobin variant (C, S, and F) alongside a S hemoglobin results in the disease[9].

Gender Distribution of Hemoglobin Variants

Among the 45 hemoglobin-variant–positive individuals, 23 were males (51.11%) and 22 were females (48.89%), demonstrating an almost equal gender distribution. The marginal male predominance of 2.22% indicates no significant gender bias in the occurrence of hemoglobin variants. This observation is consistent with the genetic nature of hemoglobinopathies, which are inherited in an autosomal manner and are therefore expected to affect both sexes equally.Jadhav says that most of the 113 patients whose blood tests were done were very anemic, including men and women with HbSS[10].

Anemia Status in Individuals with Hemoglobin Variants

Despite being asymptomatic at the time of screening, a considerable proportion of individuals with hemoglobin variants exhibited anemia of varying severity. Severe anemia was documented in 17 participants (37.78%), while moderate anemia was observed in 15 participants (33.33%), and mild anemia in 9 participants (20.0%). Only 4 participants (8.89%) maintained normal hemoglobin levels. Thus, 71.11% of hemoglobin-variant–positive individuals had moderate to severe anemia, highlighting that significant hematological compromise may exist even in the absence of clinical symptoms.

Gender-Based and Genotype-Specific Severity of Anemia

Gender-based stratification revealed a strong association between hemoglobin genotype and anemia severity in both males and females. Among male patients, the SC genotype accounted for 23 cases (46.94%), with 34.78% presenting with mild anemia and 26.09% with moderate anemia, while 30.43% remained hematologically normal. In contrast, males with the SS genotype (19 cases; 38.78%) predominantly exhibited severe anemia in 63.16%, with only 5.26% having normal hemoglobin levels. The SF genotype, though less common (7 cases; 14.29%), was associated with severe anemia in 71.43% of cases. This association between genotype and anemia severity among males was statistically significant ($p = 0.006$).HbAS was the second most common hemoglobin genotype, with a frequency distribution of 24.5%. HbA was

the most common, with a frequency distribution of 65.3%. HbAC and HbSC had frequencies of 4.0% and 1.1%, respectively[11].

Among female patients, the SS genotype was the most prevalent (29 cases; 46.03%) and was associated with severe anemia in 62.07% of individuals, followed by moderate anemia in 24.14%. Females with the SC genotype (24 cases; 38.10%) predominantly had mild anemia (37.50%) or moderate anemia (29.17%), while 20.83% remained normal. The SF genotype (10 cases; 15.87%) showed severe anemia in 50.00% of cases. The association between genotype and anemia severity among females was also statistically significant ($p = 0.004$). These findings clearly demonstrate that SS and SF genotypes are associated with more severe anemia than SC genotype in both genders.

Interpretation of Hematological Parameters

Analysis of complete blood count parameters revealed that the mean WBC count was $6.05 \pm 0.42 \times 10^3/\mu L$, indicating the absence of infection or inflammatory pathology. The mean RBC count ($4.72 \pm 0.23 \times 10^6/\mu L$) and mean hemoglobin level (13.65 ± 0.51 g/dL) were within normal reference ranges, suggesting that many individuals maintained adequate baseline hematological function despite harboring hemoglobin variants. The average hematocrit of $41.10 \pm 1.60\%$ also showed that there was enough red cell mass. People with HbS usually have a much higher average total WBC count.[12]

Red Cell Indices and Morphology

Red cell indices showed a mean MCV of 87.6 ± 1.1 fL, mean MCH of 29.1 ± 0.2 pg, and mean MCHC of 33.2 ± 0.3 g/dL, indicating a predominantly normocytic normochromic blood picture. These values suggest that structural red cell abnormalities may not be evident in the early or less severe stages of hemoglobin variants, thereby contributing to their incidental detection during routine screening.Changes in hemoglobin can lead to a wide range of phenotypic effects, such as anemia caused by protein instability and the breakdown of red blood cells[19]and blockage of the microvascular circulation, which causes tissue ischemia, infarction, and persistent hemolytic anemia[20].

Platelet Count, Differential Leukocyte Count, and RDW

The mean platelet count was $258.4 \pm 18.6 \times 10^3/\mu L$, remaining within normal physiological limits. Differential leukocyte analysis revealed a normal pattern with neutrophils at $58.3 \pm 2.1\%$, lymphocytes at $32.4 \pm 2.0\%$, monocytes at $6.1 \pm 0.7\%$, eosinophils at $3.1 \pm 0.5\%$, and basophils at $1.0 \pm 0.2\%$. Additionally, RDW-SD (45.1 ± 1.2 fL) and RDW-CV ($13.2 \pm 0.3\%$) values indicated minimal anisocytosis, suggesting a relatively uniform red cell population despite the presence of hemoglobin variants.

Clinical Implications

The presence of moderate to severe anemia in over 70% of hemoglobin-variant–positive individuals, despite largely normal CBC indices, underscores the importance of routine hemoglobin variant screening. Early identification allows for appropriate counseling, monitoring, and prevention of long-term complications, particularly in individuals with SS and SF genotypes, which showed the highest association with severe anemia.

CONCLUSION

This study shows that accidental hemoglobin variations are not very common in those who don't have any symptoms, with a prevalence of 1.09%. A significant number of affected patients displayed moderate to severe anemia, especially those with SS and SF genotypes, whereas the SC genotype was more commonly linked to milder anemia or normal hemoglobin levels. Even while most of the total blood count measures were normal, there was a lot of genotype-specific hematological variability. These results underscore the necessity of regular hemoglobin variant screening and thorough hematological assessment, especially in asymptomatic cohorts, to facilitate early identification, suitable counseling, and prompt action to avert possible long-term consequences.

DECLARATION

Conflicts of Interests: The authors declare no conflicts of interest.
Author Contribution: All authors have contributed in the manuscript.
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