Genetic Disorders: Global Impacts, Healthcare Disparities, and Challenges in Bangladesh

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Abstract

Background: Genetic disorders significantly contribute to infant mortality and childhood morbidity, disproportionately affecting low- and middle-income countries (LMICs). With congenital disorders causing approximately 410,000 child deaths annually, the burden is intensified by healthcare disparities, limited genetic research, and insufficient services in LMICs like Bangladesh. Advances in genetic research, particularly post-Human Genome Project, have expanded understanding but highlighted the challenges in diagnosis, treatment, and prevention, with over 95% of rare genetic diseases lacking FDA-approved therapies. Methods: This review evaluates the global and regional burden of genetic disorders, focusing on Bangladesh's challenges. It synthesizes data from genetic studies, healthcare evaluations, and international reports to assess disparities in service availability, resource allocation, and healthcare outcomes. Historical and current trends in genetic disorder management were analyzed to propose targeted interventions for resource-constrained settings. Results: Genetic disorders remain underdiagnosed in Bangladesh due to inadequate healthcare infrastructure, absence of a genetic registry, and limited public awareness. Common conditions include hemoglobin-pathies, congenital heart defects, and muscular dystrophies. The maternal mortality rate (240/100,000 live births) and life expectancy (70 years) further underscore systemic inadequacies. Despite economic growth, gaps in neonatal screening, genetic counseling, and universal health coverage persist. Conclusion: Addressing genetic disorders in Bangladesh requires establishing a genetic disease registry, implementing neonatal screening, and enhancing healthcare training. Investments in public awareness and international collaborations can bridge gaps, reducing disparities and advancing equitable healthcare for LMICs. This model offers a framework for addressing genetic diseases in similar contexts globally.

Keywords: Genetic Disorders, Infant Mortality, Congenital Conditions, Healthcare Disparities, Neonatal Screening

Significance | Genetic disorders is crucial for reducing infant mortality, improving healthcare strategies, and addressing disparities in resource-limited settings globally.

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1. Introduction

Genetic disorders have emerged as a significant contributor to infant mortality and childhood morbidity worldwide. Recent research highlights that 41% of 112 infant deaths were linked to genetic disorders, underscoring a larger burden than previously recognized (Owen et al., 2023). Each year, congenital disorders account for nearly 240,000 neonatal deaths within the first 28 days of life globally (Zhou et al., 2024). Beyond the neonatal period, congenital disorders contribute to an additional 170,000 deaths in children aged one month to five years, with profound implications for families, healthcare systems, and societies (Zhou et al., 2024). While all genetic disorders are congenital, not all congenital disorders originate from genetic factors; some result from infections or environmental influences. This distinction is crucial for understanding the multifaceted nature of congenital conditions

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and their underlying causes.

A genetic disorder arises from abnormalities in DNA, which is the blueprint for our characteristics and biological functions inherited from our parents. Advances in genetics, particularly following the completion of the Human Genome Project (HGP), have significantly enhanced our understanding of the interplay between genetics and health. The HGP has enabled researchers to identify over 6,500 inherited disorders, 15,000 monogenic diseases, and 20,442 coding genes (Akter et al., 2022; Hosen et al., 2021). Despite these achievements, genetic diseases remain a growing public health concern. Rare genetic disorders affect nearly 350 million individuals globally, yet fewer than 200,000 people have received a diagnosis (Bienstock, 2019). Tragically, over 95% of these rare diseases lack FDA-approved treatments and more than 80% are rooted in genetic origins (Lopes-Júnior et al., 2022).

Genetic diseases exhibit significant variability across populations and regions. According to the World Health Organization (WHO), about 2–3% of all births globally are affected by genetic disorders, with approximately 70% of these conditions being preventable (Akter et al., 2022). However, the burden is disproportionately high in low- and middle-income countries (LMICs), which account for 94% of severe congenital disorder cases (Moges et al., 2023). These disparities are exacerbated by limited access to healthcare, insufficient genetic research, and underdeveloped genetic services in LMICs. For example, while high-income countries (HICs) like the United States benefit from advanced healthcare infrastructure, including government-funded programs like Medicare and Medicaid, LMICs struggle with underfunded healthcare systems, limited research capabilities, and inadequate resources to address genetic disorders effectively (Akter et al., 2022; Jobanputra et al., 2024). Additionally, countries like Bangladesh lack comprehensive genetic disease databases, further hampering efforts to tackle these challenges (Akter et al., 2022).

This review provides a detailed examination of the state of genetic diseases and their management in both HICs and LMICs. It delves into the historical context of genetic disorders, evaluates existing genetic service delivery systems, and highlights the critical gaps and opportunities for improvement in Bangladesh. By presenting this information, we aim to offer valuable insights into the challenges and potential strategies for addressing genetic diseases, particularly in resource-constrained settings. The proposed framework could serve as a model for implementing genetic services in other LMICs with similar health and cultural contexts, contributing to a more equitable global healthcare landscape.

2. History of Genetic Disorders

Genetic disorders, resulting from abnormalities in an individual's genetic material, have been a significant focus of medical and scientific research. Subtle mutations in the genetic code can give rise to numerous severe illnesses, illustrating the profound impact of genetics on human health.

2.1 Early Discoveries in Genetic Disorders

The historical understanding of genetic disorders dates back to the early 20th century. In 1902, British physician Archibald Garrod first observed the hereditary nature of alkaptonuria, a rare metabolic disorder caused by a recessive mutation. Garrod's work was groundbreaking; he proposed that alkaptonuria followed Mendelian inheritance patterns, referencing Gregor Mendel's principles of genetic transmission from 1865. His seminal publication in *The Lancet* not only identified alkaptonuria as a recessively inherited condition but also linked human disease to genetic inheritance, establishing the field of medical genetics (National Human Genome Research Institute, n.d.).

Interestingly, the recognition of genetic disorders predates modern genetics. Ancient art, including paintings, sculptures, and sketches, depicts individuals with conditions such as achondroplasia, neurofibromatosis, Robert’s syndrome, and hermaphroditism. These observations underscore that genetic anomalies have been part of human history long before they were scientifically understood (Urban, 1999).

2.2 Advancements in Understanding Genetic Disorders

The identification of alkaptonuria marked the beginning of systematic efforts to understand inborn errors of metabolism. This discovery emphasized the link between genetic mutations and metabolic abnormalities, pioneering the study of genetic diseases. By the late 20th century, researchers had established that over 5% of live births and a significant proportion of miscarriages could be attributed to genetic disorders. These conditions represent a considerable burden on human health, resulting from mutations and variations in the human genome (Roth & Marson, 2021a).

In the 1980s and 1990s, advances in molecular biology enabled researchers to identify genes responsible for rare, single-gene diseases. Techniques such as linkage analysis and fine-scale mapping within large families facilitated the pinpointing of these genes. Pathogenic variants were identified by studying their presence in affected individuals and their absence in healthy controls. Functional studies in cellular and animal models often confirmed these variants’ roles in disease pathogenesis (Claussnitzer et al., 2020).

2.3 The Genomic Era and Beyond

By the year 2000, researchers had identified the genetic basis for over 1,000 of the approximately 7,000 known single-gene hereditary diseases, including major disorders such as Huntington's disease and cystic fibrosis. This progress laid the foundation for modern genomics and personalized medicine, significantly enhancing our understanding of the genetic underpinnings of disease (Claussnitzer et al., 2020).

2.4 Genetic Disorder Classification

Our genetic makeup, which defines our characteristics and physical appearance, is inherited from our parents through genes. These genes, composed of DNA, play a crucial role in our biological functions and traits. However, deviations in these genetic structures such as missing altered or mutated genes can lead to various genetic disorders. Advances in medical science have significantly enhanced our understanding of genetic disorders, and discoveries in this field are accelerating at an unprecedented pace.

2.5 Types of Genetic Disorders

Genetic disorders are broadly categorized into three main types: **single-gene disorders (monogenic), chromosomal disorders, and complex disorders (multifactorial) as shown in table 1**. Each category has distinct causes and characteristics, as detailed below:

2.5.1 Single-Gene Disorders

Single-gene disorders result from mutations in a single gene. These disorders are often inherited in Mendelian patterns dominant, recessive, or X-linked. Examples include: **Cystic Fibrosis**: A condition affecting the respiratory and digestive systems. **Phenylketonuria (PKU)**: A metabolic disorder caused by a deficiency in the enzyme phenylalanine hydroxylase. **Hereditary Breast Cancer**: Often associated with mutations in the BRCA1 and BRCA2 genes. Despite being individually rare, single-gene disorders collectively account for about 80% of all rare diseases, which number in the thousands (Jackson et al., 2018). Studies reveal that single-gene mutations affect approximately 1 in 50 individuals (Akter et al., 2022).

2.5.1.1 Chromosomal Disorders

Chromosomal disorders originate from abnormalities in the structure or number of chromosomes, which are the cellular components housing our DNA and genes. These abnormalities can lead to the addition, deletion, or rearrangement of genetic material. Common examples include: **Down Syndrome (Trisomy 21)**: Caused by an extra copy of chromosome 21. **Turner Syndrome**: Affects females who have only one X chromosome. **Klinefelter Syndrome**: Occurs in males with an extra X chromosome (XXY). Chromosomal disorders affect approximately 1 in 263 individuals (Akter et al., 2022). The presence of missing or extra chromosomes disrupts normal development and function.

2.5.2 Complex Disorders

Complex disorders arise from interplay between genetic predispositions and environmental factors such as: **Dietary habits, Exposure to chemicals, Use of medications or drugs and Substance abuse.** Conditions like heart disease, diabetes, and certain cancers fall into this category. Unlike single-gene or chromosomal disorders, these conditions do not follow simple inheritance patterns.

2.5.3 Prevalence and Impact

A staggering 65% of individuals are estimated to experience health issues related to genetic mutations at some point (Akter et al., 2022). Genetic disorders, when combined with congenital conditions such as birth defects, fetal abnormalities, and growth restrictions, represent a significant burden. According to estimates, 5% of pregnancies result in newborns with serious congenital or genetic issues (Roy & Shengelia, 2016).

Longevity Differences between Men and Women

Globally, women tend to live longer than men, a trend observed consistently across populations. Historical and contemporary analyses have highlighted these differences in life expectancy, with statistical data indicating that women born in the late 19th century often outlive their male counterparts. Improved public health measures, advancements in medical science, and societal changes have disproportionately benefited women in terms of longevity. These factors have further enhanced their life expectancy compared to men, particularly in the 20th century, when significant strides were made in reducing maternal mortality and addressing gender-specific health needs (Zeng et al., 2024).

The 1970s to 1990s marked the peak of gender disparity in life expectancy. During this period, women experienced greater reductions in mortality, while men faced higher risks from cardiovascular disease (CVD) and lifestyle-related factors such as smoking and alcohol consumption (Ostan et al., 2016). However, the gap has gradually narrowed due to reductions in male CVD mortality rates and a convergence in health risk behaviors between the sexes.

2.5.4 Health Challenges by Gender

The prevalence and impact of age-related illnesses differ significantly between men and women, influenced by biological, social, and environmental factors. **Women**: After menopause, the incidence of several chronic conditions increases among women. Diseases like Alzheimer's disease (AD), septicemia, hypertension-related infections, influenza, pneumonia, and chronic lower respiratory disorders disproportionately affect women. This increased susceptibility may be linked to hormonal changes, immune system differences, and longer life spans, which expose women to age-related degenerative conditions (Ostan et al., 2016). Men are at higher risk of mortality from stroke, ischemic heart disease (IHD), and certain cancers. While genetic predispositions such as those involving the second X chromosome may offer some protection to women, men often experience higher mortality rates from conditions related to lifestyle factors and comorbidities (Zhao & Crimmins, 2022).

3. Historical Trends and Shifts in Mortality Causes

Infectious diseases were the leading causes of death for both sexes in the early 20th century. However, as medical advancements controlled these diseases, chronic conditions like cancer and cardiovascular illnesses emerged as the dominant causes of mortality. This transition disproportionately affected men due to higher rates of tobacco use, alcohol consumption, and occupational hazards (Zeng et al., 2024; Zhao & Crimmins, 2022).

The significant gender disparities in life expectancy during the late 20th century were largely attributable to higher male mortality rates over age 40. Socioeconomic and behavioral factors compounded this disparity, with men engaging in more high-risk behaviors compared to women. Conversely, the improving health and social status of women during this period contributed to their enhanced longevity (Ostan et al., 2016).

3.1 Role of Genetic and Biological Factors

Chromosomal differences may also contribute to disparities in mortality risk. Women possess two X chromosomes, which are thought to provide a genetic buffer against certain diseases. For example, this chromosomal advantage is believed to influence outcomes in stroke and other cardiovascular conditions. However, the benefit diminishes with age and hormonal changes, leading to a higher prevalence of some conditions among elderly women (Zhao & Crimmins, 2022).

Strokes, while not directly influenced by genetic disorders, are significantly affected by age, pre-existing health conditions, and stroke severity. Meta-analyses reveal that men who suffer strokes face higher mortality rates than women in both short- and long-term scenarios. Factors like atrial fibrillation and pre-stroke functional limitations often exacerbate outcomes for men (Zhao & Crimmins, 2022).

3.2 Genetic Diseases in Bangladesh: Challenges and Realities

Bangladesh, unlike developed nations such as the USA and UK, or even some low- and lower-middle-income countries, faces significant challenges in addressing genetic diseases due to the absence of a comprehensive database and insufficient healthcare infrastructure. While developed nations have established systems for monitoring and managing genetic disorders, Bangladesh struggles with a lack of data, limited awareness, and constrained resources. Despite these challenges, genetic disorders are estimated to affect a substantial portion of the population, contributing significantly to morbidity and mortality as shown in table 2.

With a population of approximately **173 million**, Bangladesh is the **eighth most densely populated country in the world**, with a density of **1,328 people per square kilometer** (S. M. S. Islam et al., 2023). As a lower-middle-income nation in Asia, it is burdened by a dual spectrum of infectious and non-infectious diseases. Among the non-infectious conditions, genetic disorders and congenital malformations pose a major yet under diagnosed public health challenge. Many cases remain unidentified due to the lack of systematic screening and diagnostic facilities. Estimates based on global genetic disease prevalence suggest that a significant number of Bangladeshis are likely living with undiagnosed genetic conditions (Akter et al., 2022).

The healthcare system in Bangladesh is insufficiently equipped to address these issues. The country's life expectancy is approximately **70 years**, notably lower than the average of **75 years in developed nations** (Sarker, 2021). Maternal and infant health outcomes further highlight systemic inadequacies; only **25% of mothers deliver in medical institutions**, leaving both mothers and newborns vulnerable to complications. The maternal mortality rate is high, with over **240 deaths per 100,000 live births**, while infant mortality remains significant (Hosen et al., 2021). These statistics reflect broader challenges in healthcare access and quality, further compounded by the absence of a national health insurance policy. Despite a GDP growth rate of **7.2% in 2022**, one of the fastest in Asia, Bangladesh ranked **151st out of 188 nations** in the Global Burden of Disease study, which evaluated health-related Sustainable Development Goal indicators (S. M. S. Islam et al., 2023; Hosen et al., 2021).

Among the genetic disorders prevalent in Bangladesh, **hemoglobinopathies**, congenital heart defects, muscular dystrophies, cystic fibrosis, and metabolic disorders such as phenylketonuria (PKU) are prominent. Specific conditions include **thalassemia**, a severe form of anemia; **sickle cell anemia**, though less common, presents severe complications; and congenital heart defects such as **atrial septal defects (ASD)** and **tetralogy of Fallot**. Muscular dystrophies, including **Duchenne and Becker muscular dystrophies** and **spinal muscular atrophy**, significantly impair mobility and quality of life. Other prevalent conditions include **chronic diseases with genetic predispositions** like cardiovascular diseases (CVD), cancer, diabetes mellitus (DM), and chronic respiratory diseases (Hosen et al., 2021).

Genetic disorders in Bangladesh require urgent interventions. A **national genetic disease registry** must be established to collect data and inform policy decisions. **Neonatal screening programs** should be implemented to detect and manage congenital and metabolic disorders early. The government must invest in specialized diagnostic facilities, genetic counseling services, and training programs for healthcare professionals to enhance diagnostic accuracy and patient care. Public awareness campaigns are essential to reduce stigma and increase understanding of genetic diseases, while partnerships with international organizations can support research and resource sharing. Lastly, introducing **universal health coverage** to include genetic testing and treatment would provide essential financial support to affected families.

Genetic diseases are a significant but under recognized public health challenge in Bangladesh. Despite economic progress, systemic weaknesses in the healthcare sector leave the population vulnerable to the impacts of genetic disorders. By addressing policy gaps, improving healthcare infrastructure, and investing in preventive measures, Bangladesh can reduce the burden of genetic diseases and improve the overall health outcomes of its population.

4. Hemoglobinopathies

Hemoglobinopathies are among the most common human monogenic diseases, resulting from genetic abnormalities in hemoglobin (Hb) production. These conditions are caused by more than 700 mutations in globin genes, with approximately 7% of the global population carrying these genetic variations. It is estimated that over 25,000 individuals are born annually with hemoglobinopathies (Sachdev et al., 2021; Inheritance of β Hemoglobin Gene Mutation 2 / 5, 2022; S. A. Rahman et al., 2017). Among the most prevalent hemoglobinopathies are sickle cell disease (SCD) and β-thalassemia, both of which are characterized by mutations in the β-globin gene (S. A. Rahman et al., 2017; Sachdev et al., 2021).

Sickle cell disease (SCD) is a genetic disorder that leads to the production of sickle-shaped red blood cells, which are rigid and fragile, impairing blood flow and leading to a range of complications (Elendu et al., 2023). It is an inherited hemoglobinopathy caused by a single base mutation in the β-globin gene, resulting in the formation of hemoglobin S (HbS) (Brandow & Liem, 2022; Darshana et al., 2021). SCD ranks among the most common severe genetic disorders globally, affecting more than 20 million individuals, with the highest prevalence in sub-Saharan Africa, where it is estimated that 75% of those affected live (Pace et al., 2021; Rees et al., 2022). The disease was first described by James Herrick in 1910, who observed elongated, sickle-shaped red blood cells in affected individuals (Germino-Watnick et al., 2022). A major scientific breakthrough occurred in the late 1940s when electrophoresis revealed the link between an altered protein structure and sickle cell anemia, marking the first instance of a heritable protein change being associated with a disease (Roth & Marson, 2021b).

The global incidence of SCD is difficult to determine precisely, but it is estimated that over 300,000 children are born with the disorder each year (Rees et al., 2022). In the United States, approximately 100,000 individuals, predominantly African Americans are affected by SCD, with a prevalence of 1 in 365 births among African Americans and 1 in 16,300 births among Hispanic Americans (Sachdev et al., 2021). The clinical manifestations of SCD are severe and primarily arise from vaso-occlusion and tissue ischemia. Pain crises, caused by blocked blood vessels, are the most common and debilitating symptom, with the frequency and severity of pain increasing with age. About 30–40% of adolescents and adults experience pain crises (Brandow & Liem, 2022; Sachdev et al., 2021). The pathophysiology of SCD is marked by the polymerization of HbS, leading to red blood cell dehydration, increased rigidity, and a propensity for hemolysis. This results in a cascade of pathological events, including vascular damage, inflammation, coagulopathy, and platelet activation (Rees et al., 2022).

SCD incidence varies significantly across regions and demographics. The highest burden is concentrated in sub-Saharan Africa, where countries such as Nigeria, Benin, and Burkina Faso have incidence rates exceeding 2000 cases per 100,000 live births (Thomson et al., 2023). The disease is also prevalent in India, parts of the Mediterranean, and some areas of the Middle East, such as Saudi Arabia, where the incidence can reach up to 4% (Elendu et al., 2023). Additionally, there have been reports of SCD in countries like Pakistan, Sri Lanka, and Bangladesh, although the full extent and nature of the disease in these regions remain poorly understood (Darshana et al., 2021). In high-resource countries, more than 95% of children with SCD survive into adulthood, thanks to advances in neonatal screening and treatment. In contrast, in low-income countries, where access to healthcare is limited, most children with SCD die before reaching the age of five (Sachdev et al., 2021; Inheritance of β Hemoglobin Gene Mutation 2 / 5, 2022).

In countries like Bangladesh, where the disease burden is particularly high, SCD has resulted in significant morbidity and mortality, with recent reports indicating that the disease has claimed the lives of millions, particularly women and children (S. A. Rahman et al., 2017). Anemia, often exacerbated by iron deficiencies, significantly impacts the quality of life, particularly among the poor, affecting their physical health and mental well-being. While high-income nations have developed extensive screening programs to identify and treat SCD in newborns, low-income nations like Bangladesh struggle with limited resources and lack of infrastructure to address the disease adequately (S. A. Rahman et al., 2017). This disparity highlights the urgent need for global health initiatives aimed at improving early diagnosis, treatment access, and public health awareness, particularly in resource-poor regions.

5. Comprehensive Overview of Sickle Cell Disease (SCD) and Its Treatment

Sickle cell disease (SCD) profoundly impacts the health and quality of life of affected individuals, necessitating a comprehensive understanding of its underlying causes, symptoms, and available treatment options. This understanding is vital not only for healthcare professionals but also for patients and their families to effectively manage the disease and its associated complications (Elendu et al., 2023).

5.1 Causes of Sickle Cell Disease

SCD is primarily caused by a genetic mutation in the *HBB* gene, which encodes hemoglobin. This mutation leads to the production of abnormal hemoglobin known as hemoglobin S. When oxygen levels are low, hemoglobin S molecules polymerize, causing red blood cells to assume a sickle or crescent shape. These misshapen cells are less flexible, leading to blockages in blood flow, chronic hemolysis, and various complications associated with SCD. Beyond the genetic basis, co-morbid conditions such as depression and anxiety often exacerbate the disease's impact, intensifying pain and impairing coping mechanisms. These psychological factors can amplify pain-related distress and interfere with effective disease management (Brandow & Liem, 2022; Elendu et al., 2023).

5.2 Symptoms and Complications

The symptoms of SCD are diverse and vary widely among individuals. **Pain crises:** Episodic severe pain caused by vaso-occlusion, where sickled cells block blood flow to organs and tissues. **Anemia:** Chronic hemolytic anemia due to the destruction of abnormal red blood cells, leading to fatigue and weakness. **Infections:** Increased susceptibility to infections because of spleen dysfunction. **Acute chest syndrome:** A life-threatening condition characterized by chest pain, fever, and difficulty breathing, often triggered by infection or vaso-occlusion in the lungs. **Delayed growth and development:** A result of chronic anemia and poor oxygen delivery to tissues. **Stroke:** A major risk, particularly in children, due to occluded blood vessels in the brain. Other complications include leg ulcers, retinopathy, and priapism, which significantly affect quality of life (Elendu et al., 2023).

5.3 Treatment Approaches

The management of SCD has advanced considerably, although it remains complex. Current treatment strategies include: **Symptom Management and Preventive Care:** Regular blood transfusions to prevent complications like stroke and severe anemia. Pain management using analgesics, including opioids and non-opioid medications. Preventive measures such as vaccination and prophylactic antibiotics to reduce infection risk. **Disease-Modifying Therapies: Hydroxyurea (HU):** A widely used medication that increases fetal hemoglobin (HbF) levels, reducing the polymerization of hemoglobin S and the frequency of pain crises. HU also decreases hospitalizations and improves overall quality of life. **Advanced Therapeutic Interventions: Hematopoietic Stem Cell Transplantation (HSCT):** A potentially curative option for a subset of patients, particularly those with compatible donors. HSCT can replace the defective hematopoietic system with healthy cells capable of producing normal hemoglobin. **Gene Therapy:** An emerging near-curative approach involving the correction or replacement of the defective gene. While still experimental and available to a limited number of patients, gene therapy holds immense promise for revolutionizing SCD treatment (Darshana et al., 2021).

5.4 Holistic Management

Effective SCD care also involves addressing psychological and social dimensions of the disease. Comprehensive care plans often integrate mental health support, counseling, and educational initiatives to enhance coping mechanisms for patients and their families. This approach acknowledges that SCD's impact extends beyond physical health, affecting emotional well-being and social functioning.

6. Thalassemia

Thalassemia a genetic blood disorder first described by Whipple and Bradford in 1932, derives its name from its prevalence among individuals from the Mediterranean region (Shafique et al., 2023). It is one of the most common inherited hematological conditions globally, characterized by the body's inability to produce sufficient hemoglobin, the critical protein in red blood cells responsible for oxygen transport. Thalassemia manifests in two main forms: alpha (α) and beta (β). These arise from mutations in the globin genes, leading to deficient or defective production of the α- or β-globin chains of adult hemoglobin (Hb), respectively (Musallam et al., 2024). Severe cases of α- and β-thalassemia often require lifelong blood transfusions to sustain life, significantly improving survival rates and life expectancy for affected individuals, especially when coupled with proper medical management (R. Chowdhury et al., 2023).

Globally, thalassemia is a critical health concern, identified as the most prevalent chronic genetic disease in over 60 countries, according to the World Health Organization (WHO). WHO estimates that approximately 40,000 children are born annually with β-thalassemia, with 25,500 of these cases being transfusion-dependent (Tuo et al., 2024). Epidemiological data from 2021 highlight that the global prevalence of thalassemia is 18 cases per 100,000 people, affecting over 1.3 million individuals worldwide. Moreover, about 15% of global fatalities are linked to complications arising from this condition (Tuo et al., 2024). In Bangladesh, thalassemia presents a significant public health challenge, with 6–12% of the population, or around 10–19 million people, being carriers of the thalassemia-causing gene. Each year, an estimated 6,000 to 8,000 infants are born with thalassemia in the country (R. Chowdhury et al., 2023; Mitro et al., 2024). Regional statistics from the Bangladesh Bureau of Statistics (BBS) 2024 survey reveal varying carrier rates: Rangpur records the highest at 27.7%, while Sylhet has the lowest at 4.8%. Other regions such as Rajshahi, Chattogram, and Dhaka report moderate carrier rates, highlighting the geographical disparities in gene distribution.

Thalassemia carriers often display increased iron absorption, elevated serum ferritin levels, and reduced hepcidin levels, necessitating careful management. Guidelines recommend against routine iron supplementation unless specific iron deficiencies are identified (S. Rahman et al., 2023). Alpha-thalassemia affects approximately 5–20% of the global population, while β-thalassemia impacts about 1.5% (Musallam et al., 2024). In Bangladesh, β-thalassemia is among the most common genetic blood disorders.

The condition manifests in varying severities, from beta-thalassemia intermedia, caused by certain genetic configurations such as two copies of the β+ gene or a combination of β0 and β+ genes, to beta-thalassemia minor, which arises from partial insufficiency of the HBB gene (Mitro et al., 2024). These disorders result in chronic anemia of varying severity, necessitating tailored treatment approaches for each phenotype (Musallam et al., 2021).

6.1 Treatment of β-Thalassemia

Patients with β-thalassemia, a hereditary blood disorder characterized by reduced or absent synthesis of the β-globin chain of hemoglobin, are typically classified as having **transfusion-dependent β-thalassemia (TDT)** or **non-transfusion-dependent β-thalassemia (NTDT)**. Those with severe forms of HbE/β-thalassemia or β-thalassemia major are categorized under TDT. These patients often present with severe anemia early in childhood, necessitating lifelong transfusion therapy to maintain normal hemoglobin levels and ensure survival (Musallam et al., 2021).

6.2 Diagnostic Approaches

Accurate diagnosis of thalassemia requires a combination of clinical evaluation and laboratory investigations. Key diagnostic tests include: **Quantification of Hemoglobin Fractions**: Measurement of **HbA2** and **HbF** levels aids in identifying abnormal hemoglobin patterns characteristic of thalassemia syndromes. **Hemoglobin Analysis**: Techniques such as high-performance liquid chromatography (HPLC) or capillary electrophoresis are used to confirm hemoglobin variants and levels. **Assessment of Red Blood Cell Indices**: Automated hematology analyzers measure parameters like mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), which are typically reduced in thalassemia. **Genetic Testing**: Molecular analysis can identify mutations in the β-globin gene, further confirming the diagnosis and aiding in subtype classification (Munkongdee et al., 2020).

6.3 Treatment Modalities

Managing β-thalassemia is complex and requires a multidisciplinary approach due to its chronic nature and associated complications. The treatment landscape includes: **Allogeneic Bone Marrow Transplantation (BMT)**: Currently, BMT is the only curative option for β-thalassemia. It involves replacing the defective bone marrow with healthy marrow from a compatible donor. However, the high costs and requirement for a suitable donor make it inaccessible for many patients (Suresh et al., 2023). **Blood Transfusion Therapy**: Regular transfusions are the cornerstone of treatment for TDT. These help maintain hemoglobin levels and prevent complications like growth retardation and cardiac issues. **Iron Chelation Therapy**: Repeated transfusions can lead to iron overload, necessitating the use of iron chelators such as **deferoxamine**, **deferiprone**, or **deferasirox** to prevent organ damage. **Folic Acid Supplements**: Folic acid supports red blood cell production and is commonly prescribed to thalassemia patients. **Gene Therapy**: Emerging gene-editing technologies, such as CRISPR-Cas9, hold promise as potential curative strategies by correcting the underlying genetic defect. **Combination Approaches**: Genetic counseling and prenatal screening are vital in preventing new cases. For at-risk couples, **prenatal diagnostic techniques** such as chorionic villus sampling (CVS) or amniocentesis can detect thalassemia in the fetus.

6.4 Challenges and Future Directions

The treatment of β-thalassemia remains challenging due to the high cost, limited availability of curative options, and long-term complications of existing therapies. Advances in gene therapy and improvements in transplantation techniques offer hope for better outcomes. Additionally, increasing awareness and implementing community-based screening programs can play a pivotal role in reducing the burden of the disease.

Congenital disorders, also known as congenital anomalies, refer to a broad spectrum of pathological conditions that develop during fetal development. These conditions may become evident at birth or manifest later in life, significantly impacting individuals' health and quality of life (Moorthie et al., 2018). As global maternal age continues to rise, congenital anomalies have emerged as a pressing public health concern. While the exact causes of many congenital disorders remain unknown, recognized factors include chromosomal abnormalities, environmental exposures during pregnancy, and single-gene mutations (Ahn et al., 2022). According to the World Health Organization (WHO), congenital anomalies affect 3% of live births globally, equating to one in 33 newborns. These conditions account for an estimated 295,000 neonatal deaths annually and leave millions more children with long-term disabilities, placing significant emotional, social, and economic burdens on families and healthcare systems (Ahn et al., 2022; Haghighi et al., 2021).

The rising average age of pregnancy has further amplified concerns surrounding congenital anomalies. In the United States, the average maternal age increased from 27.7 years in 2010 to 29.1 years in 2019, with a marked rise in the proportion of mothers aged 35 and older. Similar trends are observed in Europe, where the average maternal age increased from 28.8 years in 2013 to 29.4 years in 2019, and in South Korea, where births to mothers aged 35 or older rose sharply from 15.4% in 2009 to 33.4% in 2019 (Ahn et al., 2022). Among the most common congenital anomalies are Hirschsprung's disease (HD) and Anorectal Malformations (ARMs). HD is characterized by a lack of nerve cells in the colon, leading to functional blockages, while ARMs involve structural abnormalities of the anus that hinder the normal passage of feces (Diana Farmer, 2015).

The economic impact of congenital anomalies is immense. In the United States alone, healthcare costs associated with these conditions are estimated to exceed $2.6 billion annually. Importantly, over 70% of congenital anomalies are preventable, underscoring the potential of effective public health interventions (Ahn et al., 2022; Roy & Shengelia, 2016). Comprehensive Genetic Services (CGS) play a vital role in prevention and management, but their implementation in resource-constrained settings faces numerous challenges. Developing countries like Bangladesh, for instance, struggle with limited healthcare funding, societal barriers, and competing public health priorities. Bangladesh, with a population of 166 million, allocates only 3.6% of its GDP to public health. The country also has a high prevalence of home births (72%) and contraceptive use (61%), contributing to an infant mortality rate of 33 per 1,000 live births (Akter et al., 2022; Roy & Shengelia, 2016).

Cultural practices further exacerbate the burden of congenital disorders in certain regions. Consanguineous marriages, defined as unions between closely related individuals such as first or second cousins, are a significant risk factor for genetic conditions. In Bangladesh, 10% of marriages are between first cousins, and 8% are between more distant relatives (Shenk et al., 2016). These practices increase the likelihood of recessive genetic disorders such as bronchial asthma, hearing impairments, and congenital heart defects. Children born to related parents also face nearly double the risk of infant mortality (Hosen et al., 2021). Addressing congenital anomalies requires a multifaceted approach that includes improving healthcare infrastructure, increasing public awareness, and promoting culturally sensitive prevention strategies.

7. Treatment of Congenital Conditions and Contributing Factors to Their Development

Congenital conditions those present at birth can occur in any pregnancy. However, several factors significantly increase the likelihood of their occurrence, with a combination of genetic, environmental, and maternal health issues playing a key role. Understanding these factors and their implications is vital in managing and preventing congenital disorders. **Risk Factors for Congenital Problems:** The development of congenital problems can be influenced by various maternal health and environmental factors. According to the National Institute of Child Health and Human Development (NICHD), several modifiable and non-modifiable factors contribute to the risk of congenital conditions: **Lack of Folic Acid:** Folic acid is a crucial nutrient during pregnancy, especially in the first trimester. Deficiencies in folic acid can increase the risk of neural tube defects (NTDs), such as spina bifida and anencephaly. This is why folic acid supplementation is universally recommended for women before and during pregnancy. **Alcohol Consumption:** Drinking alcohol during pregnancy can lead to fetal alcohol spectrum disorders (FASDs), which can cause lifelong developmental delays, intellectual disabilities, and physical abnormalities. **Cigarette Smoking:** Smoking during pregnancy increases the risk of preterm birth, low birth weight, and congenital heart defects. It also impairs fetal lung development and increases the risk of respiratory problems after birth. **Drug Use:** The use of illicit drugs or prescription medications not approved during pregnancy (such as opioids or some anti-seizure medications) can lead to congenital abnormalities, growth restrictions, and withdrawal symptoms in newborns. **Infections:** Certain infections during pregnancy, such as rubella, cytomegalovirus, or Zika virus, can harm the developing fetus, leading to a range of congenital conditions including heart defects, hearing loss, and microcephaly. **Obesity:** Maternal obesity is associated with an increased risk of congenital defects, including neural tube defects, heart defects, and other developmental issues. It also increases the risk of gestational diabetes and hypertension, both of which can affect fetal health. **Uncontrolled Diabetes:** Poorly controlled diabetes in pregnancy can lead to several complications for the baby, including congenital heart defects, neural tube defects, and macrosomia (excessive birth weight). Managing blood sugar levels is essential for reducing these risks. **Environmental Challenges in Low-Resource Settings:** In many low-income countries (LICs) and low- and middle-income countries (LMICs), pregnant women face additional challenges that increase the risk of maternal and infant mortality. According to Haghighi et al. (2021), **extreme heat** a condition exacerbated by climate change can significantly impact maternal health. In regions with limited resources, pregnant women may not have access to cooling methods or air conditioning, increasing the risk of heat stress, dehydration, and related complications. This is particularly critical in settings where health care infrastructure is already fragile, and the capacity to manage heat-related illnesses is often insufficient. Furthermore, in such environments, access to proper prenatal care, nutrition, and emergency obstetric services may be limited, compounding the risks of adverse outcomes. **Diagnostic and Treatment Challenges for Congenital Conditions:** The diagnosis and treatment of congenital disorders vary depending on the specific condition, but the process is generally guided by a combination of physical examination and diagnostic tests. **Arterial Root Malformation (ARMs):** ARMs are typically diagnosed through a thorough physical examination by a pediatrician or neonatal specialist. In some cases, additional imaging may be used to confirm the diagnosis, especially if the condition affects internal structures like blood vessels or the heart. **Hirschsprung Disease (HD):** HD is a congenital condition that affects the large intestine, leading to severe constipation and intestinal dysfunction. Clinical indicators of HD include vomiting, delayed passage of meconium, severe intestinal infection, enterocolitis, and feeding intolerance (Diana Farmer, 2015). A rectal biopsy is the definitive diagnostic tool for HD, as it identifies the absence of ganglion cells in the colon, which is characteristic of the disorder. However, due to the high costs and limited availability of pathology services, particularly in LICs and LMICs, access to timely diagnosis may be restricted

(Diana Farmer, 2015). In these settings, early diagnosis and intervention may be delayed, potentially leading to severe complications. **Surgical and Non-Surgical Treatments for Congenital Conditions:** Some congenital conditions, such as **clubfoot**, **hernias**, and **cleft lip and palate**, can be managed effectively through surgical or non-surgical treatments. These interventions can dramatically improve the child's quality of life and reduce long-term disability. For example, clubfoot can often be corrected through non-invasive casting methods or surgery, and cleft lip/palate can be treated with reconstructive surgery to improve both function and appearance. However, more complex conditions, such as **Down syndrome**, congenital **heart defects**, and **neural tube defects**, may require lifelong management. These conditions can involve significant medical, social, and psychological challenges for both the child and their family. For instance, children with Down syndrome may need ongoing physical, occupational, and speech therapies to aid in their development, while congenital heart defects may require multiple surgeries and lifelong follow-up care. **Global Disparities in Treatment Access:** While some congenital conditions can be treated effectively with surgery or medication, others require lifelong care and support. According to the World Health Organization (WHO), global disparities in access to healthcare, including diagnostic tools and surgical interventions, pose significant barriers to the management of congenital disorders, particularly in low-resource settings. In many LICs and LMICs, there are insufficient trained healthcare professionals, surgical facilities, and access to specialized treatments. This lack of infrastructure results in poorer health outcomes for both mothers and babies, contributing to higher rates of maternal and infant mortality and long-term disability. Moreover, the social stigma associated with certain congenital conditions, such as Down syndrome or cerebral palsy, can further isolate families in these communities, limiting access to social support and early intervention programs.

8. Down syndrome

Down syndrome (DS), also known as trisomy 21, is the most common genetic condition caused by the presence of an extra copy of chromosome 21. This leads to the characteristic features associated with DS, which include intellectual disabilities, physical abnormalities, and an increased risk for certain health conditions (Akhtar et al., 2024). The condition is named after British physician John Langdon Down, who first described it in 1866, and was later identified as a chromosomal disorder by French geneticist Jérôme Lejeune in 1959 (Akhtar et al., 2024).

Chromosomally, individuals with Down syndrome have 47 chromosomes, rather than the typical 46, with the extra chromosome being a third copy of chromosome 21. As of 2000, researchers cataloged approximately 329 genes on chromosome 21, helping to clarify the genetic underpinnings of the disorder (National Down Syndrome Society [NDSS], 2024). Unlike many genetic conditions, Down syndrome does not follow a predictable autosomal dominant or recessive inheritance pattern. It arises randomly during the formation of reproductive cells, making its occurrence unpredictable, and can affect anyone, regardless of family history.

While the exact causes of Down syndrome are not entirely understood, it is associated with an increased risk for certain health conditions. Interestingly, despite an overall increased vulnerability to some cancers, individuals with Down syndrome face a significantly lower lifetime risk of most cancers, though they are more susceptible to childhood leukemias (Fries & Hermiston, 2023). Down syndrome is typically diagnosed during prenatal development, with an estimated occurrence of one case for every 1,000 births worldwide (Chen et al., 2022).

8.1 Physical and Cognitive Challenges

The disabilities associated with Down syndrome can vary in severity, but common challenges include visual impairments, hearing loss, hyperactivity, learning difficulties, and delayed speech and language development (Islam et al., 2022). In addition, individuals with Down syndrome are at higher risk for respiratory infections, which remain the leading cause of death in children with DS. However, as individuals age, dementia becomes the primary cause of death for approximately 70% of individuals with Down syndrome aged 40 and above (Chen et al., 2022).

Life expectancy for individuals with Down syndrome has greatly improved over the past century, rising from an average of 9 years in the 1920s to approximately 60 years today. Advances in healthcare, including better infection control, surgical interventions for heart defects, and improved general care, have contributed to this remarkable increase in life expectancy (Shields, 2021). It is expected that, within a generation, individuals with Down syndrome may experience life expectancies closer to those of the general population (Shields, 2021).

8.2 Prevalence and Global Impact

According to the World Health Organization (WHO), approximately 5,000 babies with Down syndrome are born in Bangladesh every year, with a total population of over 200,000 individuals living with the condition in the country (Islam et al., 2022). In Australia, about 11,000 people live with Down syndrome, and in the United States, the number is approximately 250,000 (Shields, 2021). In terms of worldwide prevalence, an estimated 3,000 to 5,000 infants are born with Down syndrome annually (United Nations, 2022).

8.3 Sex-Based Differences in Down syndrome

Notably, there are some gender-based differences in the manifestation of Down syndrome. Studies have shown that while male individuals with Down syndrome generally have a longer life expectancy, females with DS tend to exhibit fewer repetitive and externalizing behaviors than their male counterparts (Islam et al., 2022). This observation highlights the importance of considering gender-specific needs and challenges in the care and treatment of individuals with Down syndrome.

8.4 Health Complications and Management

Congenital heart defects are present in approximately 40-55% of babies born with Down syndrome, making cardiovascular care a critical aspect of managing the condition (Shields, 2021). Respiratory illnesses, such as pneumonia, are common causes of hospitalization in children and are often fatal in older individuals with Down syndrome (Shields, 2021). Early intervention in the form of physical therapy, speech therapy, and specialized educational programs can help improve quality of life and address developmental delays (Fries & Hermiston, 2023).

Adults with Down syndrome are at a higher risk of developing dementia. Research shows that while the general population has a 20–35% chance of developing dementia by age 75, adults with Down syndrome have a 45% chance by age 55 and an 80% chance by age 65 (Shields, 2021). This stark contrast underscores the importance of specialized care for older individuals with Down syndrome.

8.5 Screening and Diagnosis

For expectant parents, screening for Down syndrome is an essential part of prenatal care. The American College of Obstetricians and Gynecologists recommends that all pregnant women, regardless of age, be offered the opportunity to undergo screening and diagnostic tests for Down syndrome. Screening tests, while not conclusive, can help assess the likelihood of the condition, while diagnostic tests can provide a definitive diagnosis (American College of Obstetricians and Gynecologists, 2023).

8.6 Treatment

Currently, there are no treatments for Down syndrome (DS) that are directly based on an in-depth understanding of the disease's molecular pathology (Antonarakis et al., 2020). This highlights the pressing need for continued research to gain a better understanding of the biological mechanisms underlying the diverse symptoms and characteristics of the condition. Such insights are crucial for the development of effective therapies (Antonarakis et al., 2020).

It is important to recognize that treatment for Down syndrome is typically multidisciplinary, and while a cure remains elusive, management focuses on alleviating symptoms and enhancing quality of life (Faisal Akhtar et al., 2024). Treatment plans are highly individualized, taking into account the unique physical, cognitive, and emotional strengths and limitations of each person. As a result, people with DS may have varied needs, and a one-size-fits-all approach is not feasible.

Several therapeutic interventions are commonly used in the management of DS, including physical therapy, speech-language therapy, occupational therapy, and behavioral or emotional therapies. These interventions are tailored to support the development of functional skills and to improve daily living activities. For optimal growth and development, individuals with Down syndrome benefit from a balanced diet, regular physical activity, and physical therapy. It is worth noting that feeding issues, which are common among infants with DS, are often addressed following heart surgery, a procedure frequently necessary in early childhood due to congenital heart defects (Faisal Akhtar et al., 2024).

These therapies, medical care may include the use of medications, supplements, and assistive devices to address specific health challenges associated with Down syndrome. The course of treatment can vary greatly, as individuals with DS can experience a wide range of health and developmental outcomes. Some may require extensive medical care from birth, while others may experience few health problems. As individuals with DS age, some may continue to require social and medical support throughout adulthood, while others may live relatively independent lives (Antonarakis et al., 2020).

9. Muscular Dystrophy

Muscular dystrophy (MD) is a group of genetic disorders characterized by progressive muscle weakening and degeneration. It is caused by mutations in the genes responsible for muscle structure and function, leading to the gradual loss of muscle fibers. MD affects skeletal and cardiac muscles, and over time, individuals may lose their ability to walk and experience other systemic complications. MD is not contagious and is not caused by injury or physical activity. There are more than 30 distinct types of muscular dystrophy, each with its unique patterns of muscle involvement, severity, and onset. These include Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), Emery-Dreifuss muscular dystrophy (EDMD), and myotonic dystrophy, among others (LaPelusa et al., 2024).

9.1 Prevalence and Global Impact

Globally, muscular dystrophy affects approximately 1 in 5,000 to 10,000 individuals (LaPelusa et al., 2024). In the United States, it is estimated that about 250,000 people are living with some form of MD. The disease can manifest at any age, but it is most often diagnosed in childhood. The progression and severity of MD depend on the specific type and the underlying genetic mutation (LaPelusa et al., 2024).

9.2 Genetic Basis of Muscular Dystrophy

Muscular dystrophy is inherited in three primary ways: X-linked, autosomal dominant, and autosomal recessive. X-linked MD, the most common form, affects males more frequently due to the nature of X chromosome inheritance. The condition is caused by defects in genes that produce proteins crucial for maintaining muscle fiber integrity. In the case of Duchenne muscular dystrophy (DMD), the defect is in the dystrophin gene, leading to a complete absence of dystrophin protein, which is essential for muscle cell stability.

Duchenne muscular dystrophy (DMD) is the most severe form of muscular dystrophy. It affects approximately 1 in 5,000 to 1 in 6,000 live male births worldwide and is caused by mutations in the dystrophin gene, which is one of the largest human genes, comprising 79 exons and over 2.4 million base pairs. DMD leads to the complete loss of dystrophin, resulting in progressive muscle degeneration, starting in early childhood. Children with DMD typically exhibit difficulty climbing stairs, frequent falls, and a characteristic "duck-like" gait. By the age of 10-12 years, most affected individuals will require a wheelchair, and by their late teens or early twenties, respiratory and cardiac complications often necessitate additional medical support (Duan et al., 2021).

9.3 Duchenne Muscular Dystrophy (DMD)

DMD is caused by mutations in the dystrophin gene, which encodes a protein that plays a critical role in stabilizing the muscle cell membrane during contraction. Without dystrophin, muscle fibers become damaged, leading to muscle weakness and, over time, muscle atrophy. DMD is an X-linked recessive condition, meaning that it predominantly affects males. Females can be carriers but are typically unaffected, as they have a second, functioning X chromosome that compensates for the defective one. However, in rare instances, females can be affected if one of their X chromosomes carries a mutation or if X-inactivation occurs abnormally (LaPelusa et al., 2024).

In individuals with DMD, symptoms usually appear between the ages of 2 and 3 years, with affected children struggling with basic motor skills such as running or climbing stairs. As the disease progresses, the loss of muscle function leads to difficulty with breathing and swallowing. Despite advances in medical care, most individuals with DMD experience a significantly reduced lifespan, with many surviving into their 20s or early 30s, often succumbing to heart or respiratory failure (Duan et al., 2021). The dystrophin gene, with its extensive size and complexity, is known to harbor a large number of mutations, and more than 7,000 distinct mutations have been identified in individuals with DMD (Bez Batti Angulski et al., 2023; Łoboda & Dulak, 2020).

9.4 Historical Context

Muscular dystrophy was first described by Edward Meryon in 1807, but it was not until the 19th century that the disease was characterized in detail by Guillaume B.A. Duchenne de Boulogne, who studied the condition extensively. Duchenne's research on "progressive muscular atrophy with degeneration" eventually led to the condition being named Duchenne muscular dystrophy in his honor (Elangkovan & Dickson, 2021; Sun et al., 2020).

9.5 Female Carriers and Rare Cases

While Duchenne muscular dystrophy is most commonly associated with males, females can also be affected in rare cases. This occurs when there is an X-autosome translocation or abnormal X-inactivation, resulting in a loss of the protective effect typically seen in female carriers. In such cases, a genetic imbalance in the cells can lead to severe manifestations of the disease (LaPelusa et al., 2024). The prevalence of DMD in males is relatively consistent across different geographical regions, with less than 10 cases per 100,000 males (Duan et al., 2021).

9.6 Treatment of Muscular Dystrophy

Muscular dystrophy, a group of genetic disorders characterized by progressive muscle weakness and degeneration, currently has no known cure (LaPelusa A et al., 2024). Despite this, medical advancements have provided various treatments aimed at managing symptoms, slowing disease progression, and improving quality of life. These treatments address muscle weakness, mobility challenges, and secondary complications. Corticosteroids, such as prednisone and deflazacort, are often prescribed to enhance muscle strength and slow degeneration, providing temporary improvements in functionality. Rehabilitation therapies, including physical therapy, occupational therapy, and speech therapy, play a critical role in preserving mobility, maintaining flexibility, and supporting communication or swallowing difficulties associated with weakened muscles. For respiratory complications arising from weakened diaphragm muscles, ventilatory support, such as non-invasive ventilation or mechanical aids, can be life-saving. Emerging treatments like gene therapy offer hope for targeting the underlying genetic mutations responsible for muscular dystrophy. These therapies, along with advancements in stem cell research, aim to repair or regenerate damaged muscle tissues. Holistic care approaches, combining medical, physical, and technological interventions, are crucial in enhancing the lives of individuals with muscular dystrophy while research continues to advance toward potential cures.

10. Diabetes

Diabetes mellitus, a chronic metabolic disorder, arises when the pancreas fails to produce sufficient insulin or the body cannot effectively utilize the insulin it produces (Magliano DJ & Boyko EJ, 2021). Insulin is vital for glucose uptake into cells, which serves as a primary energy source. The condition, which affects people of all ages, can result from several factors, including insulin resistance, autoimmune responses, hormonal imbalances, pancreatic damage, or genetic mutations. Since the discovery of insulin by Dr. Frederick Banting in 1921, ongoing research has significantly enhanced the quality and availability of insulin treatments (M. S. Rahman et al., 2021).

There are two primary forms of diabetes. Type 1 diabetes, an autoimmune condition, occurs when the immune system mistakenly attacks insulin-producing beta cells in the pancreas, leading to complete insulin deficiency. It typically manifests in childhood or adolescence and necessitates lifelong insulin therapy. Type 2 diabetes, more common and often associated with obesity and sedentary lifestyles, results from a combination of insulin resistance and the gradual failure of pancreatic beta cells. It is strongly influenced by genetic, environmental, and lifestyle factors. Type 2 diabetes also contributes to a significant public health burden due to its association with complications like cardiovascular disease and hepatocellular carcinoma (Halder et al., 2024).

Globally, diabetes prevalence is rising, with the International Diabetes Federation (IDF) reporting 537 million cases in 2021, nearly half of which remain undiagnosed (Ong et al., 2023). In Bangladesh, diabetes prevalence increased from 5% in 2001 to nearly 14% in 2017, reflecting the profound impact of urbanization and lifestyle changes (M. B. Hossain et al., 2022). The condition disproportionately affects economically active age groups, with the highest prevalence among individuals aged 65-74 as of 2018. Regional disparities in Bangladesh reveal lower rates in Rangpur and Khulna, likely due to differing economic and lifestyle factors, whereas urban areas like Dhaka have seen significant increases in diabetes rates (M. A. B. Chowdhury et al., 2022).

Diabetes is diagnosed using plasma glucose tests, including fasting plasma glucose (FPG), oral glucose tolerance tests (OGTT), or HbA1c measurements, which assess average blood sugar levels over three months (Elsayed et al., 2023). Early detection is critical to preventing complications and managing prediabetes, a precursor to type 2 diabetes.

Management strategies for diabetes emphasize a combination of medical interventions and lifestyle modifications. Insulin therapy is indispensable for type 1 diabetes, while type 2 diabetes management often begins with lifestyle changes such as increased physical activity, healthy diets, and weight loss, alongside oral hypoglycemic agents like metformin. Advanced cases may also require insulin supplementation. Preventive measures for type 2 diabetes include regular exercise, limiting alcohol, avoiding smoking, managing stress, and consuming a balanced diet rich in whole grains and lean proteins. Despite these measures, diabetes imposes a substantial economic burden, with type 2 diabetes patients incurring average annual costs of $865, primarily for medications and hospitalizations (Afroz et al., 2019).

The rising global prevalence of diabetes underscores the urgent need for public health initiatives, improved diagnostic access, and ongoing research into novel treatments and preventive strategies. By addressing lifestyle factors and investing in early detection and education, significant progress can be made in mitigating the impact of this pervasive condition.

10.1 Improvement of Treatment

Genetic factors play a pivotal role in the development and management of diabetes, a complex condition that manifests differently in each individual. This variability necessitates highly personalized approaches to treatment and management, which may include blood sugar monitoring, insulin therapy, oral medications, and lifestyle interventions such as healthy eating, regular physical activity, and weight management (Feingold KR et al., 2024; Sapra A & Bhandari P., 2024).

Treatment strategies differ based on the type of diabetes but often involve a combination of medication and lifestyle adjustments. For individuals with type 1 diabetes, insulin is indispensable for survival, as it helps maintain blood sugar levels within a healthy range. In contrast, for type 2 diabetes, lifestyle modifications such as adopting a balanced diet, engaging in regular exercise, and achieving weight loss are critical. These changes are often complemented by medications like metformin, sulfonylureas, or sodium-glucose co-transporters type 2 (SGLT-2) inhibitors to help manage blood sugar levels effectively (Mayo Clinic, 2024).

Encouragingly, research highlights the possibility of remission for some individuals with type 2 diabetes. For instance, a study by Captieux et al. (2021) reported that approximately 5% of participants equating to 7,710 individuals achieved remission. This was defined as maintaining hemoglobin A1c levels below 48 mmol/mol for over a year without the use of glucose-lowering medications (Riddle et al., 2021).

Although diabetes cannot currently be cured or completely eradicated, advancements in treatment and management strategies enable many individuals to achieve significant improvement or even reverse their condition, enhancing their overall quality of life.

11. Cancer: A Multifaceted Global Challenge

Cancer is a complex disease characterized by the uncontrolled proliferation of cells, which may invade surrounding tissues and metastasize to distant body sites. According to the World Health Organization (WHO), cancer was responsible for approximately 9.96 million deaths in 2020, accounting for one in six deaths globally, making it the second leading cause of mortality worldwide (Frick et al., 2023; Sung et al., 2021). In Bangladesh, the burden of cancer is significant, with over 200,000 individuals diagnosed annually, and approximately 150,000 succumbing to the disease each year (Alam, 2020). A 2013 study estimated between 1.3 to 1.5 million cancer patients in the country, with 200,000 new cases emerging each year (Alam, 2020). Despite a paucity of comprehensive scientific data, reports from the National Institute of Cancer Research and Hospital highlight the urgent need for effective interventions.

Table 1. Classification of Genetic Disorders with Representative Disease Examples

Name	Chromosomal Disorders	Single-Gene Disorders	Complex Disorders
1.	Down syndrome	Sickle cell anemia	Alzheimer's disease
2.	Klinefelter syndrome	Thalassemia	Cancer
3.	Triple X syndrome	Cystic fibrosis	Diabetes
4.	Turner syndrome	Huntington's disease	Hypercholesterolemia
5.	FragileX syndrome.	Hemophilia	Coronary artery disease
6.	Trisomy 18	Phenylketonuria (PKU)	Arthritis

Table 2. Prevalent Genetic Disorders in Bangladesh and Associated Health Challenges

Disease Category	Specific Diseases	Prevalence	Impact
Hemoglobinopathies	Thalassemia, Sickle cell anemia	High	Anemia, fatigue, pain
Congenital Heart Defects	Atrial septal defect, ventricular septal defect, tetralogy of Fallot	Moderate	Heart problems, breathing difficulties
Muscular Dystrophy	Duchenne muscular dystrophy, Becker muscular dystrophy, spinal muscular atrophy	Moderate	Muscle weakness, difficulty walking
Cystic Fibrosis	Cystic fibrosis	Low	Respiratory problems, digestive issues
Phenylketonuria (PKU)	PKU	Low	Intellectual disability, seizures

11.1 Prevalence and Types of Cancer

The term "cancer" encompasses a wide variety of malignancies, classified based on their origin and affected organs, such as stomach, liver, prostate, colon, lung, and breast cancers. Globally, breast cancer is the most frequently diagnosed cancer among women, accounting for 24.2% of female cancer cases, with approximately 2.1 million new diagnoses each year (Francies et al., 2020). Lung cancer, responsible for 18.0% of all cancer-related deaths, remains the leading cause of cancer mortality, followed by stomach, liver, and colon cancers (Sung et al., 2021).

11.2 Genetic Factors in Cancer Development

Hereditary cancer genes play a pivotal role in cancer susceptibility and familial transmission. Over the past two decades, significant progress has been made in identifying and characterizing these genes, including tumor suppressors, oncogenes, and DNA repair genes. Mutations in these genes disrupt cellular regulation, promoting carcinogenesis and increasing an individual's cancer risk.

High-penetrance genes such as **BRCA1** and **BRCA2** are associated with breast cancer in both men and women. Other critical genes include **MLH1**, **MSH2**, and **MSH6**, which are linked to up to a 70% risk of endometrial cancer and hereditary nonpolyposis colon cancer (HNPCC) (Ramsoekh et al., 2009). Syndromic cancers such as medullary thyroid cancer, associated with the **RET** oncogene in multiple endocrine neoplasia type 2, further illustrate the genetic basis of certain malignancies. Moderate-penetrance genes like **ATM**, **CDKN2A**, and **BARD1** have also been implicated in common cancers, including breast and ovarian cancers.

11.3 Viral Contributions to Cancer

Infectious agents, particularly DNA viruses, significantly contribute to cancer development. Chronic hepatitis B virus (HBV) infection induces necro-inflammatory processes in the liver, increasing the risk of genetic mutations and hepatocellular carcinoma (HCC). HCC is the third leading cause of cancer-related deaths globally and the sixth most common cancer type (Panneerselvam et al., 2023; Halder et al., 2024).

11.4 Addressing the Global Cancer Burden

Cancer remains a critical public health challenge worldwide, requiring advancements in prevention, early detection, and treatment. Enhanced understanding of genetic and environmental factors, along with targeted therapies, can improve outcomes and reduce the global cancer burden. In regions like Bangladesh, where cancer prevalence is high, investment in healthcare infrastructure, research, and education is essential to mitigate this growing crisis.

Understanding the genetic factors of cancer is crucial for effective prevention, treatment planning, and assessing its familial implications. This knowledge helps identify individuals at higher risk due to genetic predisposition or family history, facilitates early detection through enhanced surveillance, and enables tailored therapeutic approaches.

World Cancer Day serves as a global platform to raise awareness and advocate for cancer prevention, diagnosis, and treatment. However, Bangladesh faces significant challenges in providing adequate cancer care. Barriers include high treatment costs, misdiagnoses, flawed treatment plans, and a shortage of trained healthcare professionals and specialized facilities.

Currently, only one-third of cancer patients in Bangladesh have access to essential services such as primary care, treatment, and routine follow-ups. This is largely due to limited diagnostic infrastructure, lack of awareness, and prohibitively expensive treatments (Alam, 2020). According to the country has only one palliative care facility, four specialized hospitals, and a single radiotherapy center. The absence of a national protocol for cancer management and insufficient skilled manpower further compounds the crisis.

Addressing these gaps is imperative for improving cancer care outcomes and ensuring equitable access to life-saving treatments in Bangladesh.

12. The current condition of genetic counseling and testing in Bangladesh

The current state of genetic counseling and testing in Bangladesh highlights both challenges and opportunities in addressing hereditary diseases. Genetic counseling is pivotal for providing patients with insights into their conditions, supporting diagnosis and management, offering therapy when available, and assessing familial risks for genetic disorders. However, a significant portion of the Bangladeshi population remains unaware of the genetic risks posed by practices such as consanguineous marriages. Counseling before marriage is a critical preventive measure to mitigate these risks, as evidenced by successful awareness campaigns in other countries. For instance, premarital counseling programs have achieved remarkable reductions in the incidence of β-thalassemia, with a 95% decrease in affected births in regions like the Middle East. Similar successes in Greece, Italy, and Iran underscore the transformative potential of such initiatives. In Bangladesh, however, the implementation of comparable programs remains limited, stymied by cultural norms, insufficient awareness, and inadequate infrastructure.

The limited availability of genetic testing infrastructure exacerbates the challenges in combating hereditary diseases. Most hospitals in Bangladesh lack the equipment for advanced genetic testing, restricting access to essential prenatal screenings for congenital anomalies such as Down syndrome. Premarital screening emerges as a more feasible alternative, particularly in light of resource constraints. Moreover, newborn screening (NBS), which is instrumental in detecting treatable genetic disorders early, faces significant barriers to adoption in Bangladesh. While widely implemented in high-income countries, NBS programs in low- and middle-income countries (LMICs) like Bangladesh are hindered by socioeconomic challenges, inadequate health policies, and cultural factors such as the preference for home births. Although the government has piloted NBS initiatives, particularly for congenital hypothyroidism, the absence of a robust national program limits their effectiveness.

Molecular genetic testing in Bangladesh remains concentrated in public universities and specialized institutions like BIRDEM and ICDDRB. A few private hospitals and diagnostic centers are beginning to offer comprehensive testing, but these services are neither widespread nor affordable for most citizens. The reliance on external institutions for complex tests underscores the need for an autonomous, government-supported molecular testing infrastructure. Efforts are underway to address this gap, but significant investments are required to make genetic testing accessible nationwide.

Another critical need is the establishment of a national genetic disease database to support disease management and research. While genetic databases such as OMIM and the Human Gene Mutation Database provide invaluable resources globally, Bangladesh lacks a localized database to document the prevalence and transmission of genetic disorders within its population. Countries participating in initiatives like the Genome Asia 100K Project such as China, India, and Pakistan are advancing genome-wide association research through the collection of population-specific data. In Bangladesh, the absence of such a resource hampers research and complicates healthcare delivery, particularly in rural areas where access to diagnostic methods is limited. A genetic disease database tailored to Bangladesh would enable better genetic counseling, mutation analysis, and the development of molecular diagnostic tools. It would also facilitate genotype-phenotype correlation studies, benefiting not only the healthcare sector but also researchers investigating region-specific genetic variations.

13. Conclusion

Genetic disorders in resource-constrained settings like Bangladesh are both a challenge and an opportunity to improve healthcare equity globally. Establishing a genetic disease registry, neonatal screening programs, and strengthening genetic counseling are critical steps. These initiatives, coupled with targeted healthcare training and public awareness campaigns, can transform outcomes for affected populations. Bangladesh's unique challenges such as limited infrastructure and lack of universal health coverage highlight the need for international collaborations and strategic investments in genetic research and healthcare delivery. By prioritizing these efforts, Bangladesh can reduce disparities, improve maternal and child health outcomes, and serve as a model for similar low- and middle-income countries. Genetic disorders holistically will not only save lives but also foster a more inclusive approach to global healthcare innovation.

Author contributions

T.J. conceptualized the study and developed the methodology. T.H., A.I., and M.U.P. prepared the original draft and contributed to its review and editing. R.M., S.A., and A.R. conducted data analysis and further refined and edited the manuscript.

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