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Prevalence And Impact Of Albinism, Hemophilia, Thalassemia Among Consanguineous Marriages In District Khairpur Sindh, Pakistan

Majeeda Ruk[1*], Khalida Unar[2] , Ayaz Ali Unar[3]

[1*] Department of Zoology, Shah Abdul Latif University Khairpur, Sindh, Pakistan
[2] Institute of Microbiology, Shah Abdul Latif University Khairpur, Sindh, Pakistan
[3] Institute of Pharmacy, Shaheed Mohtarma Benazir Bhutto Medical University Larkana, Sindh, Pakistan
Email: drunar.ayaz@smbbmu.edu.pk

ABSTRACT
This research, conducted in specific areas of the district Khairpur Mirs' in Sindh, Pakistan on three genetic disorders Albinism, Hemophilia and Thalassemia, from March 1, 2023, to August 28, 2023. Albinism primarily affects pigmentation, Thalassemia and Hemophilia have significant impacts on blood. This study aimed to determine the prevalence and primary focus was on the consanguinity association with these three genetic conditions in the population of specific areas within the district. The results revealed that Thalassemia was the most prevalent genetic condition, affecting a significant 33.36% of the population, with a cumulative prevalence of 40.23% when considering all three conditions. Gender distribution analysis showed changing patterns across the three genetic conditions. Markedly, Albinism predominantly affected males, with 70% of cases occurring in males and 30% in females. In contrast, Hemophilia showed a more balanced gender distribution, with 57.19% of cases in males and 42.81% in females. Thalassemia, had a greater prevalence in males, with 60.09% affected, while 39.91% were female. Age-wise analysis revealed patterns, specifying that Albinism primarily affected individuals in the 2-12 age group, comprising 25% of all cases in this category. Hemophilia, on the other hand, exhibited the highest number of cases in the 44-52 age group. Constituting 30.17% of all Hemophilia cases. Thalassemia mainly affected individuals in the 13-22 age group, making up 33.67% of all Thalassemia cases. Moreover, the study explored the prevalence of consanguineous in marriages among individuals with these genetic conditions. The data highlighted that consanguineous marriages, particularly in cases of Thalassemia, were prevalent, with 97.43% of marriages involving close relatives. These findings suggest a potential link between consanguinity and the prevalence of these genetic conditions, emphasizing the need for further research into genetic factors and family history.

Keywords: Prevalence; Consanguineous; Hemoglobin (Hb) disorders; Thalassemia; Albinism

Introduction

It is important to understand that Thalassemia, Hemophilia, and Albinism are all genetic disorders caused by mutations in particular genes. Albinism mostly affects pigmentation, although Hemophilia and Thalassemia have major effects on blood and general health. Examining these conditions as a group can help clarify the genetic influences on human health and offer important new understandings of how biology, genetics, and health outcomes interact.

Global Prevalence

Albinism prevalence varies among populations and regions. It is estimated that approximately 1 in 17,000 to 20,000 people worldwide are affected by some form of Albinism (World Health Organization, 2023).Since Hemophilia varies in prevalence among various demographics and geographical areas, it is regarded as an uncommon disorder. The prevalence of Hemophilia B is predicted to be between 1 in 20,000 and 1 in 34,000 male births, whereas Hemophilia A affects between 1 in 5,000 to 1 in 10,000 male births globally, according to the World Federation of Hemophilia (WFH) (WFH, 2021). Regarding Thalassemia, only 1.7% of people globally exhibit the signs and symptoms of the Thalassemia trait, which is caused by a gene mutation, whereas 5% of people have a variation in hemoglobin protein (Smith, 2022).

The pigment responsible for the color of the skin, hair, and eyes, melanin, is either absent or deficient in Albinism, an inherited genetic condition. People who are albino have always piqued curiosity and created misconceptions. The name "Albinism," which derives from the Latin word "albus," which means "white," has been connected to superstitions and myths across many cultural contexts. There have occasionally been false connections made between people with Albinism and curses or supernatural powers (Disability Rights International, 2017).Deciphering the genetic foundation of Albinism is essential to comprehending the intricacies of this illness.

Gene alterations that are essential for the generation and distribution of melanin are the main cause of Albinism. Tyrosinase, an enzyme essential to melanin formation, is encoded by the well-studied gene TYR, which is linked to Albinism (Sturm, 2009). Mutations in various genes, which each have a different effect on melanin, are associated to different kinds of Albinism, such as Ocular Albinism (OA) and Oculocutaneous Albinism (OCA) (Gronskov et al., 2007). There are several different clinical indications of Albinism that affect both look and vision. Albinos usually have pale to white skin, light-colored hair, and pinkish-white or light-colored eyes. Nystagmus, or involuntary eye movements, strabismus, or crossed eyes,

and photophobia, or excessive light sensitivity, are common visual impairments (Summers, 2009). Each person experiences vision impairment to a different degree. Researchers' investigation of the frequency of Albinism in Pakistan, mainly in Punjab province, and its connection to genetic variables focused on the influence of consanguinity in Pakistani matrimony on the incidence of recessive genetic disorders such as OCA. A higher prevalence of recessive illnesses affects groups, and consanguineous marriages account for 62.7% of marriages in Pakistan.

Findings from the study demonstrate the genetic variability in Albinism among Pakistani linguistic and ethnic groupings, demonstrating the widespread distribution of certain OCA alleles that are not enriched within specific clans. (Mohsin S. et al., 2017).

Hemophilia is a rare and complex hereditary condition characterized by a lack of clotting factors that has long fascinated medical professionals and researchers. This disorder, which mainly affects men, can cause prolonged, uncontrollable bleeding, even in cases of minor wounds. The ailment known as "the royal disease" was first identified in European royal families, where Hemophilia was common and gave rise to the moniker. This thorough introduction will examine the genetic foundation of Hemophilia, its clinical manifestations, and the significant advancements in Hemophilia management over time as we delve into its intricacies.

Hemophilia has a long history; ancient manuscripts have references to bleeding illnesses that resemble Hemophilia. Still, in the 19th century, there were reported incidences of Hemophilia among European royal families. Hemophilia is caused by a genetic abnormality that Queen Victoria carried and passed on to many of her descendants, establishing a hereditary connection between European aristocracy and the condition. Hemophilia has a significant historical relevance because notable historical figures like Tsarevich Alexei Romanov of Russia suffered from it (Rogaev et al., 1996).

Mutations in the genes encoding clotting factors, namely Factor VIII (Hemophilia A) or Factor IX (Hemophilia B), are the primary cause of Hemophilia. Blood clot formation is hampered by certain genetic abnormalities because they cause a lack or malfunction of key clotting factors. Because Hemophilia is an X-linked recessive condition, affecting only one X and one Y chromosome, it is more common in men. Usually carriers, females with one defective X chromosome may show milder symptoms. The hereditary aspect of Hemophilia is highlighted by the fact that the disorder develops in the son of a female carrier of the defective X chromosome.

Excessive bleeding is the defining feature of Hemophilia, and it can happen on its own or after little traumas. Hemophiliacs may suffer from nosebleeds, easy bruising, joint and muscle bleeding, and, in extreme situations, potentially fatal internal bleeding. The degree of clotting factor deficiency determines the mild, moderate, and severe forms of Hemophilia (Srivastava et al., 2013).

A class of genetic blood disorder known as Thalassemia affect people and their families greatly and present a complex and compelling medical challenge. The protein responsible for carrying oxygen in red blood cells, hemoglobin, is produced insufficiently in several illnesses. Thalassemia is a genetic disorder that affects people all over the world. It can cause a wide range of clinical manifestations, from asymptomatic carriers to severe anemia that could be fatal. This introduction sheds light on Thalassemia, a syndrome that has drawn interest from medical researchers and healthcare professionals worldwide by examining its genetic roots, clinical presentations, and developments in management.

Genetic abnormalities influencing the synthesis of hemoglobin are the fundamental cause of Thalassemia. Mutations in the genes that control the synthesis of the alpha (α) and beta (β) globin chains, which make up hemoglobin, cause the condition. Thalassemia is classified as either beta- or alpha-Thalassemia based on the particular genes affected. These genetic variations cause an imbalance between the creation of beta and alpha globin chains, which results in hemoglobin that is either defective or inadequate. The quantity of mutated genes and their type determine how severe Thalassemia is. (Weatherall & Clegg, 2001).

Thalassemia presents with a highly variable clinical presentation. People with Thalassemia traits—those with one faulty gene—can either stay asymptomatic or develop moderate anemia. On the other hand, those who have Thalassemia major—a condition caused by two faulty genes—often struggle with severe anemia, which can lead to pallor, exhaustion, stunted growth in children, and other issues. Between these two extremes, Thalassemia intermedia causes moderate to severe anemia that requires medical attention. Possible side effects include splenomegaly, bone abnormalities, and an increased risk of organ damage from iron excess brought on by repeated blood transfusions.

Thalassemia is one of the most common inherited hemoglobin disorders in Pakistan, according to research. The carrier accounts for about 5.4% of the frequency. To identify the spectrum of -globin gene defects that cause -Thalassemia, they analyzed a representative sample of 602 alleles from six ethnic groups in Pakistan; 99.2% of the alleles were characterized, while 0.8 percent remained unexplained. The entire range of heterogeneous mutations consists of 19 different mutations. The four most common mutations, IVS-I-5 (GC) (37.7%), codons 8/9 (+G) (21.1%), the 619 bp deletion (12.4%), and IVS-I-1 (GT) (9.5%), affect 87% of the alleles. There are differences among and between ethnic groups as well as within provinces. The rates of the IVS-I-5 (GC) mutation are higher in Sindh and Baluchistan, two of Pakistan's four provinces that border India on the south and Iran on the southwest, respectively, than they are in Punjab and the Northwest Frontier Province, two other provinces that border India on the northeast and Afghanistan, respectively, with higher rates of the codons 8/9 (+G) mutation. Compared to other ethnic groups, Gujaratis and Memons in the Province of Sindh, which is adjacent to the Indian Gujrat, have a higher (619 bp deletion) rate (46%). (Shah et al, 2020).

Methodology

The research study, which focused on three genetic conditions Albinism, Hemophilia, and Thalassemia—was carried out in specific areas of district Khairpur Mir between March 1, 2023, and August 28, 2023. The purpose of the study was to determine the prevalence of these genetic diseases and their consanguinity associations in particular areas within district

Khairpur, which is located in the Sukkur division of Sindh province in Pakistan.. It is situated in the region between the middle and northern parts of Sindh. The district's revised area is 15910 km², covering an estimated 2,000 km², or 200,000 hectares. Within this large area, villages in the District Khairpur Mir's, such as Long Fakir Dharejo, Moulded Dharejo, Dhani Bux, Abdul Razzaq, Aziz Ali Panhwar, Manzoor Khan Wassan, Khuda Bux Rajper, Hadi Bux Rajper, and others, were visited in order to gather data. An estimate of the district's area was made, which was useful in determining the population size.

From a population of 10,182 people, 160 cases of Albinism were found during the survey. Face-to-face interviews were held with those who had the condition and their families, and questionnaires were used to gather information on names, ages, genders, consanguinity, family histories, and other relevant factors. After that, proper statistical analysis was performed on the gathered data using SPSS version 20 in order to determine means, frequency distributions, and percentages.
Hemophilia and Thalassemia research was carried out at Gambat in District Khairpur, Sindh, Pakistan. Data was collected from the GIMS Hospital and Civil hospital Gambat. In a population of 5381 people, it sought to ascertain the incidence of these disorders and their relationships to consanguinity. Of these, 285 instances of Hemophilia and 1796 cases of Thalassemia were detected, while the remaining individuals had various blood issues. Relevant patients were given questionnaires to complete in order to collect data for this study on blood diseases, consanguinity, family history, name, age, gender, and associated factors. Hemophilia and Thalassemia data were analyzed in the same way as Albinism data.
In order to evaluate the impact of consanguinity on these three genetic disorders, medical histories, consanguineous marriages, and cases of genetic conditions were recorded. Genetic history and consanguineous ties were visualized through pedigree charts using pedigree analysis. As required by ethical rules and principles guiding research on human beings, informed consent was obtained from each participant prior to the administration of the questionnaires. Assessing the prevalence of Hemophilia and Thalassemia in the study population and investigating the connection between these blood disorders and consanguinity were the main goals of the research.

Results

Table 1: Shows Prevalence of genetic conditions in given population size

Genetic conditions	Total Frequency (N)	Population size	Percentage (%)	Valid percentage (%)	Cumulative Percentage (%)
Albinism	160	10182	1.57	1.57	1.57
Hemophilia	285	5381	5.30	5.30	6.87
Thalassemia	1796	5381	33.36	33.36	40.23

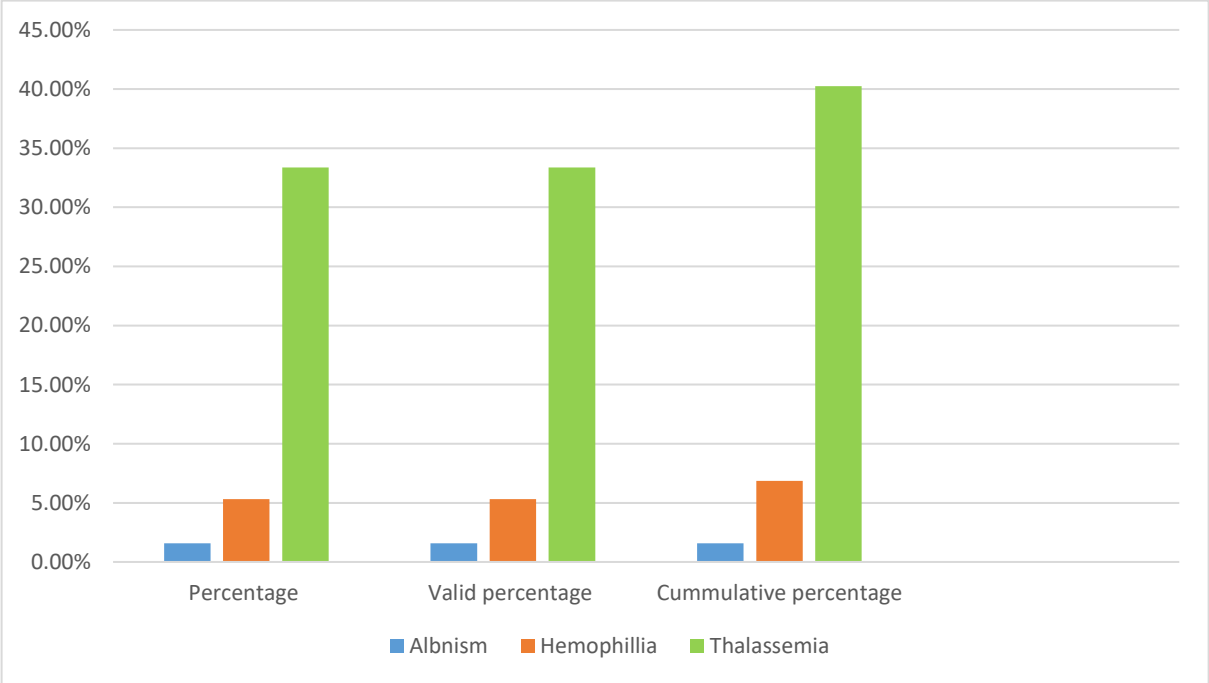

Figure 1: Shows graphical representation of prevalence of three genetic conditions

Table 2: Shows Gender wise percentage of three genetic conditions:

Genetic Conditions	Male frequency (N)	Female frequency (N)	Male percentage (%)	Female Percentage (%)
Albinism	112	48	70.00	30.00
Hemophilia	163	122	57.19	42.81
Thalassemia	1079	717	60.09	39.91

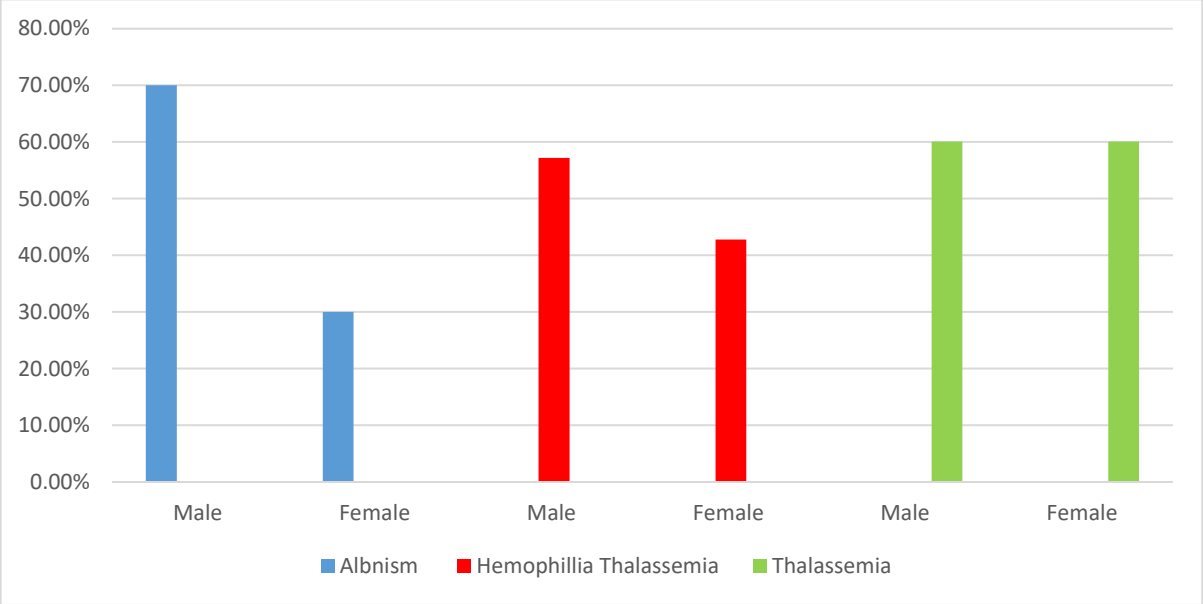

Figure 2: Shows graphical representation of gender wise percentages of three genetic conditions

Table 3: Shows Age distribution of individuals with Albinisms

Age groups (in years)	Frequency (n)	Percentage (%)	Valid percentage	Cumulative Percentage
2-12	40	25.0	25.00	25.0
13-22	34	21.25	21.25	46.0
23-32	32	20.0	20.0	66.25
33-42	31	19.38	19.38	85.63
44-52	23	14.37	14.37	100.0
Total	160	100	100	100.0

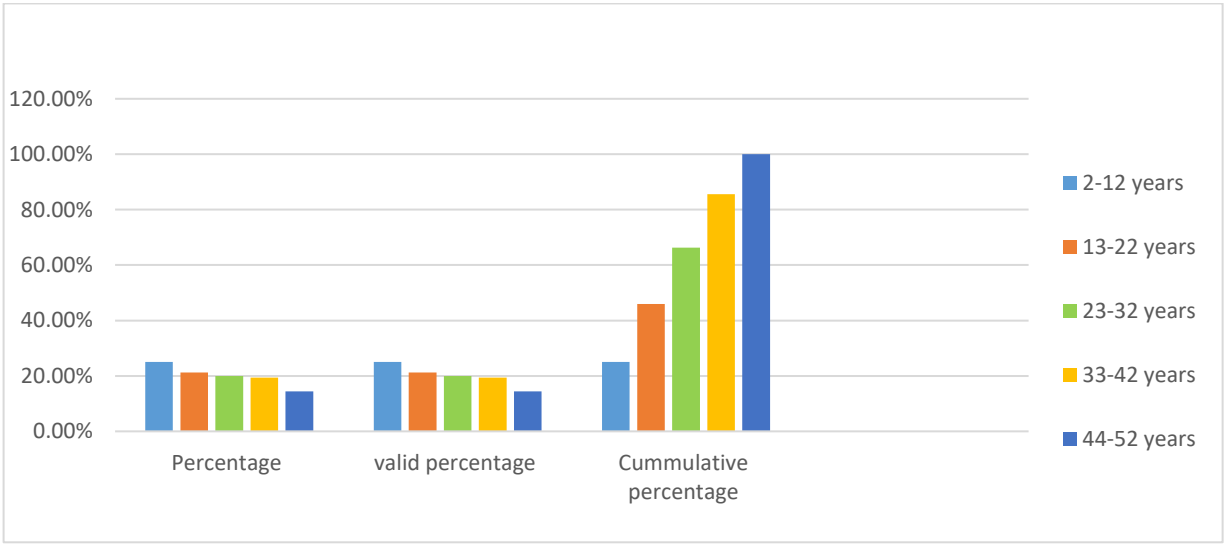

Figure 3: Shows graphical representation of age distribution of individuals with Albinism

Table 4: Shows Age distribution of individuals with Hemophilia

Age groups (in years)	Frequency (n)	Percentage (%)	Valid percentage (%)	Cumulative Percentage (%)

2-12	32	11.23	11.23	11.23
13-22	45	15.79	15.79	27.2
23-32	57	20.0	20.00	47.02
33-42	65	22.81	22.21	69.83
44-52	86	30.17	30.17	100.0
Total	285	100.0	100.0	100.0

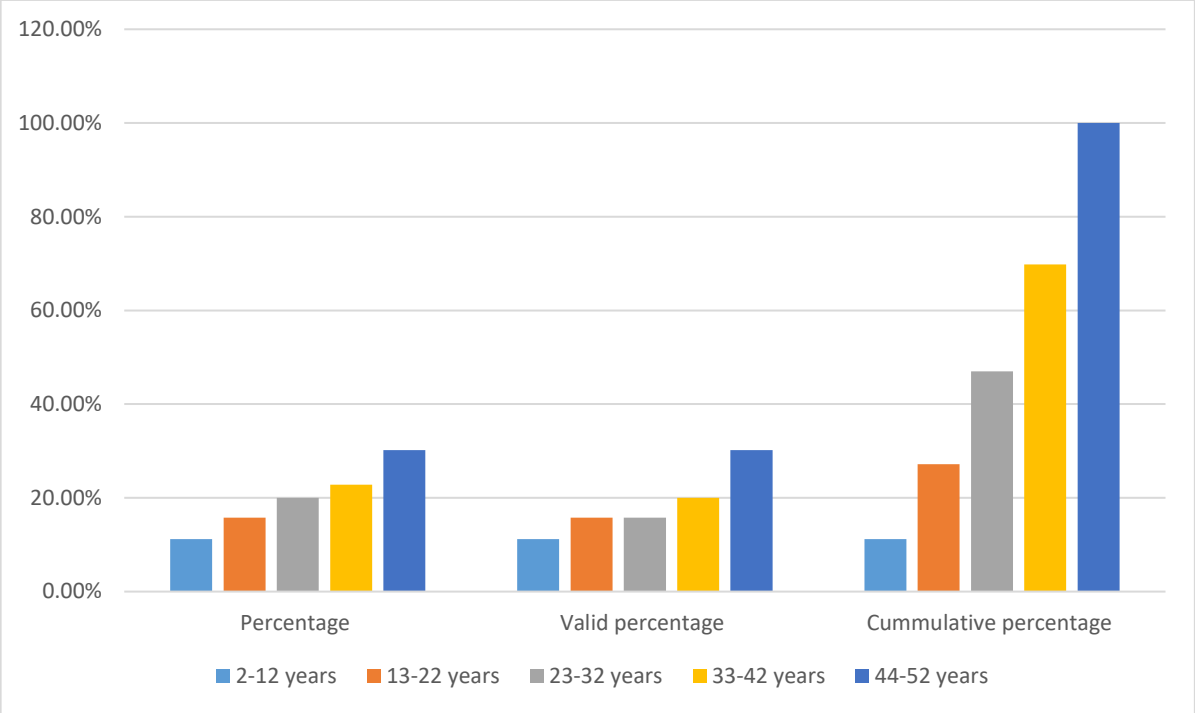

Figure 4: Shows graphical representation of age distribution of individuals with Hemophilia

Table 5: Shows Age distribution of individuals with Thalassemia

Age groups (in years)	Frequency (n)	Percentage (%)	Valid percentage (%)	Cumulative Percentage (%)
2-12	592	32.96	32.96	32.96
13-22	605	33.67	33.67	66.63
23-32	599	33.37	33.37	100.00
33-42	0	0.00	0.0	0.0
44-52	0	0.00	0.0	0.0
Total	1796	100.0	100.0	100.0

Figure 5: Shows graphical representation of age distribution of individuals with Thalassemia.

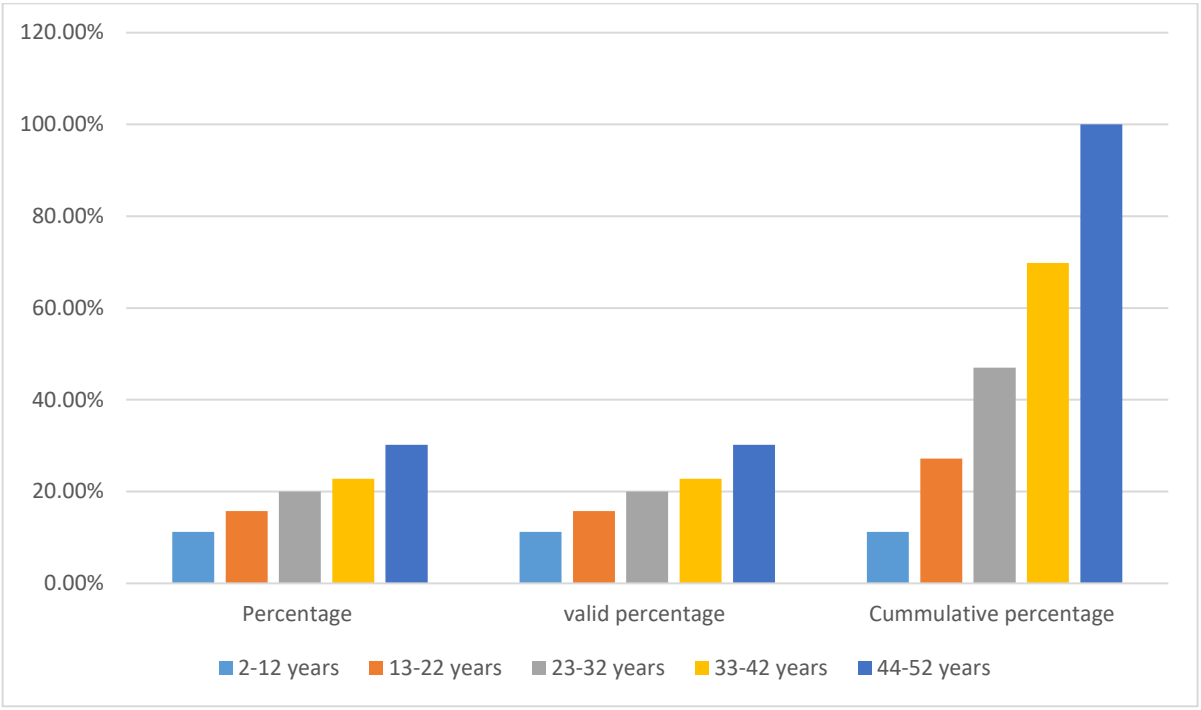

Table 6: Shows Prevalence of consanguinity and non-consanguinity

Genetic condition	Consanguineous marriages (N)	Non-consanguineous marriages (N)	Percentage of consanguineous marriages (%)	Percentage of non-consanguineous marriages (%)
Albinism	110	50	68.75	31.25
Hemophilia	218	67	76.50	23.50
Thalassemia	1750	46	97.43	2.57

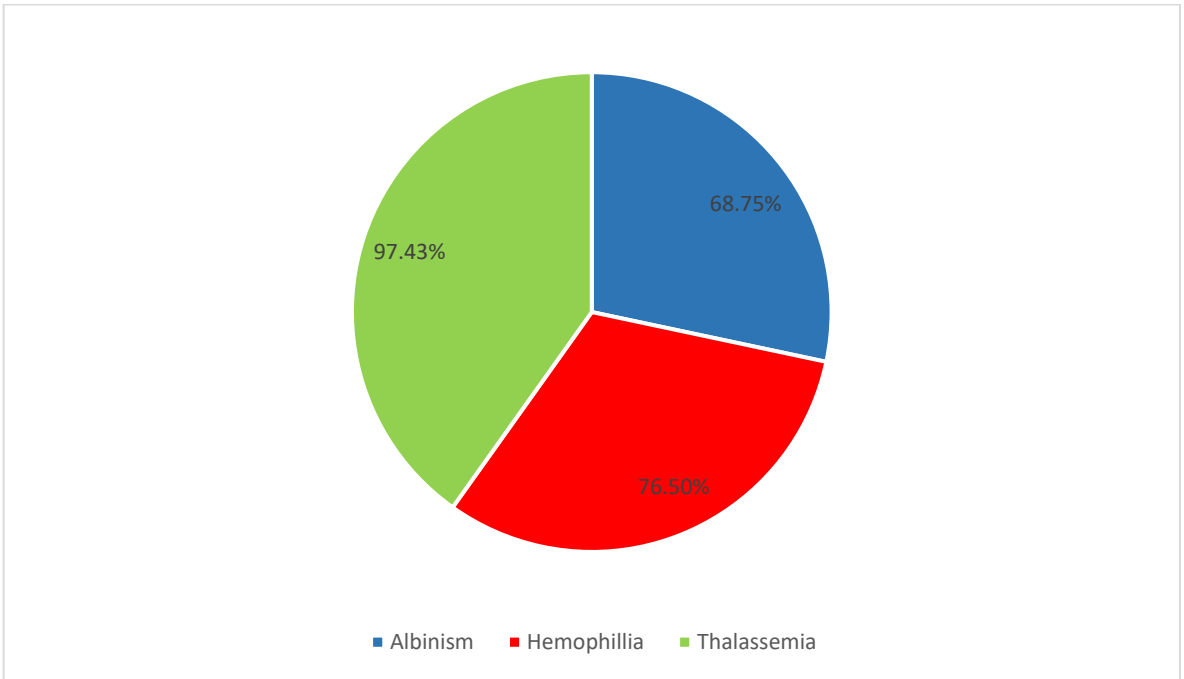

Figure 6: Shows graphical representation consanguinity and non-consanguinity percentages

Table 1 provides the prevalence of three genetic conditions Albinism, Hemophilia and Thalassemia within their respective population size. Most prevalent Thalassemia affecting 33.36% of population while the other conditions are rare. Cumulative percentage shows collectively these three genetic conditions affect 40.23% of population. Table 2 provides a breakdown of

how these genetic conditions are distributed among males and females showing gender specific prevalence of each genetic condition. Table 3 Table represent age distribution of individuals with Albinism highest number of individuals with Albinism falls in 2-12 age group. Table 4 provides insight into the age distribution of individuals with Hemophilia highest number of individuals with Hemophilia falls in 44-52 age group. Table 5: provides insight into the age distribution of individuals with Thalassemia highest number of individuals with Thalassemia falls in 13-22 age group. Table 6 provides insight into the consanguinity rates marriages in close relatives for individuals with three genetic conditions. Data can assist in accessing risk of genetic condition in populations with a tradition of consanguineous marriage.

Discussion:

Three genetic disorders were the focus of this study carried out in the district of Khairpur Mir in Sindh, Pakistan: Thalassemia, Hemophilia, and Albinism. According to this study, Thalassemia affects a noteworthy 33.36% of the population, making it the most common genetic illness. With a cumulative frequency of 40.23% when taking into account all three disorders, this suggests a significant burden of this genetic ailment on the community.

Upon analyzing the gender distribution, it was discovered that men are mostly affected by Albinism, accounting for 70% of instances in men and 30% in women. Conversely, the gender distribution of Hemophilia cases was more balanced, with 42.81% of cases occurring in females and 57.19% in males. Similar to Albinism, Thalassemia was more common in men (60.09% versus 39.91%), with a higher incidence rate in men.

An examination by age showed some interesting trends. With 25% of occurrences occurring in this age range, those with Albinism are most affected by this condition. With 30.18% of all cases, the age group of 44 to 52 had the greatest number of cases with Hemophilia. The age range of 13 to 22 years old accounted for 33.67% of all cases of Thalassemia patients.

The study also looked at the prevalence of consanguinity in unions between people who have certain genetic disorders. Particularly in cases of Thalassemia, where 97.43% of marriages were consanguineous, the results demonstrated the predominance of consanguineous marriages. Further investigation into genetic variables and family history is necessary, as this information points to a potential correlation between consanguinity and the occurrence of various genetic diseases.

Conclusion: The research carried out in specific areas of the district of Khairpur Mir in Sindh, Pakistan, has provided significant information regarding the frequency of three hereditary disorders: Thalassemia, Hemophilia, and Albinism. The high frequency of consanguineous marriages—97.43% of marriages in cases of Thalassemia, for example—is particularly noteworthy.

The custom of marrying near relatives, or consanguinity, seems to be a major contributing cause to the high frequency of certain genetic disorders in the area. The research suggests that those born into consanguineous marriages had a higher frequency of certain genetic illnesses, specifically Thalassemia. In order to reduce the risk of such genetic diseases in the community, this emphasizes the vital need for public health measures, education, and awareness campaigns targeted at minimizing consanguineous marriages

Recommendations:

Community Awareness: it is recommended that there should be public awareness efforts to inform the public about the possible health hazards connected to consanguineous marriages. All locals should be able to access these efforts, and they should be culturally sensitive.

Genetic Counselling Services: There should be genetic counselling centers in the district to give couples and individual advice and information about the possible hereditary risks associated with consanguinity. Family planning advice and premarital counselling ought to be provided by these agencies.

Healthcare Access: To help people make educated decisions regarding marriage and family planning, it should guarantee better access to healthcare services, such as genetic testing and counselling.

Promote Non-Consanguineous Marriages: Encourage non-consanguineous marriages within the society and provide incentives for them, stressing the advantages for future generations' health and well-being..

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