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A STUDY OF PATIENTS SUFFERING FROM SICKLE CELL DISORDER

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ABSTRACT

Screening for sickle cell disease and thalassemia is an important part of preventative healthcare that tries to help those at risk by finding them early so they can get treatment and have better results. Thalassemia and sickle cell condition are both hereditary blood illnesses that have different biological roots but may cause serious health problems if left untreated. Screening allows for the systematic identification of people who contain the genetic variants linked to certain ailments. This allows for genetic counseling, early medical intervention, and even prevention in some situations. Standard screening procedures for sickle cell disease include looking for aberrant hemoglobin levels, especially hemoglobin S, a marker of the disease. Molecular genetic testing, hemoglobin electrophoresis, and high-performance liquid chromatography (HPLC) are some of the methods used to decipher the genetic secrets of sickle cell disease. Screening may take place in a variety of contexts, such as preconception counseling, regular health checkups, and screenings for newborns. In order to make educated choices about family planning and individualised medical treatment, it is necessary to identify people who have sickle cell trait or sickle cell disease. In a similar vein, thalassemia screening looks for people whose genes alter their ability to make certain types of hemoglobin. Molecular genetic testing, hemoglobin electrophoresis, and complete blood counts are the basic screening tools for the two main kinds of thalassemia, alpha and beta. People might be categorized as carriers (thalassemia trait) with minor symptoms or as having thalassemia major or intermedia with moderate to severe symptoms based on the results of the test. Screening allows for early detection, which in turn allows for medical treatment options to be tailored, difficulties to be anticipated, and genetic counseling to influence reproductive choices. In addition to making diagnoses, screenings may lead people in need to more extensive forms of treatment and assistance.

Keywords: Patients Suffering, Sickle Cell Disorder, thalassemia, treatment.

INTRODUCTION

Thalassemia is considered one of the most challenging and controversial hematologic diseases. β-thalassemia is an autosomal recessive disorder characterized by microcytosis and hemolytic anemia. This occurs due to a reduction in the synthesis of hemoglobin, namely in the b-globin chain. This condition affects more than 150 million people in the Mediterranean area, West Africa, and a large part of Asia. Over 180 distinct -thalassemia mutations have been discovered so far. However, in the majority of populations and ethnic groups, the illness is mostly caused by a smaller range of alleles that result in the deactivation of the majority of b-globin genes. Turkey, a prominent Middle Eastern country, encompasses the whole of medieval Asia Minor (Anatolia) as well as a small portion of Eastern Thrace in Europe. An intercontinental gathering spot for individuals hailing from Asia and Europe. The location has facilitated extensive interaction among individuals from many races and cultural backgrounds from the earliest stages of human habitation. Beta-thalassemia in Turkey is distinguished by a gene frequency of 2% and encompasses a wide spectrum of clinical symptoms ranging from moderate to severe. Regular blood transfusions are necessary for individuals with major b-thalassemia.

Recent molecular examinations of genes in Turkey have identified over 30 different variants associated with b-thalassemia. Thalassemias are the most prevalent single-gene illnesses affecting public health in India. Over the last thirty years. The use of regular transfusion therapy and iron chelation has significantly improved the quality of life for those suffering from thalassemia, resulting in a substantial increase in their average lifespan from a few years to 55. An major public health concern in India is haemoglobinopathies, a set of genetic blood diseases, which are mostly reliant on strict adherence to recommended medication. Based on a population of 1 billion in the year 2000 and a birth rate of 25 per thousand, it has been estimated that India will have 45 million individuals carrying haemoglobinopathies and 15,000 infants with haemoglobinopathies per year. The prevalence of haemoglobinopathy carriers varies from 3% to 17% among different Indian communities. Approximately 5.35 percent of the Indian population is believed to possess the genetic makeup for the three most prevalent abnormal forms of hemoglobin, namely sickle cell anemia, hemoglobin D, and hemoglobin E. Haemoglobinopathies exert a significant burden on India.

Hemoglobin, a vital protein composed of an iron molecule called "heme" and a protein component called "globin," plays a critical role in the transportation of oxygen into red blood cells. Errors in the coding DNA of hemoglobin are responsible for both sickle cell disease and thalassemia. These disorders may cause fatigue, jaundice, and mild to severe pain episodes. The defective gene is inherited by each new generation from both sets of parents, and it is transmitted down through generations. The subsequent diseases may be quite severe, sometimes even fatal.

During the early 1900s, scientists discovered "peculiar, elongated sickle-shaped erythrocytes," which were subsequently recognized as the defining characteristic of sickle cell disease, a blood cell abnormality. Subsequent investigations conducted by a distinguished pathologist revealed that the agony experienced by individuals with sickle cell disease was a result of the constriction of capillaries. Hemoglobin S, the variant type of hemoglobin identified by Dr. Linus Pauling in 1949, is the primary cause of sickle cell disease. Scientists identified that the presence of sickled hemoglobin is a result of a single amino acid error in hemoglobin S. This finding establishes it as one of the first disorders to be fully elucidated at the molecular level.

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Despite having identified the core molecular cause of the condition about fifty years ago, there has been a lack of significant progress in using this information to improve patient therapy. This serves as an indicator of the inherent difficulty in treating the illness. However, this is mostly due to the fact that sickle cell disease has a greater impact on individuals belonging to racial and ethnic minority groups in the United States. These groups have traditionally been inadequately represented in health research and treatment. The recognition of the racial discrepancy in healthcare, shown by the mistreatment of these patients, was not publicly accepted until the civil rights movement in the early 1970s. The formation of the Sickle Cell Disease Association of America was a direct reaction to the situation. This group actively contributed to the enactment of the Sickle Cell Anemia Control Act in 1972. The legislation provided government financing for the prevention, diagnosis, and treatment of sickle cell disease.

THALASSEMIA

Thalassemia is a hereditary blood illness defined by the generation of defective hemoglobin, which results in inadequate synthesis of red blood cells and consequent anemia. This illness mostly affects persons of Mediterranean, African, Middle Eastern, and Southeast Asian ancestry. The term "thalassemia" originates from the Greek terms "thalassa," which translates to sea, and "emia," which refers to blood. The condition originally had a high occurrence among communities living in the vicinity of the Mediterranean Sea, where it was first recognized.

Thalassemia causes an interruption in the usual production of hemoglobin, the protein that carries oxygen in red blood cells. Thalassemia is characterized by an unequal synthesis of the alpha and beta protein chains that make up hemoglobin. Alpha thalassemia is caused by mutations in the genes that control the production of alpha globin, while beta thalassemia is caused by mutations in the genes that regulate the synthesis of beta globin.

Thalassemia may manifest with a broad spectrum of severity, ranging from moderate anemia to potentially fatal consequences. Thalassemia major, in its most severe manifestation, need frequent blood transfusions for afflicted patients to maintain their lives. Thalassemia intermedia is a condition that is between the main and minor kinds, characterized by symptoms that are intermediate in severity. Thalassemia minor, sometimes referred to as thalassemia trait, generally results in a moderate form of anemia and is frequently overlooked.

Thalassemia is caused by mutations in certain genes found on chromosomes 11 and 16. These genes are responsible for producing the alpha and beta globin chains. Thalassemia is inherited in an autosomal recessive fashion, which requires both parents to possess a defective gene for their children to be impacted. Individuals with thalassemia trait, often known as carriers of thalassemia, typically do not exhibit severe symptoms but may transmit the faulty gene to their offspring.

Thalassemia has a wide range of clinical presentations, with symptoms appearing at various points during a person's life. Infants with more severe conditions may exhibit signs such as stunted development, yellowing of the skin and eyes, and an enlarged spleen. With advancing age, people may encounter symptoms such as tiredness, debility, and heightened vulnerability to infections as a result of their blood's insufficient ability to transport oxygen.

The diagnosis of thalassemia entails a comprehensive evaluation that includes clinical evaluations, laboratory testing, and genetic analysis. Thalassemia-related abnormalities may be identified using blood tests, such as a complete blood count (CBC) and hemoglobin electrophoresis. Genetic testing is essential for verifying the diagnosis and identifying the precise subtype of thalassemia. Couples with a familial background of thalassemia may get prenatal testing, which allows them to make well-informed choices on family planning.

The management techniques for thalassemia focus on mitigating symptoms, enhancing quality of life, and averting consequences. Blood transfusions are a vital medical treatment for persons suffering with thalassemia major, as they effectively maintain sufficient amounts of hemoglobin and reduce symptoms associated with anemia. Regular transfusions may result in an excessive accumulation of iron in the body, which requires the implementation of chelation treatment to eliminate the surplus iron and safeguard against organ harm.

Stem cell transplantation, or bone marrow transplantation, provides a promising remedy for thalassemia by substituting faulty bone marrow with healthy cells from a donor. The efficacy of this technique is most when conducted during the early stages of life. However, it is accompanied by inherent hazards and difficulties, such as the need to locate a compatible donor and handle any consequences.

IMPACT OF THALASSEMIA

Thalassemia, a hereditary blood illness that originates from the complex molecular processes involved in hemoglobin production, has a significant and enduring effect on people, families, and communities. This intricate illness, distinguished by the synthesis of aberrant hemoglobin, results in a variety of clinical symptoms that span from moderate anemia to severe consequences that may be life-threatening. Thalassemia has a profound impact on the physical health, mental well-being, and economical elements of people afflicted.

Physiologically, thalassemia primarily affects the body's capacity to create fully functioning red blood cells. Hemoglobin, the vital protein accountable for the transportation of oxygen, is adversely affected by genetic abnormalities, resulting in a reduced ability to convey and distribute oxygen to tissues and organs. This leads to chronic anemia, a disease marked by weariness, weakness, and a continuous feeling of lethargy. The physiological ramifications go beyond simple pain, into everyday life as a persistent reminder of the body's ongoing battle to maintain balance.

Thalassemia major, in its most severe form, places a constant and demanding load on persons afflicted by it, necessitating frequent blood transfusions to offset the faulty hemoglobin. Although these transfusions provide temporary relief from anemia-related symptoms, they also introduce a new set of difficulties. Iron overload, a predictable outcome of recurring transfusions, poses a risk to critical organs such as the heart, liver, and endocrine glands. If not addressed, the subsequent problems may lead to organ failure and greatly diminish life expectancy.

Thalassemia has a profound effect not only on the medical well-being of people, but also on their mental state as they struggle with the difficulties presented by the condition. During the early stages of life, children with thalassemia have a significant psychological burden due to the challenges of managing medical procedures, frequent hospital visits, and the continual awareness of their own fragility. The ability to face these problems with emotional resilience is a clear indication of the fortitude possessed by people and their families, who often establish close-knit support systems to endure the difficulties of chronic disease.

As people go into adolescence and adulthood, the emotional consequences persist and change over time. The responsibility of overseeing a persistent ailment coincides with the inherent need for autonomy and a feeling of regularity. Managing the requirements of medical care with the pursuit of education, job goals, and personal relationships requires skillful multitasking. The prospect of a lifetime medical treatment plan and the ambiguity surrounding future well-being may have a negative impact on one's goals, requiring not just physical strength but also a strong mental and emotional support network.

The condition of thalassemia has a significant and wide-ranging influence on the families of affected persons. The fluctuating emotions of optimism and pessimism are experienced with every medical intervention, and the additional burden of financial pressure arises from the need to maintain a routine of blood transfusions, drugs, and supplementary therapies, which further complicates the difficulties. The responsibility of providing care, which is often taken on by parents and family members, requires a careful equilibrium between offering assistance and promoting self-reliance. The deep emotional commitment expected from families highlights the need for all-encompassing support services that go beyond the therapeutic domain.

APPLICATION OF THALASSEMIA

Thalassemia is a hereditary blood illness that involves the creation of defective hemoglobin. It has important implications in many areas of medical research, including diagnostics, therapy, genetics, and public health. The use of thalassemia-related information and technology has extensive implications, including patient treatment, research efforts, and preventative measures. The complexity of this condition has led to the emergence of new ideas and progress in several important domains, influencing the way thalassemia is managed and contributing to wider improvements in the field of hematology.

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Diagnostics and Screening: An important use of thalassemia-related information is in the field of diagnostics and screening. The development of accurate and dependable diagnostic techniques has fundamentally transformed the process of identifying and categorizing thalassemia. Hemoglobin electrophoresis, high-performance liquid chromatography (HPLC), and genetic testing are essential tools for detecting various forms of thalassemia and identifying the precise genetic mutations responsible. These diagnostic methods assist in both establishing the existence of thalassemia and customizing treatment approaches according to the unique genetic changes found in a person.

Furthermore, the implementation of thalassemia screening programs has been crucial in locations with a high frequency of the disease and among people with a recognized genetic risk. Through the use of focused screening, healthcare practitioners may detect individuals who have thalassemia characteristics, enabling them to make educated choices about reproduction and intervene early in situations of afflicted pregnancies. The use of sophisticated molecular tools into screening programs has improved the precision and effectiveness of detecting carriers, therefore aiding in the prevention and early treatment of thalassemia.

Therapeutic Interventions: Therapeutic treatments for managing thalassemia have made notable progress, with the goal of reducing symptoms, enhancing quality of life, and targeting the genetic defects at the root of the condition. Blood transfusions are a fundamental aspect of treating thalassemia major, offering a temporary resolution to the anemia linked to the condition. The implementation of this life-preserving measure depends on careful blood type, cross-matching, and iron-chelation therapy to mitigate the possible effects of iron excess.

Genetic Counseling and Family Planning: Thalassemia-related knowledge is used in genetic counseling and family planning to provide individuals and couples with the necessary information to make well-informed decisions on their reproductive options. Genetic counseling is a thorough evaluation of an individual's or a couple's likelihood of harboring thalassemia features, taking into account their family history, ethnic background, and the findings of genetic testing.

Research and Innovation: Thalassemia is a subject of continuous study and innovation, which is advancing scientific investigation into the molecular and genetic causes of the condition. The clarification of the intricate genetic processes involved in hemoglobin production has facilitated the development of focused treatment approaches. Scientists are now investigating the capacity of gene editing technologies, such as CRISPR-Cas9, to accurately rectify the genetic abnormalities that give rise to thalassemia. Although these technologies are now in the experimental phase, they have great potential for the advancement of targeted and curative therapies.

Public Health Initiatives: Thalassemia has effects that go beyond only the clinic and research laboratory, as it also influences public health programs that focus on prevention, education, and advocacy. Thalassemia awareness campaigns are crucial in spreading knowledge about the condition, its genetic foundation, and the need of screening. Healthcare providers may expedite early diagnosis, prompt intervention, and the adoption of preventative measures by increasing awareness among populations at risk.

Challenges and Considerations: The use of thalassemia-related information has resulted in significant progress, yet obstacles remain, affecting the availability, price, and fair allocation of these gains. Restricted availability of specialist medical services, such as stem cell transplantation and developing gene treatments, in certain areas results in unequal treatment results. The economic factors, together with the expensive nature of sophisticated treatments, provide obstacles to the general implementation of state-of-the-art interventions. This highlights the need of worldwide cooperation and promotion.

SICKLE CELL

Sickle cell disease (SCD) exemplifies the complex interplay of genetics, molecular biology, and clinical aspects within the broad field of hematology. Sickle cell anemia, an inherited blood illness caused by defective hemoglobin, has a significant and wide-ranging influence on people' lives, affecting their health and impacting different aspects of medical research. Sickle cell illness encompasses a captivating narrative that spans generations, including the intricate details of hemoglobin structure and the intricate interplay of symptoms and consequences. This tale develops from the cellular level to the wider context of healthcare and social institutions.

Sickle cell disease is mostly caused by a genetic mutation that significantly affects the structure of hemoglobin, a crucial protein that transports oxygen in red blood cells. Hemoglobin, an intricate molecule composed of four protein subunits, typically exists in two variations: hemoglobin A (HbA) and hemoglobin S (HbS). Within the complex genetic process, persons affected by sickle cell disease possess a mutation in the HBB gene located on chromosome 11. This mutation causes the creation of abnormal hemoglobin S. The anomalous hemoglobin undergoes polymerization, resulting in the transformation of the formerly pliable, discoidal red blood cells into inflexible, crescent or sickle-shaped cells. This structural transformation resonates throughout the body, disturbing the normal circulation of blood, impairing the supply of oxygen, and creating a series of physiological difficulties.

The clinical presentations of sickle cell disease are diverse and complex, including a wide range of symptoms and consequences that affect numerous organ systems. Pain crises, like thunderstorms in the turbulent story of this illness, occur when sickle-shaped red blood cells block blood arteries, causing reduced blood flow and intense waves of agony. These vaso-occlusive episodes not only cause immediate pain but also serve as the basis for many of the long-term consequences associated with sickle cell disease, including as organ damage, stunted development, and neurological impairments.

Moreover, the atypical red blood cells have a significantly reduced lifetime, resulting in hemolytic anemia. This condition, known as chronic anemia, is defined by the early

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breakdown of red blood cells. It is accompanied by symptoms such as weariness, weakness, and a pale complexion, which reflect the underlying difficulties occurring in the bloodstream. The impaired capacity of sickle cells to transport oxygen makes persons more vulnerable to infections, especially those caused by encapsulated bacteria, which further complicates the complex clinical progression of the condition.

However, sickle cell disease is not a uniform entity; it is a complex composition of several genotypes and phenotypes, each exhibiting distinct clinical characteristics and varying degrees of severity. Homozygous sickle cell disease (HbSS) is characterized by people who have two copies of the defective gene. This condition often results in more severe symptoms compared to persons with heterozygous variants, such as sickle cell trait (HbAS) or compound heterozygous states (e.g., HbSC or HbSβ thalassemia). The wide range of ways in which the illness presents itself highlights the complex relationship between genetics and clinical results, highlighting the need of customized and subtle treatment that is specifically designed for the distinct manifestation of the disease in each person.

PATIENTS SUFFERING FROM SICKLE CELL

Sickle cell disease (SCD) significantly impacts the lives of persons dealing with this persistent hereditary blood ailment, influencing their experiences in ways that go beyond the boundaries of medical facilities. Every individual afflicted with sickle cell disease goes on a unique journey, maneuvering through the intricacies of a sickness that profoundly affects their everyday life. The experience of persons with sickle cell disease encompasses the complex interplay between defective hemoglobin at the molecular level and the complicated progression of pain crises and organ damage. It is a multilayered story that requires empathy, comprehension, and a comprehensive approach to healthcare.

The central element of this complex narrative is the genetic abnormality that characterizes sickle cell sickness. Individuals afflicted with this disorder have a profound impact on all aspects of their lives due to the modified composition of hemoglobin, the molecule responsible for transporting oxygen in red blood cells. The voyage starts at a minuscule scale, where the HBB gene located on chromosome 11 bears the burden of a genetic alteration that converts hemoglobin A (HbA) into its abnormal variant, hemoglobin S (HbS). This genetic mutation initiates a series of physiological difficulties that result in the unique sickle shape of red blood cells. This compromises their ability to be flexible and leads to various clinical symptoms.

Individuals with sickle cell disease often experience a precarious equilibrium between times of stability and intense pain crises in their everyday lives. The crises occur due to vaso-occlusive events caused by the obstruction of blood arteries by sickle-shaped red blood cells, resulting in tissue oxygen deprivation and severe pain. Pain's story transcends the confines of the physical domain, infiltrating the emotional and psychological essence of persons, molding their relationships, goals, and perspective on life.

Nevertheless, pain does not exclusively dominate the narrative of sickle cell illness. The persistent anemia resulting from the early breakdown of erythrocytes adds an additional level of intricacy. The constant exhaustion, debility, and paleness become quiet companions, affecting everyday activities and overshadowing even the most basic of chores. The impaired immune system leads to increased vulnerability to infections, which requires ongoing monitoring and cautious navigation in a world full of possible health threats.

Individuals with sickle cell disease navigate not just the physical aspects of their condition, but also the complex network of interpersonal connections and social interactions. Families assume a crucial role in this tale, often serving as unwavering advocates and caretakers. The parents are deeply affected by the emotional burden of seeing their children's suffering, while siblings strive to strike a difficult equilibrium between empathy and the want for normality. The responsibility of providing care, especially during episodes of intense pain and hospital stays, influences the relationships within families and highlights the strength of these support systems.

CONCLUSION

Sickle cell anemia and thalassemia are prevalent worldwide. Thalassemias, including α-thalassemia and β-thalassemia, are the most prevalent inherited single-gene illnesses globally. They are particularly frequent in regions where malaria was or is now prevalent. The prevalence of this condition in several locations is so significant that it becomes a significant public health issue. In some countries in the Mediterranean area where a certain disease is prevalent, control strategies that have been in place for a long time have successfully prevented 80-100% of new cases from occurring at birth. The disorders of sickle cell anemia and Thalassemia are prevalent in almost all states of India. The state of Gujarat had the greatest incidence of b-thalassemia trait, followed by Punjab, Tamil Nadu, and South India. The prevalence rate of this trait was found to be highest in Central India, specifically ranging from 2.4% to 4.4%. (Mean frequency). The prevalence of b-thalassemia in Maharashtra was around 1.9%. The prevalence of P-thalassemia trait in Western Maharashtra, which is estimated to be 7.0%, is within the range seen in Punjab and Tamil Nadu. The prevalence of thalassemia trait in the Amravati area, as determined by examining a sample, is around 0.85%.

REFERENCES

1. Hermes, Sebastian & Riasanow, Tobias & Clemons, Eric & Böhm, Markus & Krcmar, Helmut. (2020). The digital transformation of the healthcare industry: exploring the rise of emerging platform ecosystems and their influence on the role of patients. BuR - Business Research. 13. 1-37. 10.1007/s40685-020-00125-x.

2. Soyez, Katja & Gurtner, Sebastian. (2014). Challenges and Opportunities in Health Care Management. 10.1007/978-3-319-12178-9.

3. Akenroye, Temidayo. (2012). Factors Influencing Innovation in Healthcare: A conceptual synthesis.. Innovation Journal. 17.

4. mobley smith, Miriam & Koronkowski, Michael & Petersen, Nicole. (2004). INNOVATIONS IN TEACHING Enhancing Student Learning Through Integrating Community-Based Geriatric Educational Outreach Into Ambulatory Care Advanced Practice Experiential Training. American journal of pharmaceutical education. 68. 10.5688/aj680120.

5. Han, Eui-Ryoung & Yeo, Sanghee & Kim, Min-Jeong & Lee, Young-Hee & Park, Kwi-Hwa & Roh, Hyerin. (2019). Medical education trends for future physicians in the era of advanced technology and artificial intelligence: an integrative review. BMC Medical Education. 19. 460. 10.1186/s12909-019-1891-5.

6. Torab-Miandoab, Amir & Samad-Soltani, Taha & Rezaei, Peyman. (2021). Open Innovation in Healthcare Ecosystem – a systematic review (Accepted Paper : Journal of Health Management(Sage)). 10.21203/rs.3.rs-640164/v1.

7. Paul, Shuva & Riffat, Muhtasim & Yasir, Abrar & Mahim, Mir & Sharnali, Bushra & Naheen, Intisar Tahmid & Rahman, Akhlaqur & Kulkarni, Ambarish. (2021). Industry 4.0 Applications for Medical/Healthcare Services. Journal of Sensor and Actuator Networks. 10. 43. 10.3390/jsan10030043.

8. Omachonu, Vincent & Einspruch, Norman. (2010). Innovation in Healthcare Delivery Systems: A Conceptual Framework. The Innovation Journal: The public sector Innovation Journal. 15.

9. Berry, Leonard. (2019). Service innovation is urgent in healthcare. AMS Review. 9. 10.1007/s13162-019-00135-x.

10. Berwick, Donald. (2003). Disseminating Innovations in Health Care. JAMA : the journal of the American Medical Association. 289. 1969-75. 10.1001/jama.289.15.1969.

11. Anderson, MSc & Mossialos, Elias & Richards, Mike & Ucl, & Sheikh, Sir Aziz & Anderson, Michael & Albala, Sarah & Casadei, Barbara & Dean, Bryony & Richards, Mike & Taylor, David & Tibble, Holly & Mossialos, Elias. (2021). Health Policy Health information technology and digital innovation for national learning health and care systems. The Lancet. Digital health. 3. 10.1016/S2589-7500(21)00005-4.