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Prevalence of Haemoglobinopathies among Different Populations

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Abstract: ***Aim: To establish the prevalence of hemoglobinopathies among different populations. Hemoglobinopathies are the prevalent hereditary illnesses found worldwide. Their frequency varies considerably with geographic location and ethnic group. This paper reviews the literature on the prevalence of hemoglobinopathies among different populations. Design and methods: A systematic literature review to identify peer-reviewed studies on hemoglobinopathies was performed. The inclusion criteria for the search included finding an English-language article published in a peer-reviewed journal that included our keywords and discussed the prevalence of hemoglobinopathies among different populations, including early works pertinent to the current review. For India's tribal communities, sickle cell disease and thalassemia pose serious problems. Of India's total population, the tribal population makes up about 8.5%. As several authors have shown, hemoglobinopathies of various kinds were identified in many Indian tribal communities; sickle cell anemia and beta-thalassemia were the most prevalent illnesses. These illnesses are genetic or hereditary, tend to run in families, and are primarily brought on by consanguineous unions within the tribal society.***

Keywords: Hemoglobinopathies, sickle cell anemia, prevalence, tribes, thalassemia, haemoglobin variants.

Abbreviations

BTT - Beta Thalassemia Trait
DNA - Deoxyribonucleic acid
G6PD- Glucose – 6 – Phosphate Dehydrogenase
Hb - Haemoglobin
HbA - Haemoglobin A
HbA2 - Haemoglobin A2
HbAS - Haemoglobin AS
HbD - Hemoglobin D
HbDβ - Haemoglobin Dβ
HbE- Haemoglobin E
HbF - Haemoglobin F
HbS - Haemoglobin S
HbSD - Haemoglobin SD
HbSS - Haemoglobin SS
HCT - Haematocrit
HPLC - High Performance Liquid Chromatography
MCH - Mean Corpuscular Haemoglobin
MCHC - Mean Cell Haemoglobin Concentration
MCV - Mean Cell Volume
MPV - Mean Platelet Volume
PCR - Polymerase Chain Reaction
RBC - Red Blood Cell
RDW-CV - Red Cell Distribution Width-Coefficient of Variation
SCD - Sickle Cell Disease
WHO - World Health Organisation

1. Introduction

A group of proteins known as hemoglobin (Hb) molecules are formed when alpha (α) and beta (β) globin polypeptide chains are paired and formed into a tetrameric unit[1]. The oxygen delivered from the lungs to tissues is primarily carried by the α2β2 molecule, which is the most significant adult haemoglobin unit. The α-globin gene, which is located on chromosome 16, codes for the adult α-globin and, consequently, the ζ-globin chain, which represents the α-globin's embryonic form. The β-globin gene, located on chromosome 11, encodes four distinct globin molecules: foetal γ-globin, adult δ-globin, adult β-globin, and embryonic ε-globin. Each of these molecules is expressed differently at different stages.There are 141 amino acids in each of the two alpha chains. The two beta chains are each made up of 146 amino acids. Genes within the alpha gene cluster on chromosome 16 are the source of the two alpha chains. Genes in the beta gene cluster on chromosome 11 are the source of the two beta chains[2].

2. The Hemoglobinopathies

The synthesis of hemoglobin with structural defects as a result of anomalies in the globin moiety of the molecule characterizes hemoglobinopathies. Hemoglobin's biological function may be impacted by mutations in the genes encoding the beta and alpha chains. Hemoglobinopathy is the term for the disorder that results from a mutation in the Hb gene that alters biological function[3].

The hemoglobinopathies that are most prevalent are thalassemia, HbD, HbE, and HbS.[4]There are two categories for inherited abnormalities of Hb synthesis. Hemoglobinopathies are those that are defined by structurally aberrant variations of Hb. Thalassemia is a disease in which the synthesis of one or more of the normal polypeptide chains of hemoglobin occurs at a reduced rate.[5] Changes in the globin gene's primary structure have been triggered by gene substitution, mutation, and fusion, which affects hemoglobin's solubility, oxygen affinity, molecular structure, and stability, among other biological characteristics.[6]According to WHO estimates, between 3 and 7% of people worldwide are at risk of hemoglobinopathies that are inherited[7]. It is already well known that individuals who choose consanguineous marriage have a higher incidence of abnormal hemoglobin[8], and that having high levels of abnormal hemoglobin can protect against diseases like malaria.[9]

3. Sickle Cell Anemia

The genetic disorder known as sickle cell disease (SCD) and its variants are caused by a mutated form of haemoglobin called haemoglobin S (HbS)[10]. It is inherited in an autosomal recessive manner.[11]A point mutation at position six in the beta-globin chain, where valine replaces glutamic acid, causes a group of diseases known as sickle cell disorder. As a result, when erythrocytes are deoxygenated, their shape changes to a sickle shape, and their cell membrane becomes more fragile[12]. It also causes varying degrees of hemolytic anemia and acute and chronic tissue damage from vaso-occulsion, which can lead to many serious complications[13].It only appears in the homozygous or doubly heterozygous states and is inherited in an autosomal recessive manner. The HbS gene can be passed down to the progeny, but sickle cell trait, also referred to as sickle cell carrier (HbAS), is not considered a sickle cell disease because it typically does not show clinical symptoms[14].The main pathophysiology is based on the polymerization of deoxyHbS in red blood cells (RBCs), which results in the formation of long fibers inside the cells and distorts the sickle shape. This ultimately causes increased hemolysis and sickle red cell vaso-occulsion. Nonetheless, the way SCD patients present clinically varies greatly, and several things can cause vaso-occulsion. In the pathophysiology of this multi-organ disease, recent research has demonstrated the significance of red cell dehydration, aberrant RBC adhesion to the vascular endothelium, inflammatory events, activation of all vessel cells, and abnormalities of nitric oxide metabolism.[15]

4. Thalassemia

A thalassemia is a group of inherited autosomal recessive disorders of hemoglobin synthesis in which one or more hemoglobin chains are absent or reduced. The structural variations arise from structural modifications such as the substitution of one or more amino acids in the hemoglobin's globin chains. Thalassemias are divided into four types α, β, γ, and δ thalassemia. Due to the ethnic diversity of India, numerous haemoglobin variants are common there. In the Indian population, these hemoglobinopathies cause significant morbidity and mortality and are typically inherited recessively from the parents. HbS, HbD-Punjab, and HbE are the common variants that are most common in India. The common variants that are common among Indian tribal people are HbS and HbE.[16,17]

5. Methodology

Hemoglobinopathies, sickle cell anaemia, prevalence, and tribes were the keywords used in a thorough literature search for pertinent articles published up to 2023 in the PubMed, Scopus, and Google Scholar databases. The inclusion criteria for the search included finding an English-language article published in a peer-reviewed journal that included our keywords and discussed the prevalence of hemoglobinopathies among tribal people, including early works that were pertinent to the current review. If the case studies and clinical reports related to our interest theme, they were included.

6. Review of Literature

Sujatha Dixit et al. conducted a community-based study on hemoglobinopathies and G6PD deficiency among particularly vulnerable tribal groups in hard-to-reach malaria endemic areas of Odisha, India; implications on malaria control. Their findings suggest that a high frequency of alleles associated with malaria, such as G6PD deficiency, HbS, and alpha thalassemia, are prevalent among the aforementioned tribal groups in Odisha.[18]

Abozer Y. Elderly et al. found that HbSS and AS were relatively common among the migrant patients attending the Khartoum Teaching Hospital,Western Sudanin their study "tribal distribution of Hemoglobinopathies in a Sudanese patient population." Patients from the Sudanese tribes of the Blue Nile were found to have a higher prevalence of HbAS.[19]

The study conducted by N I Ugwa et al. in a tertiary health institution in South Eastern Nigeria examined the chromatographic pattern of haemoglobin types among individuals with sickle cell trait and those with sickle cell anaemia. The findings indicated that individuals with the HbSS phenotype had a significantly higher level than those with the HbAS phenotype. Among the two groups, males had higher HbS but lower HbA2 and HbF than females, though the differences were not statistically significant. To distinguish between people with HbSS and those with HbAS phenotype, the establishment level of HbS, HbA2, and HbF will act as a guide.[20]

A study on the "prevalence of hemoglobinopathies in tribal regions of India" was carried out by Naveen Dulhani. An observational study was conducted in the past. According to their research, hemoglobin disorders pose a serious risk to the tribal population in India. As few as 10% of the tribes living in India may have gone extinct. The majority of hemoglobinopathies have varied degrees of anemia. However, they were unable to supply any hemoglobin data, which was a crucial study limitation. After the hereditary persistence of fetal hemoglobin, the prevalence of HbAS was higher in their study than in sickled beta-thalassemia. Compared to tribal communities, the non-tribal community is more widespread.[21]

Sichuan province in southwest China has a higher carrier rate of beta thalassemia, according to research done by Xia Yu on the genetics of hemoglobinopathies in a sizable cohort of asymptomatic people.13298 individuals in Sichuan province, ranging in age from 5 to 73, who did not exhibit any clinical symptoms were included in the study. Genes were sequenced to determine genotypes and aberrant hemoglobin was screened using electrophoresis.PCR and shunt hybridization were used to diagnose the alpha-thalassemia genotype. Sixty-three people were suspected of having hemoglobinopathy. According to DNA sequencing, six individuals had aberrant hemoglobin genotypes and fifteen had HbE. In Sichuan province, the frequency of thalassemia heterozygosity was 4.12%. The five most prevalent mutations make up the alpha thalassemia mutation spectrum. This study found seven different types of beta-thalassemia mutations. In Sichuan, the carrier rate for

beta-thalassemia was greater than that for alpha-thalassemia.[22]

A study on "the prevalence of sickle cell disease and anemia in tribal school students from central India " was carried out by Gunjal Sandeep et al. According to their findings, boys had a higher prevalence of SCD than girls.[23]

A study titled "A demographic prevalence of beta thalassemia carrier and other hemoglobinopathies in adolescents of Tharu population" was carried out by Nitu Nigam et al. They discovered that the Tharu community in Lakhimpur Kheric district, Uttar Pradesh, India, had an increased incidence of thalassemias and hemoglobinopathies. According to their research, the most prevalent hemoglobinopathies in the general population were beta thalassemia trait, HbE trait, and HbS/beta thalassemia trait.[24]

The research conducted by Shirley Henderson on the "Incidence of haemoglobinopathies in various populations — The impact of immigration" revealed the following findings: The UK population has more β- and α-thalassemia mutations than any of the 60 other countries with a published spectrum of mutations, including both endemic and non-endemic Northern European countries. This is a direct result of immigration. The provision of a molecular diagnostic prenatal diagnosis service is made more difficult by the racial heterogeneity of the immigrant population in a non-endemic country, which greatly increases the spectrum of haemoglobinopathy mutations and their combinations found in individuals.[25]

"Thalassemia and hemoglobinopathy prevalence in a community-based sample in Sylhet, Bangladesh" was the title of a study done by Amanda S. Wendt. According to their research, alpha thalassemia is more common in women and children in rural Sylhet, Bangladesh, than it is in all other hemoglobinopathies put together. Although there are few community-based estimates of the prevalence of alpha thalassemia in Bangladesh, their results imply that in certain areas of the nation, alpha thalassemia may account for the majority of inherited blood disorders.[26]

Virender Singh et al.'s study, "Prevalence of hemoglobinopathies using high-performance liquid chromatography as a diagnostic tool in anemic patients of tertiary care center of Western India," found that, of 2698 cases, 543 (20.12%) cases had abnormal haemoglobin fractions and 2155 (79.88%) cases were free from hemoglobinopathies. Of the total hemoglobinopathies detected, 250 (46%) were male and 293 (54%) were female. The major abnormality detected was beta-thalassemia trait, accounting for 425 (15.75%) cases, followed by sickle cell disorders (58, 2.15%), HbE 38 (1.41%), hereditary persistence of foetal haemoglobin 6 (0.22%), HbD Punjab 13 (0.48%), HbD Iran 2 cases, and 4 cases of compound heterozygous for HbS beta-thalassemia. Forty (1.48%) cases were detected as borderline with HbA2 level.Hemoglobinopathies were found to be highly prevalent in anaemic subjects in their study. BTT was the most frequently identified disorder. Using HPLC, a quick, sensitive, and repeatable technique for identifying various hemoglobinopathies, the majority of the hemoglobinopathies discovered in their investigation could be precisely measured.[27]

Research on the topic "burden and distribution of sickle cell anemia in the tribal and non-tribal population of state Chhattisgarh, India" by LAD H et al. revealed a higher prevalence of sickle gene in the non-tribal group as compared to the tribal group in Chattisgarh.[28]

Dipika Mohanty et al. assessed the spectrum of hemoglobinopathies among primitive tribal groups from four states in India for their study, Spectrum of Hemoglobinopathies Among the Primitive Tribes: A Multicentric Study in India. Automated high-performance liquid chromatography was used to examine 15,200 individuals from 14 primitive tribal groups. Frequencies of the haemoglobin S (HbS) and β-thalassemia alleles ranged from 0.011 to 0.120 and 0.005 to 0.024, respectively. Remarkably, compared to Austro-Asiatic speaking tribal groups (0.011-0.022), a very high HbS allele frequency was found among Dravidian (0.060-0.120) and Indo-European (0.060-0.076) speakers. While there were no ethnic differences found within the states based on statistical analysis of the data, there were regional variations for both HbS and β-thalassemia traits between the states. It was discovered that β-thalassemia and HbS were the two most prevalent hemoglobinopathies.[29]

According to Vineeta Gupta et al.'s research, "Profile of Haemoglobin D (HbD) Disease in Eastern Uttar Pradesh: A Single-Center Experience," hemoglobin D disease was found in 31 samples (1.20%) from 15 families. Three patients had HbDβ, five had HbSD disease, and twenty-three had HbD trait. Two of the patients with HbSD disease were siblings from one of the four families to which they belonged. Every family lived in the Sonebhadra district, which is home to a sizable number of tribal people.[30]

According to Feroze M's study, "Sickle cell disease among tribals of attappady," the Irula, Kurumba, and Muduga tribal communities in the area all had high prevalence rates of the sickle cell gene. This population does not have a significant prevalence of other hemoglobinopathies or thalassaemias. Compared to sickle cell anaemia in Africa or among African immigrants in the US, Attappady's disease is comparatively mild. It is comparable to what is observed in Wayanad.[31]

Ashish Jawarkar and Varsha Bhatia conducted a study on the topic “A study of HPLC patterns in patients of sickle cell anemia with analysis of red cell parameters” Theirfindings suggest that ‘In sickle cell trait(SCT) patients,there is a significant higher level of HbA2 and HbS and significantly lower level of HbA,both sickle cell trait and sickle cell disease patient had a significantly lower level ofhematocrit, MCH and higher RDW-CV. Concluded thatthere wasa statistical difference in levels of Hb, HCT, MCH, and RDW-CV between the case and controls. A high index of suspicion should be maintained when these parameters are on the lower side, especially in the population who is prone to have sickle cell disorders such as tribal.[32]

Vidhyanand Gaikvad et al, in their study "Clinical and haematological profile of sickle cell disorder patients in a tertiary hospital of Central India". This study showed that the hematological profile of sickle cell disorder patients has a low value of Hb%, HCT, total RBC count, MCH, MCHC with normal MCV, MPV, platelets count, and high RDW. Peripheral smear showed predominantly hypo-chromic and anisopoikilocytosis cells. Symptoms like weakness and fatigability were mostly seen in sickle cell disease patients, same symptoms were also commonly seen in sickle cell trait patients. Some patients with sicklecell trait had also the same clinical features of sickle cell disease along with anemia.So patients having weakness and fatigability, recurrent fever with cough, breathlessness, bone pain, painful, swollen digits of hands and feet, periodic abdominal pain, jaundice along with low values of Hb%, HCT, total RBC count, MCH, MCHC, and high value of RDW in presence of anisopoikilocytosis, hypo-chromic cells on peripheral smear strongly suspect sickle cell disorder.[33]

AI Shakour and AI Suhail in their study "Percentage of HbS among cases of sickle cell trait in Basra, Iraq" revealed that the three best predictors of HbS% in sickle-cell trait were: Hb concentration, MCH, and target cell percentage. The Hb concentration and MCH have a positive function, indicating that higher HbS percentages are associated with higher Hb concentration and MCH values and vice versa. This is explained by the fact that the lower HbS percentages in sickle-cell trait are mostly caused by thalassemia, which in turn also causes a decrease in Hb concentration and MCH. Similarly, the target cell percentage also has a positive effect as higher amounts of this abnormal hemoglobin are associated with an increase in the number of target cells.[34]

7. Discussion

The prevalence of hemoglobinopathies varies from stateto state and country to countryas demonstrated by various authors, many tribal communities in India wererecognized to have various types of hemoglobinopathies and the commonest recognizable diseases were sickle cell anemia and β thalassemia.Hemoglobinopathies were found in scheduled casts, scheduled tribes, and,Other Back-ward Classes and General categories of Jabalpur, Madhya Pradesh, according to a study by Pande et al. Yet, Scheduled Tribes had the highest rate of hemoglobinopathies.[35]Some authors observed that hemoglobinopathies continue to be common in ethnic populations as a result of population internal migration.[36,37]

Henderson's study indicates that immigration has led to a higher prevalence of β- and α-thalassemia mutations in the UK population, encompassing both endemic andnon-endemicNorthern European countries. The spectrum of hemoglobinopathy is markedly expanded in non-endemic countries due to the racial heterogeneity of the immigrant population.[38]

According to Ashtiani et al,Iran appears to have a distinct pattern of hemoglobinopathy with a high prevalence of Hb D compared to other parts of the world.[39]

According to Promil et al, among 4275 total cases surveyed, normal hemoglobin pattern was observed in 90.3%, and abnormal hemoglobin fractions on HPLC were detected at 9.7%. β thalassemia trait was the predominant abnormality found. Other abnormal patterns found were HbE, Hb S, and Hb D Punjab.

8. Conclusion

The most prevalent single-gene hereditary disease worldwide is hemoglobinopathy, which is characterized by abnormal haemoglobin frequency that varies with geographic location and ethnic groupings. The current study examined the prevalence of hemoglobinopathies across a range of population groups, and the data analysis showed that the highest incidence of hemoglobinopathies was found in tribes, possibly as a result of endogamy within the tribal population. The majority of studies found that sickle cell anemia and thalassemia were the most common hemoglobinopathies; other hemoglobinopathies are also found in both tribal and non-tribal populations worldwide. Additionally, the prevalence of hemoglobinopathies is increased due to human migration.

Consent
It is not applicable.

Ethical Approval
It is not applicable.

Competing Interests
The authors have declared that no competing interests exist.

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