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A Population-Based Study on the Epidemiological Trends, Molecular Diagnosis, and Disease Burden of Hemoglobinopathies: Assessing the Impact of Hemoglobin Variants on Public Health Outcomes

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Abstract

Introduction: Hemoglobinopathies, including sickle cell disease and thalassemia, represent a significant public health challenge, particularly in regions with high prevalence. This study aims to examine the epidemiological trends, molecular diagnosis, and disease burden of hemoglobinopathies, focusing on how different hemoglobin variants impact public health outcomes. Understanding the genetic diversity and its effect on disease progression is critical to formulating targeted health interventions and improving care for affected populations. The study evaluates both genotypic and phenotypic variations of hemoglobinopathies and their long-term effects on public health metrics such as mortality, morbidity, and healthcare costs. **Objective:** To assess the prevalence and distribution of hemoglobinopathies, identify molecular variants, and understand the impact on public health outcomes and healthcare systems. **Methodology:** This prospective cohort study was conducted at Sudan during jnauray 2024 till October 2024, including 550 patients diagnosed with hemoglobinopathies. **Results:** This study of **550 patients** found **HbS** to be the most common hemoglobinopathy (**54.5%**), followed by **HbC (27.3%)** and **β-thalassemia (18.2%)**. The **HbS group** had the highest **hospitalization rate (52%)**, **morbidity index (4.5)**, and complications like **stroke (15%)** and **organ failure (25%)**. **HbC** and **β-thalassemia** had lower rates and complications. Genotype-phenotype analysis showed **HbS/HbS** had the most severe symptoms and **earliest onset (4.5 years)**. **Conclusion:** The study emphasizes the critical need for widespread screening and genetic counseling in high-risk populations to reduce the public health burden of hemoglobinopathies. Early molecular diagnosis and continuous medical care are key strategies in improving health outcomes and reducing the long-term economic costs associated with these diseases.

Keywords: Hemoglobinopathies, sickle cell disease, thalassemia, epidemiological trends, molecular diagnosis, genetic variants, public health, disease burden, genetic screening, healthcare outcomes.

Introduction

Hemoglobinopathies, including sickle cell disease (SCD), β-thalassemia, and other inherited disorders of hemoglobin, are among the most prevalent genetic diseases globally, particularly in regions with high rates of consanguinity, such as Sub-Saharan Africa, South Asia, and the Middle East. These disorders, resulting from mutations in the **globin genes**, lead to abnormal

hemoglobin production, causing a range of clinical manifestations, including **hemolytic anemia**, **organ failure**, **pain crises**, and **increased susceptibility to infections** [1]. The prevalence of these conditions remains significantly high, affecting millions of individuals, with estimates suggesting that **300,000 to 400,000 children** are born annually with **severe forms of hemoglobinopathies** (WHO, 2014). Specifically, **Sickle Cell Disease (HbS)** is the most widespread hemoglobinopathy, with approximately **20-25 million** individuals globally affected, and it remains a leading cause of **morbidity** and **mortality** in affected populations [2]. The disease burden of hemoglobinopathies on both individuals and healthcare systems is substantial. In countries where **SCD** and **thalassemia** are endemic, the disease presents a major public health challenge due to its **chronic nature** and **complications**, including **stroke**, **acute chest syndrome**, and **organ damage**. The economic costs associated with **hospitalizations**, **blood transfusions**, and **long-term care** place a significant strain on healthcare resources. For example, **SCD** alone accounts for **approximately 10%** of the total **healthcare expenditure** in high-burden regions [3]. Additionally, patients with **thalassemia** require **regular blood transfusions** and **iron chelation therapy**, leading to significant treatment costs and prolonged medical care [4].

Recent advancements in **molecular diagnostics** have enabled more accurate and efficient identification of hemoglobinopathies. Techniques such as **next-generation sequencing (NGS)** allow for the detection of **multiple genetic variants** that cause hemoglobinopathies, which has improved early diagnosis and allowed for personalized treatment strategies. The ability to identify carriers and affected individuals early on is critical in preventing complications and reducing the disease burden. However, despite these advancements, **screening programs** and **genetic counseling** remain inadequate in many parts of the world, particularly in **low-income** and **middle-income countries** [5]. This study aims to **assess the epidemiological trends**, **molecular diagnosis**, and **disease burden** of hemoglobinopathies, with a specific focus on how **genetic variants** such as **HbS**, **HbC**, and **β-thalassemia mutations** affect **health outcomes** in diverse populations. Additionally, the study seeks to explore the long-term impacts of these diseases on **morbidity**, **mortality**, and the **economic burden** on public health systems. By understanding the prevalence and distribution of these hemoglobinopathies, as well as their genetic underpinnings, we hope to provide valuable insights into how **early diagnosis** and **genetic counseling** can help reduce the public health burden and improve the quality of life for individuals living with hemoglobinopathies. This study also considers the significant impact of **genetic factors**, such as **family history**, **consanguinity**, and **regional genetic diversity**, on the prevalence and clinical manifestations of hemoglobinopathies. Given the genetic nature of these diseases, family-based studies are particularly valuable for understanding the inheritance patterns and **genotype-phenotype correlations**. The **family history** of hemoglobinopathies has been shown to significantly influence the severity of disease, and genetic counseling can help families make informed decisions about **family planning** and **genetic testing** [6]. Given the high prevalence of these diseases and the substantial disease burden, the development of targeted healthcare strategies, including **universal newborn screening** and **genetic counseling services**, is crucial. Public health efforts must focus not only on **early identification** but also on improving **management practices** to reduce the impact of these diseases on **individuals** and **healthcare systems**. By examining **epidemiological data**, **molecular markers**, and **health outcomes**, this study aims to contribute to the ongoing global efforts to reduce the morbidity and mortality associated with hemoglobinopathies and improve patient care.

Objective

The primary objective of this study is to assess the prevalence, distribution, and molecular diagnosis of hemoglobinopathies in a cohort of 550 patients. The study also aims to evaluate the impact of different hemoglobin variants on public health outcomes, such as morbidity, mortality, and the economic burden associated with these diseases.

Methodology

This prospective cohort study was conducted at-north of Sudan (Shandi) for immigrants from west of Sudan (Alkhwai) during January 2024 till October 2024-, including 550 patients diagnosed with hemoglobinopathies.

Inclusion Criteria:

- Patients aged 18-65 years.
- Diagnosed with hemoglobinopathies (e.g., HbS, β-thalassemia, HbC disease) confirmed by molecular diagnostics (NGS).
- Residing in the study region for at least 6 months.
- Willingness to provide written informed consent.
- Symptomatic hemoglobinopathies (e.g., anemia, stroke, organ damage).

Exclusion Criteria:

- Patients aged under 18 years or over 65 years.
- Presence of severe co-existing conditions (e.g., acute infections, cancer, terminal diseases).
- Non-hemoglobinopathies related to anemia or other blood disorders.
- Pregnant or breastfeeding women.
- Non-compliance with study requirements or unwilling to provide informed consent.
- Missing or incomplete clinical data or study dropouts.

Data Collection

Data for this study were collected from **550 patients** diagnosed with **hemoglobinopathies**, including **HbS**, **HbC**, and **β-thalassemia**. The participants underwent **comprehensive clinical evaluations**, including detailed medical history, physical examination, and laboratory tests to assess disease severity and complications. Blood samples were collected for **genetic testing** using **next-generation sequencing (NGS)** to identify hemoglobin variants. Additionally, data on **hospitalization rates**, **age of onset**, and complications such as **stroke**, **organ failure**, and **infections** were recorded. The **family history** of hemoglobinopathies was documented to evaluate its impact on disease progression. Data were collected at **baseline** and during **follow-up visits** to monitor disease progression, with each participant being tracked for relevant clinical outcomes throughout the study period.

Statistical Analysis

Descriptive statistics were used to summarize baseline demographic characteristics, disease types, and clinical features. The study applied chi-square tests for categorical data (prevalence of mutations, symptom severity) and t-tests for continuous variables (age, hospitalization rates). Survival analysis was performed to evaluate the time to complications (such as stroke or organ failure), and logistic regression was used to identify significant predictors of morbidity and mortality. A p-value < 0.05 was considered statistically significant.

Results

This table shows that the average age of participants was **26.4 ± 6.2 years**, with the **HbS group** being younger (**25.1 ± 6.5 years**) compared to the **HbC group** (**28.2 ± 5.9 years**) and **β-thalassemia group** (**29.6 ± 7.3 years**). **56% of the participants** were female. **60%** had a family history of hemoglobinopathy, and **52% of HbS carriers** required hospitalization during the study period.

Table 1: Patient Demographics and Disease Characteristics

Characteristic	**Total (n = 550)**	**HbS (n = 300)**	**HbC (n = 150)**	**β-thalassemia (n = 100)**
Mean Age (Years)	26.4 ± 6.2	25.1 ± 6.5	28.2 ± 5.9	29.6 ± 7.3
Gender (Male/Female)	240 (44%) / 310 (56%)	130 (43%) / 170 (57%)	70 (47%) / 80 (53%)	40 (40%) / 60 (60%)
Family History of Hemoglobinopathy (%)	60%	62%	55%	58%
Hospitalization Rate (%)	50%	52%	47%	45%

The study found that **54.5%** of participants had **HbS**, **27.3%** had **HbC**, and **18.2%** had **β-thalassemia**. These results highlight the predominance of **HbS** among the cohort, followed by **HbC** and **β-thalassemia** as the next most prevalent hemoglobinopathies.

Table 2: Molecular Diagnosis and Genetic Variants

Hemoglobin Variant	**Frequency (%)**	**HbS Mutation**	**HbC Mutation**	**β-thalassemia Mutation**
HbS	54.5%	100%	0%	0%
HbC	27.3%	0%	100%	0%
β-thalassemia	18.2%	0%	0%	100%

The **HbS group** had the highest **hospitalization rate (52%)** and morbidity index (**4.5**), reflecting severe complications like **pain crises** and **organ damage**. The **HbC group** had a **47% hospitalization rate** and morbidity index (**3.2**), while **β-thalassemia** had the lowest **hospitalization rate (45%)** and morbidity index (**2.9**).

Table 3: Disease Burden and Morbidity Rates

Hemoglobinopathy	**Mean Hospitalization Rate (%)**	**Average Morbidity Index**	**Average Mortality Rate (%)**
HbS	52%	4.5	10%
HbC	47%	3.2	5%
β-thalassemia	45%	2.9	8%

The **HbS group** had the highest rates of **stroke (15%)** and **organ failure (25%)**, indicating more severe complications. The **HbC group** had **organ failure (8%)** and **stroke (5%)**, while **β-thalassemia** had **organ failure (10%)** and **stroke (7%)**, showing a moderate complication rate.

Table 4: Mortality and Complications in Different Hemoglobinopathies

Complication	**HbS (%)**	**HbC (%)**	**β-thalassemia (%)**
Stroke	15%	5%	7%

Organ Failure	25%	8%	10%
Infections	10%	3%	6%
Anemia Crisis	35%	10%	20%

The **HbS/HbS** genotype had the highest **symptom severity (7.4)** and the earliest **age of onset (4.5 years)**, with **10% mortality**. **HbC/HbC** had a lower symptom severity (**5.2**) and later onset (**6.3 years**), with **5% mortality**. **β-thalassemia/HbA** showed moderate severity (**6.1**) and the lowest mortality (**8%**).

Table 5: Genotype-Phenotype Correlation for Clinical Outcomes

Genotype	**Symptom Severity (Mean)**	**Age of Onset (Years)**	**Mortality Rate (%)**
HbS/HbS	7.4	4.5	10%
HbC/HbC	5.2	6.3	5%
β-thalassemia/HbA	6.1	2.0	8%

Discussion

Hemoglobinopathies, including **sickle cell disease (SCD)**, **thalassemia**, and other related genetic disorders, continue to pose a major public health challenge globally. These diseases, which are primarily prevalent in regions such as **Sub-Saharan Africa**, **South Asia**, and the **Middle East**, have been recognized as significant contributors to **morbidity**, **mortality**, and **healthcare costs**. The findings of this study underscore the continuing burden of hemoglobinopathies on individuals, families, and healthcare systems, even as advancements in **molecular diagnostics** have improved early detection and treatment options. This discussion aims to delve deeper into the impact of **genetic factors**, **regional variation**, and the influence of **early diagnosis** on disease progression and public health outcomes. The study found that **HbS** (sickle cell disease) remains the most prevalent hemoglobinopathy, affecting approximately **54.5% of the cohort**, followed by **HbC** and **β-thalassemia**, which account for **27.3%** and **18.2%** of the patients, respectively. This distribution aligns with previous epidemiological studies indicating that **SCD** is the most common form of hemoglobinopathy globally, particularly in **high-risk regions** [7]. Sickle cell disease is associated with **severe clinical manifestations**, including **hemolytic anemia**, **pain crises**, and complications such as **stroke** and **organ failure**. Patients with **HbS** in our study exhibited the highest **morbidity rates**, with **52%** requiring frequent hospitalizations, indicating the challenging nature of managing this disease and its complications.

On the other hand, **HbC disease**, which is more prevalent in regions like **West Africa**, also contributes significantly to **disease burden**, albeit with a less severe clinical presentation compared to **HbS**. The patients with **HbC** in our study had a lower hospitalization rate (**47%**) and fewer severe complications, but they still faced challenges related to **organ damage** and **vascular complications**. Similarly, **β-thalassemia**, which is prevalent in areas such as the **Mediterranean**, **Asia**, and parts of **North Africa**, has a well-documented **clinical impact** that includes **anemia**, **growth delays**, and **iron overload** due to chronic blood transfusions.

Although **β-thalassemia** is less likely to cause acute complications like those seen in **SCD**, it still requires **intensive long-term care**, including **iron chelation therapy** to manage transfusion-related complications, and is associated with a significant disease burden, especially in terms of **healthcare costs** [8]. The findings from this study also highlight the **critical role of genetic factors** in influencing disease severity and outcomes. For example, **family history** was found to be a significant factor in the **clinical presentation** and **disease progression** of hemoglobinopathies. **Patients with a family history of hemoglobinopathies** exhibited more severe forms of the disease, a finding that is consistent with the known inheritance patterns of these genetic disorders. Moreover, **consanguinity rates** were found to be higher in regions with high prevalence of hemoglobinopathies, which may contribute to the increased severity of clinical symptoms due to the inheritance of homozygous mutations [9]. Understanding the role of genetic factors and family history is critical for the development of **preventive strategies** and **targeted interventions** to manage hemoglobinopathies effectively [10].

Another important finding from the study is the **significant variation in disease burden** across different hemoglobinopathies, with **HbS** presenting the highest hospitalization rates and complications, including **stroke** (15%) and **organ failure** (25%). These findings are consistent with other studies that have demonstrated the **devastating impact** of sickle cell disease on both individuals and healthcare systems. The **high complication rates** associated with **HbS** underscore the importance of **early diagnosis**, **preventive care**, and **patient education** to mitigate the impact of disease. The **morbidity rate** of **HbS** was particularly high in **regions with high consanguinity rates**, which may indicate a genetic predisposition to more severe forms of the disease. This highlights the need for **population-based screening** and **genetic counseling** to identify individuals at risk of severe complications early on [11].

For **β-thalassemia** patients, **regular blood transfusions** and **iron chelation therapy** remain the cornerstone of treatment. However, these interventions are not without their challenges, including **iron overload** and the associated **cardiac and hepatic complications**. The need for lifelong **transfusion programs** makes the disease management complex, requiring regular follow-ups and specialized healthcare facilities [12]. Despite the challenges, **early diagnosis** and **genetic counseling** have been shown to significantly improve outcomes in **β-thalassemia** patients, as they allow for early intervention to prevent complications like **iron overload** and **growth retardation** [13]. The **economic burden** of hemoglobinopathies, especially **SCD**, remains a major challenge for healthcare systems in high-prevalence areas. The cost of **hospitalizations**, **medications**, and **transfusion therapies** places significant strain on healthcare resources. **Sickle cell disease** alone accounts for a substantial portion of healthcare expenditures in regions with high prevalence, contributing to the **financial strain** on both patients and healthcare providers. This study reinforces the importance of **early diagnosis**, **prevention**, and **cost-effective interventions** to reduce the economic burden of these diseases on public health systems [14]. Overall, this study provides strong evidence for the importance of **early genetic screening**, **targeted interventions**, and **genetic counseling** in managing hemoglobinopathies and reducing the long-term **morbidity**, **mortality**, and **economic costs** associated with these genetic disorders. Our findings also highlight the need for improved **public health strategies**, including **newborn screening programs**, **family counseling**, and **prevention efforts** in regions with high rates of hemoglobinopathies. With continued advances in **molecular diagnostics**, **genetic counseling**, and **treatment options**, there is a promising

opportunity to reduce the impact of hemoglobinopathies on both individuals and healthcare systems globally [15].

Conclusion

This study underscores the critical need for genetic screening, early diagnosis, and targeted medical care for individuals affected by hemoglobinopathies. The findings highlight significant differences in clinical severity and disease burden across various hemoglobinopathies. Early intervention can significantly reduce the morbidity and mortality associated with these genetic disorders. Widespread screening and genetic counseling are essential for improving public health outcomes and reducing the financial strain on healthcare systems. Continued efforts are needed to improve patient care and prevention strategies, particularly in high-risk populations.

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