A STUDY OF INBREEDING IN ALBINO AND THALASSEMIA AFFECTED FAMILIES RESIDENT IN TUMAN LEGHARI DISTRICT DERA GHAZI KHAN

(M.Phil Thesis)

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بسم الله الرحمن الرحيم

Dedication

Each difficult work requires self endeavors and additionally direction of senior citizens particularly the individuals who were near our heart. My unassuming exertion I commit to my mother Ruqia Nazar, whose love, adoration, support and supplicates of day and night make me ready to get such achievement and honor, alongside my minding wife Rashida Ayaz, my sons Muhammad Farukh Ayaz, Muhammad Ahmad Ayaz, my daughters Nazish, Sana, Nida, Asmara, Rida and Zarish Fatima.

DECLARATION

The material containing in this thesis is my original work and I have not presented any part elsewhere for any other degree.

AYAZ AHMAD

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LIST OF ABBREVIATIONS

FC	:	First Cousin
SC	:	Second Cousin
DFC	:	Double First Cousin
DR	:	Distantly related
NR	:	Non-Related
IM	:	Inbreeding Marriage
OM	:	Outbreeding Marriage
F	:	Inbreeding Co-efficient
DGK	:	Dera Ghazi Khan
DIK	:	Dera Ismail Khan

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ABSTRACT

The inbred marriages are highly acceptable in many populations of human beings but their prevalence and configuration vary depending on ethnicity, religious conviction, learning and socioeconomic circumstances of relevant population. Such social contracts are reported as the most important cause of enhancing the occurrence of the hereditary disorders by recessive autosomal, especially Albino and Thalassemia.

The challenges of hereditary diseases trouble in the population calls for the progress of anticipation programs. But the implementations of different means require the information about types and prevalence of hereditary diseases and family system in population. These goals can be achieved through perceptive of the determinants of human population and genetic structure that is mainly determined by the different marriage lines. Furthermore, the pattern of close marriages in population along with other factors leads to develop the isolated groups having typically confined, extended and show multigenerational pedigrees. This study focuses on inbred marriages and genetic diseases in the general population of Tuman Leghari resident in district D.G. Khan, Punjab, Pakistan because of its exclusive geographical position and population arrangement.

The district D.G. Khan is located in the center of Pakistan, bordered on the North by D.I. Khan District of KPK; Musa Khel and Barkhan districts of Baluchistan are bordered on west side, the southern area is Rajan Pur, while on the Eastern side river Indus that separates it from the other districts of province Punjab. The populations of Tuman Leghari resident in D.G. Khan is mainly mixture of Leghari, Khosa included in Baloch, and Saraiki other than Baloch which represents different ethnic groups. There are many variations in societal and cultural activities in this area but the marriages are generally inbred within community or tribes. During data collection, 406 families were approached indiscriminately to study the effects of inbreeding. Ethnically the highest positive response was found in Saraiki (other than Baloch) 47.30% than Leghari (32.26%) or Khosa (20.44%). The Saraiki other than Baloch, Khosa and Leghari families were 47.30%, 32.26%, and 20.44% respectively.

Inbred marriages were more prevalent in Tuman Leghari Tribe of D.G Khan District. The ratios of such inbred marriages in different ethnic populations were studied

to be: Saraiki other than Baloch 46.24%, Leghari 35.10% and Khosa 18.66%. The comparison of inbred marriages and outbreeding marriages in different ethnic groups of Tuman Leghari tribe was found to be statistically non-significant. There was many differences found between the frequency of inbred and out bred marriages of total sample as well as within the ethnic groups, Leghari, and Khosa (X^2=10.87 P<0.001; X^2=47.45 P<0.001 and X^2=03.73 P<0.001 respectively.

Statistical analysis uncover the significant difference among various types of marriages in Leghari, Khosa and Saraiki other than Baloch (X^2=20.00 P<0.001). A significant difference was observed in Leghari and non-significant difference observed in Khosa and Saraiki other than Baloch with 10.87, 27.09 and 3.73 Chi values respectively. The calculated mean inbreeding coefficient (F) for the total population was 0.0287.

There were three groups formed on male education in order to assess the effect of education on the inbred marriages at the time of marriage in total samples represents the lower, middle and higher levels of male education comprised Leghari 81 (19.95%), 141 (34.72%) and 184 (45.32%) couples, respectively. Male education found to be statistically significant in Saraiki other than Baloch group.

Similarly in order to assess the impact of female education on the marriage types, the sample was divided in to three groups based on female schooling years at the time of marriage. In total samples, representing the lower, middle and higher levels of male education comprised Leghari 114 (19.95%), Khosa 133 (34.72%) and Saraiki other than Baloch 184 (45.32%) couples, respectively. Female education found to be statistically significant in Khosa group.

The effect of socioeconomic status of male on marriages was also studied; the sample was distributed in three groups on the basis of socioeconomic status of male at the time of marriage. The total sample representing the lower, middle, and higher levels comprised Leghari 120 (29.56%), Khosa (131 (32.26%) and Saraiki other than Baloch 155 (38.18%). The statistical analysis uncovers significant results in total and Leghari ethnic groups. In order to find the impact of socioeconomic status of female on inbred marriage, the sample was divided into three groups based on female socioeconomic status at the time of marriage. The total sample representing the lower, middle, and higher levels comprised Leghari 108 (26.60%), Khosa 152 (37.44%) and Saraiki other

than Baloch 146 (35.96%). The statistical analysis uncovers significant results in total sample, Leghari and Saraiki other than Baloch ethnic groups.

During the survey, 39 afflicted couples, having affected children or one genetically affected child with positive history, were identified. To study the effect of marriage types on specific group of genetic disorders, these couples were divided in to two groups such as albino and thalassemia. The number of albino and thalassemia couples were 13 (33.33%) and 26 (66.67%) respectively. The affected couples with Thalassemia were found widespread in the sample. On ethnic base, 33.33%, 10.26% and 56.41% of total afflicted couples were found to be related with the Leghari, Khosa and Saraiki other than Baloch groups respectively. Inbreeding marriages were found endemic in afflicted couples (100%) as compared to general population (00%). In the groups of afflicted couples based on genetic diseases, inbreeding was found 100% in both albino and thalassemia.

The frequency of inbreed marriages in the sample of afflicted couples was 100% with mean inbreeding co-efficient was found to be 0.0287. Statistically significant difference was found between Inbred and outbreed couples in the sample (X^2=00 P< 0.001). The data on marriages in normal and effected families of different ethnic groups were found statistically significant in chi-test (X^2=24.42) and in different types of marriages FC (38.92), SC (25.86%), DR (21.18%) and NR (14.04%) were also statistically significant. In case of albino and thalassemia couples, Thalassemia were found to highly significant in all marriage types (i.e. X^2=11.69) (Tables 4.12, 4.13 & 4.14).

Data on children in Leghari, Khosa and Saraiki other than Baloch were statistically significant in both affected and non-affected. In case of data on number of children in Leghari, Khosa and Saraiki other than Baloch in albino were found non-significant and in thalassemia were highly significant in chi test.

Awareness about albino, thalassemia and behavior of parents, relatives, society toward albinos and Thalassemics were found statistically significant.

INTRODUCTION

1.1 Inbreeding

We are all associated with life. Each decision we make and each belief we hold applies impact upon the entire of life. What's more, we live with the outcomes of our decision. As a component of our biological health, this one of a kind truth has physical expressions in honor, dedication, family and gathering bonds. Presumably this structures the premise of marriage, a standout amongst the most key and effective of our connections. The human population has seen current progress is still inside of family limits. One such familial-social bond is inbreeding marriage (Rao, 2009).

Inbreeding marriages are described as a social contract among the individuals which have blood relations. This includes such type of relations which are termed as first cousins, second cousins and distantly related. In a few groups, the most elevated inbreeding are come to with relational unions between double first cousins which are practiced in Arabs and uncle-niece unions are likewise by and by among South Indians (Hamamy *et al.*, 2011).

Close-kinfolk unions kept amid the ensuing moderate population development of human groupings living primarily in scattered provincial settlements, with bottlenecks brought on by intermittent scourges, starvations, and fighting. Indeed, even in mid nineteenth century Europe and North America first-cousin marriage stayed both socially acknowledged and broadly supported, particularly among the more special classes. Against this foundation it is baffling that in late eras human inbreeding has been liable to across the board negative assessment and bias in Western social orders (Lehmann, 2000; Laurent, 2001; Nicolas Perrin, 2003).

Inbreeding is helpful in the maintenance of attractive qualities or the disposal of undesirable ones; however it regularly brings about diminished power, size, and richness of the posterity as a result of the joined impact of destructive qualities that were latent in both parents. The nearest sort of inbreeding is selfing, or self-treatment, the union of male and female sex cells delivered by the same parents. Line breeding is a

type of inbreeding that includes choice of mates on the premise of their connections to a specific superior ancestor (Merrell, D.J. 1994).

1.2 Inbreeding Coefficient

Inbreeding coefficient (F) is defined as the measure of the extent of alleles with indistinguishable duplicates which are communicated in the posterity of inbreeding from both of the parents. If the inbreeding coefficient (F) is equal or more than 0.0156 then it is considered as an inbred marriage. An inbreeding marriage is a societal amalgamation between two persons who are coupled as first cousins or close relative. This incorporates such kind of unions termed as first cousins, second cousins and remotely related (Bittles, 2001).

In a few groups, the most noteworthy inbreeding coefficients are come to high when the marriages occur between DFCs which are practiced in Arabs and uncle–niece unions are likewise by and by among South Indians where inbreeding coefficient is 0.125 (Hamamy, 2011).

The populations with high inbreeding rates have high inbreeding coefficient and is progressively increasing because the families are emerging from the complex inbreeding circle of close relatives. Information concerning inbreeding rates may in some cases incorporate relational unions involving third cousins and all the further which are not directly related. In spite of the fact that this disparity influences the cumulative inbreeding velocity, the lesser coefficients of inbreeding in more distant relational marriages restrict an undeniable variation of the inbreeding coefficient. To account and evaluate inbreeding rates amongst the different populations usually two parameters are utilized, the mean inbreeding coefficient and the rates of marriages between the closely related persons (Hamamy, 2012).

1.3 Prevalence of Inbreeding in General Population

The commonness of inbreeding and rate of inbred marriages fluctuate broadly from population to population and groups, contingent upon ethnicity, religion, society at nearby level and topographical dissemination of the populations (Bittles, 1995).

Inbreeding relational unions likewise regularly happens among the emigrants people from profoundly inbreeding nations and locales, similar to Lebanon, Turkey, Pakistan and North Africa, which are presently occupant in Australia, North America and Europe (Schulpen *et al.,* 2006).

In populations of West Asia, South India and North Africa, inbred marriages are communally and generally supported and the proportion is around 20–50% of all relational unions' with first cousins relational unions represents just about 33% of the mass relational unions (Bittles, 2011; Tadmouri *et al.,* 2009).

Actually, inbreeding does not expand the chance for autosomal prevailing conditions in posterity if one of the parents is affected, similarly not for X-linked recessive character if none of the partner is affected. Moreover the writing concentrating on the relationship there is no such affiliation is existed with parental inbreeding infers the Down's syndrome (Hamamy, 2007 b).

The relationship of inbreeding relational unions with delayed onset of complex diseases, for example, cardiovascular scatters, diabetes, schizophrenia. These diseases require further studies to pinpoint any existing danger in light of the fact that as of now unambiguous confirmation based conclusions are hard to put up positively (Hamamy, 2011).

Among relational unions contracted from 1969 to 1979 in Middle East, 73.3% of 1983 relational unions were orchestrated through the assention of parents first and after that the assent of the couples, although in 18.6%, the marriage was through the couples' perceptiveness first then consent of the parents (Schulpen *et al.,* 2006).

The higher inbreeding rates, joined by the general family estimation in the minority groups, could initiate the statement of autosomal recessive diseases, including very rare or new diseases which make the general population's perception of the danger connected with ingrained relational unions. Right now, numerous youthful ingrained couples wanting to have youngsters look for previously established inclination hereditary guiding because of a paranoid fear of the results of inbreeding on their posterity (Tadmouri *et al.,* 2009).

1.4 Factors in Favor of Inbreeding

The authentic reasons given for the tendency of inbreeding relational unions are primarily communal. In groups with elevated inbreeding rates, sociological studies reveal that cousin wedding could endorse the couples' power because of superior connection in the hub of husband and wife who have the same societal and social relations after marriage as earlier than marriage, and the connection between the pair and other family members (Sekhri, 1978; Manju, 1978).

Inbreeding relational unions are greater for the female position, as well as the wife's superior relationship with her in-laws who could support her in time of necessity. There is generally trusted that marriage inside of the family diminishes the possible outcomes of obscured instabilities with reverence to security and money related matters. It is trusted that inbreeding make stronger the family as well as ties and empower the family harmony, Cousin relational unions give amazing chances to the transmission of social and social values and assume a basic part in social progression (Sandridge *et al.,* 2010).

The wellbeing criteria identified with inbreeding demonstrate that in innate relational unions rather than out reproduced relational unions, fruitfulness rate is somewhat higher among the ingrained, premature birth rate is same. Stillbirths and baby death rates are marginally higher in inbreeding and birth deformities recurrence is roughly to around 2–3% focuses more than the foundation rate among infants in the all inclusive community (around 2–3%) (Genetic Impacts of Radiation, 1962).

1.5 Hereditary Disorders

Hereditary disorder is a kind of human sickness which is brought by the genes present on the chromosomes or variations in the genes from the norm. A few disorders like malignancy are in some portion of hereditary issue yet they can likewise be brought on by ecological elements. Numerous disorders are entirely uncommon and they affect one of the individual in a million. There are a small number of types of recessive disorders which have constructive arrangement in heterozygous states in a little situation. Both hereditary and normal rudiments suppose a part being developed of any sort of

disorder. Human hereditary disease is brought on by variations in the genes from the hereditary materials of the normal people. There are four kinds of hereditary abnormalities like single-gene disorder, chromosomal disorder, multifactorial and mitochondrial disorders. Single gene disorder is caused by a single mutant gene. Such disorder can be transferred in many generations by many ways. This abnormality is brought on basically by deletion or addition of the DNA sequence in single gene (Driel *et al.,* 1957).

1.6 Single Gene Disorder

A single gene disorder is the consequence of a single transformed allele. More than 4000 human sicknesses are brought on by single-gene imperfections. Single gene disorder can be gone on to resulting generations in a few ways. Genomic engraving and uniparental disomy, not with standing, may influence legacy designs. Two duplicates of the gene must be transformed for a man to be influenced by an autosomal recessive disorder. An influenced individual for the most part has unaffected parents who express a single duplicate of the transformed gene (and are alluded to as transporters). Two unaffected individuals who transmit one duplicate of the changed gene have a 25% danger with every pregnancy of having a kid influenced by the disorder. Illustrations of this kind of disorders are Albinism, medium-chain acetyl-CoA dehydrogenase lack, cystic fibrosis, sickle-cell infection, Tay-Sachs illness, Niemann-Pick sickness, spinal solid decay, and Roberts's disorder. Certain different phenotypes, for example, wet versus dry earwax, are likewise decided in an autosomal recessive manner (Weatherall, David, J. 2000).

1.6.1 Albinism

Variety in skin, hair and Iris colour is amazing and obvious character in various human populations. Skin pigmentation is a to a great degree diverse human element with an extent from white or pink to tan, dim chestnut or dark. It shows a conspicuous contrast even inside of a specific racial group (Mollet *et al.,* 2007).

But in a few unusual neurotic cases, skin colour is the effect of three basic colors or chromophores, black, red and yellow colors are produced by melanocytes called

melanin; hemoglobin in red blood cells (RBCs) of vessels, and to a much lesser degree, nutritive carotenoids, some of the time most evident yellow colour of the palms. Generally systematic varieties in hair and skin colours are the after effect of the different substances produced by the melanocytes of skin, particularly by the shape and supply of quantity of the melanin to the skin (Abdel-Malek, 2001; Bahadoran *et al.*, 2003).

Melanin has a crucial role in skin, hair and eye colour, furthermore helps in protection from light, directing of the optic nerve tract and involved in separating of waste materials (Hill, 1992 a, b; Prota, 1992).

A glossy white skin is the consequence of the absence of colour from the epidermal layer of the skin and results into an intrinsic disorder is called albinism. Albinism is taken from the Latin word, albus, Means white (Summers, 2009).

Albinism has influenced individuals since long time. Youngsters influenced by albinism were generally feared and loathed in a few social orders, while esteemed and regarded in some communities (Cameron, 1979; Okoro, 1975; Kromberg, 1992).

Eye, skin and hair colorations are promptly observable and can offer a fraction of the least complex resources for investigative the activity of genes (Jackson, 1994).

The blend of various colours is contributed by various genes that involve in the production of various chemical substances, which offer ascent to obvious colours improvement. In view of the fact albinism is an acquired infectivity, family history is the main known hazard variable of the disorder. The union of various colours shade is controlled by numerous genes that take part in the production of various substances, which often contribute to conspicuous colour refinement (Mukhopadhyay, Yolanda, T. Moses, 2013).

1.6.2 Thalassemia

Thalassemia is an acquired disorder portrayed by irregular and low generation of hemoglobin (Hb) and unnecessary obliteration of red blood cells (RBCs). Thalassemia

causes uneven degrees of sickliness, which can broaden from massive to life-devastating. It is assessed that 1.5% of the world's population are carriers of beta-thalassemia i.e. at any rate there are 80 million to 90 million individuals with an expected 60,000 new cases being conceived every year (Chakrabart, 2012).

These genetic anaemias are brought on by transformations that decline Hb union and RBCs survival. This inherited sickliness is brought on by diminished or truant generation of one kind of globin chain, either α or β. Such hematological issue range from asymptomatic to serious iron deficiency, which can bring about noteworthy bleakness and mortality. Beta-thalassemia is common in the India, southern China, in Africa, in South America and in Mediterranean nations. The mainly significant carrier recurrence is accounted for in Cyprus (14%) and in Sardinia (10.3%). The tendency of thalassemia carriers is 5-8% in different racial gatherings which make an interpretation of into 7 to 10 million people. The normal future of β-thalassemia patients in Pakistan is 10 years. All around, endeavors have been made for the aversion of thalassemia by mass instruction and different counteractive action systems, similar to mass screening, pre-natal conclusion and end of pregnancy and pre-conjugal screening (Sandeep *et al.,* 2012).

1.7 Analysis

Because of the extensive variety of hereditary disorders that are in the blink of an eye known, finding of a hereditary disorder is generally differed and ward of the confusion. The essential parts of a hereditary disorder lay on the legacy of hereditary material. With an inside and out family history, it is conceivable to envision conceivable disarranges in youngsters who guide therapeutic experts to particular tests contingent upon the turmoil and permit parents the opportunity to get ready for potential way of life changes, foresee the likelihood of stillbirth, or mull over end. Pre-birth analysis can distinguish the nearness of trademark anomalies in fetal improvement through ultrasound, or identify the nearness of trademark substances by means of intrusive methods which include embeddings tests or needles into the uterus, for example, in amniocentesis (Milunsky, 2004).

1.8 Counseling for an Inbred Couple

In offering counseling for inbreeding couples it is essential to recognize families with a known hereditary disorders and the family without disorders can be studied by family history and developing a pedigree (Bennett *et al.,* 2002).

Reports have verified that in certain clinical tests review policy as gather data on inbreeding as a character of family history is not accessible, apart from the importance of such history in distinguishing the pregnancies at danger (Bishop *et al.,* 2008).

In families with various hereditary disorders enlightening family history by clinical tests and examinations could separate cases that are connected with inbreeding from cases. On the off chance that there is no known hereditary disorder in the family, first cousin marriages can be dangerous for birth deformities in the posterity that is twofold the population hazard, (for example, rather than 2.5%, it gets to be 5%), or the danger might be given as 1.7–2.8% higher than the population base vulnerability, for the most part due to autosomal recessive disorders (Bennett *et al.,* 1999, and Shalev, 2010).

Closely inbreeding relationship, for example, a DFCs couple might be given a higher risk for their posterity which may be evaluated at triple the rate of birth deformities in the all wide-ranging community (Christianson *et al.,* 1970).

Couples who are all the more indirectly related could have a comparable danger of birth imperfections in their posterity as first cousin couples in exceptionally innate populations. This might be because of the way that in such ingrained population the genuine relationship coefficient among two people is much higher than the one ascertained in view of data given by the couple. It additionally gives the idea that the posterity of first cousin relational unions are not at an expanded danger for birth imperfections in their kids on the off chance that they are hitched to a non-relative (Zlotogora, 2005).

The higher danger for baby mortality could be said to the couple, albeit for all intents and purposes, it is extremely troublesome for the guide to give the exact rate in

light of the fact that the danger relies on upon the all inclusive community parameters which are not generally known. Multinational studies among first cousin offspring showed that there is a mean of 1.1% abundance newborn child passing over that of the out breeding descendants, with a proportionate overabundance of 3.5% in pre-regenerative mortality (Bittles and Black, 2010 a, b).

The choice on constraining such relational unions still faces numerous disorders, and it for the most part includes individuals in the family who don't welcome conceding that the family has an "inherited disorder" because of a paranoid fear of isolation inside of the family and inside of a general public with less hereditary proficiency (Hamamy, Hanan, 2012).

New innovations including cutting edge sequencing could in the long run help in diagnosing patients influenced by conditions known not hereditarily heterogeneous. In addition, such advancements could analyze if both couple convey the same autosomal recessive genes that causes a serious disorder. It is conceived that such innovation could later on get to be achievable and reasonable to screen for transporter status and would uniquely diminish the dangers for inbred couples to have posterity influenced by genuine auto-soma latent clutters (Ringer *et al.,* 2011).

In populations that are exceedingly endogamous, hereditary directing and screening could be offered with thought of the hereditary disorders that happen with higher recurrence in that particular populations. Hereditary screening and advising programs at various levels of human services have been started in some high-chance groups (Bennett *et al.,* 2002).

In a segregated Druze town in Israel, where inbreeding rate is high, couples were screened for four uncommon acquired infections that demonstrated high bearer frequencies among patients with recognizable proof of ten at danger couples (Falik-Zaccai *et al.,* 2008).

Among the Persian Jewish group of more prominent Los Angeles, four moderately visit autosomal latent conditions were screened for, with recognizable proof of ten at

danger couples. Comparable screening ventures can be modified at whatever point an ingrained group demonstrates to have high recurrence of autosomal recessive disorders (Kabacks *et al.,* 2010).

Pre marriage hereditary guiding for inbreeding is viewed as one of the imperative viewpoints amongst the group hereditary administrations in very innate populations. Pre origination directing is another progressively requested administration in a few nations and groups where inbreeding rates are still high and specific premature birth of influenced embryo is not satisfactory and doable. Marriage in these nations is viewed as a family choice and not only the couple's choice, in spite of the fact that the recurrence of "orchestrated relational unions "are bringing lately due down to the expanding number of females achieving college level training which gives them a superior and more extensive decision of marriage accomplice (Sekhri and Manju, 1978).

But in a few nations and groups where inbreeding relational unions are standard, numerous youthful couples now a day in interview with the social insurance laborers looking for a deductively and biochemically stable answer of their inquiries including: "Will our youngsters be physically or rationally strange?" "In what manner would we be able to minimize the dangers for having influenced children?" (Bennett *et al.,* 1999).

1.8.1 Social and Instructive Boundaries in Advising for Inbreeding

In a few groups, common associations and common society deny to gather data about inbreeding in essential human services settings and in maternity care work on, limiting distinguishing proof of at-danger pregnancies (Bishop *et al.,* 2008).

The conviction that hereditary issue can just emerge through inbreeding on the fatherly side of the family is additionally entirely basic, and in the psyches of numerous individuals inbreeding may allude just to fatherly blood connections. Accordingly, amid guiding, if a couple demonstrate that they are not relatives, it is vital to explicitly ask about any mutual organic connections on their moms sides of the families (Bittles and Hamamy, 2010).

Among Pakistani settlers, a few patients had absorption of hereditary data in ways that contention with hereditary hypotheses with conceivably genuine therapeutic results. Patients alluded to hereditary qualities centers may not effectively surrender their theories or individual suspicions about the reasons for their own or their off-springs condition and their understandings of hereditary difficulties including the dangers of ingrained relational unions (Shaw and Hurst, 2008).

Instruction of the all inclusive community and of essential wellbeing authorities specifically is an imperative perspective in illuminating the wellbeing and social impacts of innate relational unions. The harmony between the conceivable hereditary issue of inbreeding and the social advantages including the non-isolation of the female accomplice in a group with insignificant hereditary training could change among different couples and diverse groups. In rustic groups, the social advantages of ingrained relational unions could exceed their effect on health and the other way around in urban areas (Bittles and Black, 2010 a).

1.9 Aims of the Proposed Study

1) To locate and identify families with hereditary disorders.

2) To study inbreeding among albino and thalassemia affected families.

3) To study the mode of inheritance of hereditary disorders.

4) To study the clinical and diagnostic features of the affected individuals.

5) Counseling of the families affected with albino and thalassemia disorders.

LITERATURE REVIEW

2.1 Albinism

Albinism results from inheritance of latent alleles and is unknown for all vertebrates, including humans. While a living being with complete nonappearance of melanin is called a pale skinned person or albino, a living being with just a lessened quantity of melanin is depicted as leucistic or albinoid (Encyclopedia Britannica Published January 27, 2015).

Tietz, W. (1963) clarified that Albinism is connected with vision imperfections, for example, amblyopia. Photophobia, and nystagmus Absence of skin pigmentation makes for more helplessness to sunburn and skin diseases. In rare cases, for example, Chédiak–Higashi disorder, albinism might be connected with lacks in the transportation of melanin granules. This additionally influences key granules present in safe cells prompting expanded vulnerability to infectivity of pale skinned person or albino.

Kruijt *et al.* (2011) concentrated on in people; there are two main types of albinism: oculocutaneous influence the eyes, hair and skin, and ocular albinism influences the eyes as it were. A great many people with oculocutaneous albinism seem white or extremely pale, as the melanin shades in charge of chestnut, dark, and some yellow hues are not display. Visual albinism results in light blue eyes and may require hereditary testing to analyze.

Kaplan and De Domenico (2008) said people with albinism have skin that completely does not have the dim color melanin, which shields the skin from the sun's bright radiation; their skin can blaze all the more effortlessly from overexposure.

Wolf, S. (2005) portrayed that human eye ordinarily produces enough colour to shading the iris blue, green or cocoa and loan obscurity to the eye. In photos, those with albinism will probably illustrate "red eye," because of the red of retina being unmistakable through the iris. Absence of color in the eyes likewise brings about issues with vision, both related and irrelevant to photosensitivity. Those tormented with albinism are by

and large as sound as whatever is left of the population (however see related scatters underneath), with development and advancement happening as typical, and albinism independent from anyone else does not bring about mortality in spite of the fact that the absence of color blocking bright radiation builds the danger of melanomas (skin diseases) and different issues.

Raymond, E. *et al.* (2007) portrayed that iris is a sphincter framed from pigmented tissue that agreements when the eye is presented to splendid light, to secure the retina by restricting the measure of light going through the understudy. In low light conditions, the iris unwinds to permit all the more light to enter the eye. In albinistic subjects, the iris does not have enough color to obstruct the light, in this way the diminishing in student breadth is just mostly fruitful in decreasing the measure of light entering the eye. Also, the disgraceful improvement of the RPE, which in ordinary eyes retains the greater part of the reflected daylight, further expands glare because of light dissipating inside of the eye. The subsequent affectability (photophobia) for the most part prompts distress in splendid light, yet this can be diminished by the utilization of shades and/or overflowed caps.

As indicated by King, R. (2001) oculocutaneous albinism is for the most part the consequence of the organic legacy of hereditarily latent alleles (genes) went from both parents of a person for instance OCA1 and OCA2. A transformation in the human TRP-1 quality may bring about the deregulation of melanocyte tyrosinase compounds, a change that is speculated to advance cocoa versus dark melanin combination, bringing about a third oculocutaneous albinism (OCA) genotype(OCA3). Some uncommon structures are acquired from one and only parent. There are other hereditary trans-formations which are ended up being connected with albinism. All adjustments, nonetheless, prompt changes in melanin generation in the body.

As indicated by Boissy, R.E. *et al.* (1996) the shot of posterity with albinism coming about because of the blending of human with albinism and one without albinism is low. Be that as it may, on the grounds that living beings (counting people) can be transporters of genes for albinism without displaying any attributes, albinistic

posterity can be delivered by two non-albinistic parents. Albinism for the most part happens with equivalent recurrence in both genders. A special case to this is visual albinism, which it is gone on to posterity through X-linked inheritance. Therefore, visual albinism happens all the more much of the time in males as they have a single X and Y chromosome, not at all like females, whose hereditary genes are portrayed by two X chromosomes.

Mollet *et al.* (2007) observed that variety in skin, hair and Iris is exceptional and obvious character in various human populaces. Skin pigmentation is a to a great degree diverse human component with a reach from white or pink to tan, dull chestnut or dark. It shows an undeniable distinction even inside of a specific ethnic gathering. But in some uncommon obsessive cases, skin shading is the aftereffect of three shades or chromophores: a chestnut/dark or red/yellow color created by melanocytes called melanin; hemoglobin in red platelets of vessels; and third, and to a much lesser degree, nutritive carotenoids, once in a while most evident as yellow shading on the palms. Overall efficient varieties in skin and hair shading are the consequence of contrasts in the melanin substance of skin, particularly by the sum, shape and supply of measure of the melanin to the skin.

Slope (1992 a); Hill (1992 b); Prota (1992) said that melanin assumes a basic part in skin, eye and hair shading furthermore helps in photograph assurance, steering of the optic nerve tracts and conceivably in separating of waste materials. A shiny white skin is the consequence of the absence of shade from the epidermal layer of the skin and results into an inborn issue called albinism. Albinism is gotten from the Latin word, 'albus', which means white.

Jackson (1994) noticed that Albinism has influenced individuals since long time. Youngsters influenced by albinism were for the most part feared and abhorred in a few social orders, while esteemed and regarded in others. Eye, hair and skin pigmentation are promptly detectable and can offer a portion of the most straightforward means for breaking down the activity of qualities.

Mukhopadhyay *et al.* (2013) watched the union of various shading colours is contributed by numerous genes that join in the creation of various sorts of substances, which offer ascent to unmistakable shading qualification. Since albinism is an acquired sickness, family history is the main known danger variable of the confusion. The amalgamation of various shading shades is contributed by numerous qualities that join in the creation of various sorts of substances, which offer ascent to obvious shading qualification.

Bahadoran *et al.* (2003) explained the variety in skin, hair and Iris shading is astounding and noticeable character in various human populaces. Skin pigmentation is a to a great degree diverse human component with an extent from white or pink to tan, dull cocoa or dark. It shows a conspicuous contrast even inside of a specific ethnic gathering.

Abdel-Malek (2001) discuss that in some uncommon neurotic cases, skin shading is the consequence of three colors or chromophores: a cocoa/dark or red/yellow shade created by melanocytes called melanin; hemoglobin in red platelets of vessels; and third, and to a much lesser degree, nutritive carotenoids, some of the time most evident as a yellow shading on the palms. Overall deliberate varieties in skin and hair shading are the aftereffect of contrasts in the melanin substance of skin, particularly by the sum, frame and supply of measure of the melanin to the skin.

Slope (1992 a); Hill (1992 b); Prota (1992) observed that melanin assumes an imperative part in skin, eye and hair shading furthermore helps in photograph assurance, directing of the optic nerve tracts and perhaps in separating of waste materials.

Summers (2009) identified that a radiant white skin is the aftereffect of the absence of color from the epidermal layer of the skin and results into an inborn issue called albinism. Albinism is gotten from the Latin word, 'albus', which means white. Albinism has influenced individuals since long time.

Garrod (1923) characterized that Albinism is a gathering of scatters brought about by weakened generation of the polymeric shade .Melanin creation is firmly managed in the body and happens in specific ectodermally-inferred cells called

melanocytes. Melanocytes might be cutaneous (hair, skin) or additional cutaneous (eye, cochlea), every getting from a particular ectodermal genealogy. The clinical classification for albinism is entangled by the way that the terms albinism. Melanin is a critical color present in the human skin, hair and eyes; and certain inner structures including the substantia nigra of the mind. It is integrated in particular cells, called melanocytes. Colors bringing about obscurity in skin, hair plumes, and so on. They are unpredictable polymeric structures and are separated into three gatherings: Allomelanins in the plant kingdom and Eumelanins and Phaeomelanins in the set of all animals. The substance offers shading to the skin and eyes. Melanin union is catalyzed by the protein tyrosinase and is controlled by TYR, TYRPI and TYRP2 genes. Melanocytes lie between the epidermis (external layer) and the dermis (inward layer) of the skin. Melanocytes start from embryonic sensory tissue and relocate into the skin by the third month of fetal life. They hold the very fanned morphology of neurons. Diverse race people groups have the same quantities of melanocytes yet the numbers and sizes of the pigmented melanosomes vary in view of the substance and concoction organization of the melanin. Melanosomes are not just found in the dendrites of the melanocytes additionally moved from them into neighboring epithelial cells.

Pliny (1942); Gellius (1952) described that Oculocutaneous albinism is a group of autosomal recessive disorder portrayed by decreased or missing melanin color in the skin, hair, and eyes, with going with optic deserts that incorporate low vision, nystagmus, strabismus, and perpetual photophobia. In light of its outwardly obvious phenotype, OCA was one of the prominent disorders.

2.2 Thalassemia

Honig *et al.* (2000) said that Thalassemia, Greek thalassa ocean and haima blood, has been geologically connected with Mediterranean in its initial point, and its pervasive-ness in different parts of the world is still considered incompletely as an outcome of the early Greek victories. Thalassemia is a genuine inherited non specific blood issue its genes are amazingly broad and are accepted to be the most pervasive of all human hereditary sicknesses.

Weatherall *et al.* (2000) observed that Thalassemia is more than a provincial issue. As indicated by the World Health Organization it is assessed that just in Thailand 250,000 beta thalassemic patients are analyzed.

De Silva *et al.* (2000) explained that there are no less than 10,000 new cases are normal, comparative appraisals are anticipated for Asian population.

Stienberg *et al.* (2001) observed that Thalassemia is an acquired autosomal passive blood malady, in which one of the globin chains is not incorporated sufficiently, accordingly bringing about the development of strange hemoglobin atoms which thus causes anemia and related blood related entanglements. The presentation of iron deficient side effects is an early sign of thalassemia giving it the portrayal of a haemaglobinopathic condition.

Provan (2003) discuss that Thalassemia is by the by not a single disorder, but instead a composite of a few deficient alterations in the hemoglobin structure, each of which prompting a particular way of complexities and anticipation. Among the significant variations, two sorts named alpha and beta thalassemia are viewed as the most imperative. As the names show, in alpha thalassemia, the alpha chains are inadequate or missing, and in beta thalassemia the beta chain is influenced. Globins are the subunit chains of hemoglobin whereby two alpha and two beta subunits are consolidated to create ordinary tetramers of hemoglobin. Diminished amalgamation of one of the subunit prompts the infection, where the hemoglobin chain lopsidedness harms and obliterates red cells subsequently creating frailty. Patients live the length of there are sufficient subunits blended with typical structure are fundamentally ordinary. The mix of subunits in ordinary hemoglobin is particular where a solitary subunit of the alpha chain and a solitary subunit from the beta chain consolidate to create a typical hemoglobin dimer. With extreme alpha thalassemia, the beta subunits start to relate into gatherings of four (tetramers) because of the deficiency of its alpha accomplice. These tetramers of beta globin subunits are practically latent and don't transport oxygen. In serious beta thalassemia, then again, no tant amount tetramers of alpha globin subunits structure and alpha subunits are quickly corrupted without a beta accomplice.

Saka *et al.* (1995) studied that Patients who have alpha thalassemia gene show milder side effects with littler, bucket red blood cells enduring a gentle form of constant weakness that does not reacts to iron supplements. Beta thalassemia, then again, can extend from gentle to extreme iron deficiency and is as needs be grouped into three classes of expanding seriousness, to be specific thalassemia minor, thalassemia intermedia and thalassemia major. A man with thalassemia minor characteristic has one typical and one changed gene. They ordinarily encounter no wellbeing disorders other than mellow pallor. In thalassemia intermedia, the influenced individual has two irregular qualities however is as yet delivering some beta globin. The seriousness of the paleness and wellbeing issues experienced relies on upon the transformations present. The separating line between thalassemia intermedia and thalassemia major is the level of sickliness and the number and recurrence of blood transfusions required to treat it. Those with thalassemia intermedia may require intermittent transfusions and thalassemia major requiring it all the time. Thalassemia major (Cooley's Anemia) initially depicted by Cooley and Lee (1925) as a consequence of lessened amalgamation of beta globin chain, it typically shows up in a newborn child following 3 months of age and causes life-undermining frailty, this pallid condition requires general blood transfusions and significant progressing restorative consideration to keep up the ordinary body capacity in patients. After some time when these transfusions surpass 20, it would prompt the development of an over the top measure of iron in the body, left untreated, this overabundance iron can store into the liver, heart and different organs typically prompting a sudden passing from organ disappointment.

Aisen (1980) enumerated that just a little extent of aggregate body iron enters or leaves the body's stores every day. Subsequently, intercellular iron transport, as a part of the iron reutilization procedure, is quantitatively more essential than the aggregate body load. The best mass of iron is found in red platelets, which contain around 80% of the aggregate body iron substance. The body framework reuses a generous measure of iron from harmed and matured red cells, for the union of new hemoglobin.

Dabbagh *et al.* (1994); Pool *et al.* (1999) watched that in thalassemia patients this iron homeostasis is irritated in light of the body's failure to deliver fresh recruits cells

keeping in mind the end goal to reabsorb iron from transfused blood. Thalassemia patients, in this manner, need exceptional restorative consideration and mediations to keep an anomalous develop of iron burden. Given that iron burden assumes the basic part in the life of a thalassemia quiet experiencing blood transfusion, one would need to ceaselessly screen different segments deciding the iron put away in the body. Iron over burden additionally lessens the levels of cancer prevention agents in plasma by meddling in the retention of other follow metals, for example, copper and zinc, diminished uptake of these metals may bring about the decrease of their compounds.

Taylor *et al.* (1988); Hulten *et al.* (1995); Halberg *et al.* (1997); Roughead and Hunt, 2000) described that the plasma ferritin fixation is a critical subjective file in the patient studies has demonstrated a converse relationship between serum ferritin focus and iron ingestion in people.

Goljan (2000) observed that for the most part, thalassemia is common in populaces that advanced in moist atmospheres where intestinal sickness was endemic, however influences all races. Thalassemia is especially connected with African Americans, individuals of Mediterranean inception, and Asians.

Maggio *et al.* (2002) Estimated that predominance of Thalassemia is 16% in Cyprus, 3-14% in Thailand, and 3-8% in population from Pakistan, India, Bangladesh, Malaysia, and China. There is additionally prevalence in individuals from Latin America, and Spain, Portugal, Italy, Greece and others. A low pervasiveness has been accounted for from individuals in Africa (0.9%), with those in northern Africa having the most elevated frequency, and in northern Europe (0.1%).

In Pakistan the predominance of thalassemia is notably higher in KPK most likely in light of the impact of Greek invasions previously (Prof. Fazl-e-Raziq. individual correspondence).

Pippard *et al.* (1979) ordered thalassemia as per which chain of the hemoglobin particle is influenced. In α thalassemia, generation of the globin chain is influenced, while in β thalassemia creation of the β chain is influenced. Thalassemia produces a

lack of α or β chain, not at all like sickle cell weakness that delivers a particular mutant type of β globin. Erasure of one of the loci has a high predominance in individuals of African-American or Asian drop, making them more prone to create α thalassemia. β thalassemia is normally present in Africans, Americans, and additionally in Greeks.

Kumar *et al.* (2004) give the hereditary proof that α thalassemia includes the qualities HBA1 and HBA2, acquired in a Mendelian latent manner. It is likewise related with the crossing out of the 16p chromosome. Alpha thalassemia result in diminished alpha-globin creation, in this way less alpha-globin chains are delivered, bringing about an abundance of β chains in grown-ups and overabundance γ chains in babies. The abundance β chains structure is called Hemoglobin of 4 beta chains that have irregular oxygen separation bends. β thalassemia are because of changes in the single gene on chromosome 11 likewise acquired in an autosomal recessive manner. The seriousness of the infection relies on upon the way of the change. Changes are portrayed as (β) on the off chance that they keep any development of β chains. In either case there is a relative overabundance of α chains, however these don't shape tetramers: rather, they tie to the erythrocytes layers, creating film harm, and at high fixations they frame dangerous totals. There are an expected 60-80 million individuals on the planet who convey the beta thalassemia quality alone. This is an unpleasant assessment and the genuine number of Thalassemia significant patients is obscure because of the pervasiveness of thalassemia in less created nations in the Middle East and Asia. Nations, for example, India, Pakistan and Iran are seeing a vast increment of thalassaemia patients because of absence of hereditary guiding and screening.

As per Pippard *et al.* (1979) and Pootrakul *et al.* iron over-burden in non transfused thalassemia intermedia patients happens in light of expanded intestinal iron retention because of erythropoiesis while in routinely transfused thalassemia major the iron over burden is expected the breakdown of red platelets however the rate of iron stacking is slower in thalassemia intermedia as contrast with thalassemia major, intermedia patients would create confusions in the long run.

Tanno *et al.* (2007) inspected 15 solid non thalassemic contributors and beta thalassemic patients, sound volunteers had mean GDF15 serum levels of 450–50 pg/ml contrasted with patients with GDF15 serum levels of 48,000 to 248,000 pg/ml, these outcomes recommended that GDF15 over expression emerging from an extended erthyroid compartment to contributes to iron overload in thalassemic syndromes by inhibiting hepicidin expression.

MATERIAL AND METHODS

3.1 Study Area

The region is named after the central command town Dera Ghazi Khan, which was established about 500 years back by Ghazi Khan Mirrani. The cumulative section of the area is 11,922 km^2, lies between 29'- 34° to 31'-20° scopes and between 69'-53° to 70'-54° East longitudes. It is limited on the North by D.I. Khan District of KPK on the West by Musa Khel and Barkhan areas of Baluchistan, on the South by Rajan Pur, and on the East by Muzaffar Garh and Leiah, isolating the later two locales by waterway Indus (Figure 3.1). This district contains three Tehsils viz. D.G Khan, Taunsa, Kot chutta and Tribal region (DGK Gazetteer, 1898; Census, 1998).

In Pakistan the information on innate marriage and its results particularly hereditary disarranges is divided. Just few studies are accessible in which inbreeding and its effects have been contemplated on preparatory levels in enormous urban areas and huge metropolitan territories. No study has been propelled in the remote and immature ranges.

This zone is very little alluring financially and geologically segregated along these lines, this is a standout amongst the most suitable zones for the investigation of inbreeding relational unions and its related impacts, including the nearness of pale skinned person and thalassaemia.

Accordingly, in the present study we mean to evaluate inbreeding in pale skinned person(albino) and thalassemia influenced families resident in Tuman Leghari District D.G Khan located in south of the Punjab, Pakistan.

3.2 Data Collection

With a specific end goal to investigation of inbreeding in albino person and thalassemia influenced families inhabitant in Tuman Leghari District Dera Ghazi Khan, a questionnaire was planned and conveyed in the study region to gather the applicable data amid the field review. For this field review, authorization was likewise acquired

from the managerial powers i.e. administrator and councilors of various Union councils of Tuman Leghari in D.G Khan to lead the study in residential communities, towns and tribal ranges, which thusly turned out to be vital to get to, contact and speak with the nearby groups. Families were drawn closer at their towns and homes where they were informed about the study, its points and targets. With the assent of the family, the information was gathered from the older folks or leader of the family accessible in the town and home. The information gathering was finished in six months beginning from September 2015 to February 2016.

During the overview, 406 families were met for information accumulation. For the present concentrate, family is characterized as an accumulation of persons related by blood or marriage, having the same salary source and living in the same home. No criteria of incorporation or prohibition were received and all the inspected families were incorporated into the investigations. The body of the information gathered includes the accompanying ranges of demography and inbreeding: data about region, ethnicity, marriage sorts, financial status of spouse, and instructive levels of companions before marriage, and word related gathering of spouse before marriage. The particular point of interest of different parameters is given underneath.

3.2.1 Ethnicity

Ethnicity implies a group of that individual fit in with as a result of shared qualities, including hereditary and geological inceptions, social conventions, and dialects. So, population is isolated into three fundamental ethnic groups i.e. Leghari, Khosa, Saraiki other than Baloch.

3.2.2 Couple's Relationship and Marriage Types

The accurate relationship between the spouse and wife preceding marriage were recorded. All the marriage sorts and parental connections were distinguished that include: marriage between first cousin (FC), second cousin (SC), indirectly related (DR), and relational unions between non-related (NR). The commonness and example of inbreeding was assessed from sort of marriage unions. The marriage sort first cousin (FC), second cousin (SC) and directly related (DR) relational unions were considered as ingrained

relational unions in light of the fact that the hereditary effect of these relational unions is purportedly substantially more genuine than other marriage sorts. Then again, non-related relational unions (NR) were thought to be out reared.

3.2.3 Socio-monetary Status of Husband

Social and monetary parameters are the key requirements characterizing different practices in our general public including the marriage design. For different reasons, both parameters are joined and can't be interestingly delimited. In this way, social and monetary components have been coordinated as financial status in the present study. Three classes were characterized concerning spouse's financial status on the premise of pay, sort and size of home, responsibility for and agrarian area, responsibility for and other life solaces. These classes are: lower, center and more elevated amounts.

3.3 Families Studied (Clinical Basis)

The families were found out by recognizing proband amid the review for inbreeding. At that point the families were gone by at their places of home. The senior citizens and relatives of the families were met to get data about the pale skinned person and thalassemia like hereditary issue and other important matters. The case history, number of influenced people, number of eras included, the related imperfections assuming any and onset of the hereditary sickness were painstakingly recorded. All the data acquired was crosschecked by talking distinctive persons. For hereditary deduction a broad family involving more than three eras was built for every family since three-era family gives a pictorial representation of turmoil inside of a family and is the most proficient approach to evaluate innate impacts on sickness and essential to perceive the example of legacy of the confusion (Puri and Verma, 2004; Wattendorf and Hadley, 2005).

3.4 Statistical Analysis

Every one of the information was broke down by utilizing chi-square test as a part of a measurable programming bundle MiniTab 17 rendition. The standard techniques and images portrayed by Bennett *et al.* (1995) were utilized for drawing family. What's more, Cyrillic form 2.1.3 (Cherwell experimental distributed 1997, www.cherwell.com) a family drawing programming was utilized for drawing family and ascertaining the inbreeding co-productive. At that point the example of legacy of genetic issue considered was concluded by watching the isolation or transmission of the turmoil inside of family.

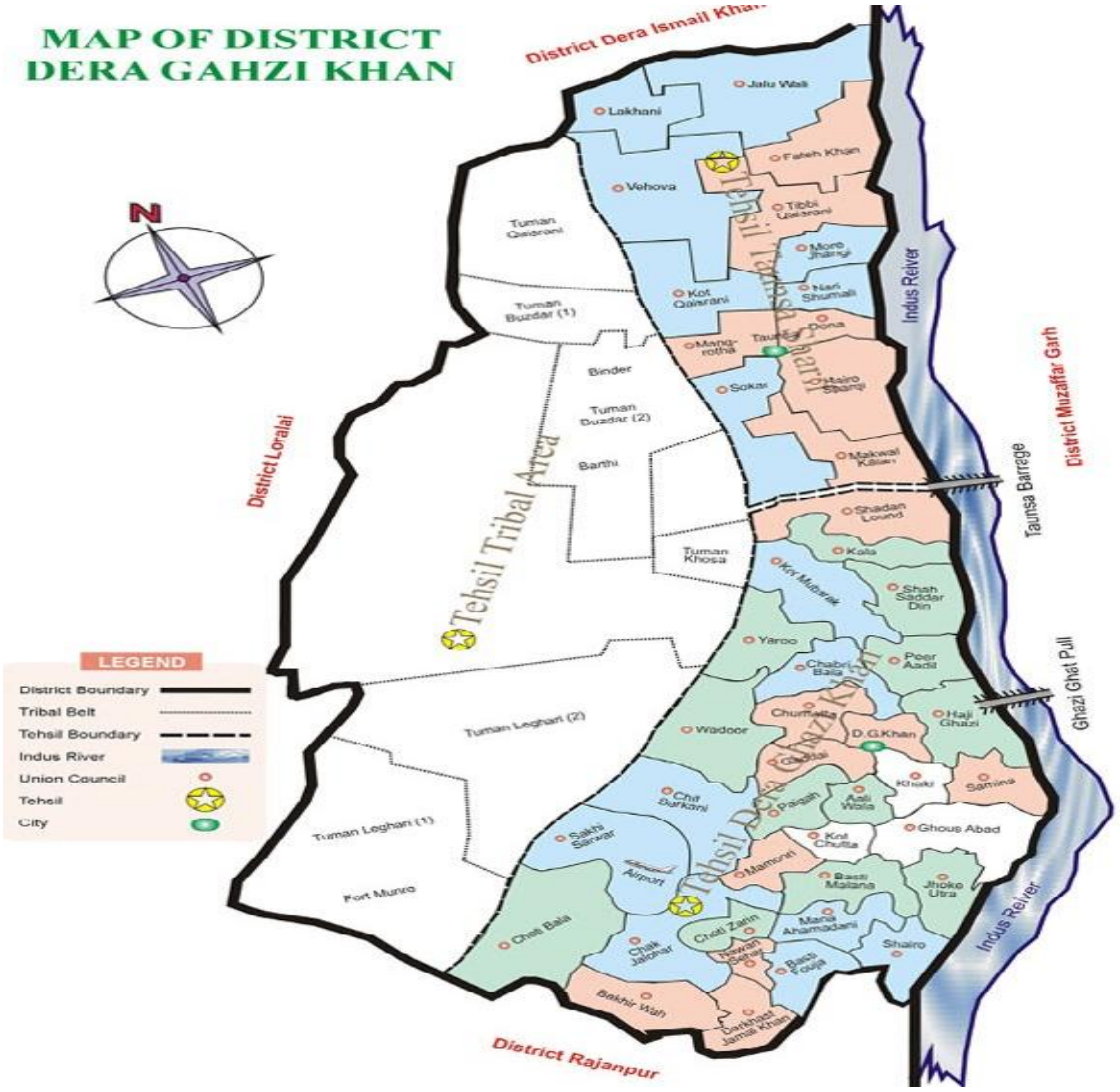


Figure 1.1: Map of Dera Ghazi Khan

RESULTS

4.1 Data Collection

During information accumulation, 406 families were drawn nearer arbitrarily to concentrate on the impacts of inbreeding. Ethnically the most astounding positive reaction was found in Saraiki (other than Baloch) 47.30% than Leghari (32.26%) or Khosa (20.44%). Table 4.1 presents relative numbers and percent frequencies of families having a place with various ethnic groups and managerial ranges inside of the example. The Saraiki other than Baloch, Khosa and Leghari families were 47.30%, 32.26% and 20.44%, respectively.

4.2 Marriages

4.2.1 Inbreed and Outbreed Marriages

Inbreeding relational unions were observed to be more common in Tuman Leghari Tribe of D.G Khan District. The frequencies of such relational unions in various ethnic groups were seen to be: Saraiki (other than Baloch) 46.24%, Leghari 35.10% and Khosa 18.66%. (Table 4.2) The correlation of inbreeding relational unions and out-breeding relational unions in various ethnic groups of Tuman Leghari tribe was observed to be factually non-noteworthy.

Be that as it may, very noteworthy contrasts were found between the pervasive-ness of inbreeding and outbreeding relational unions in all out example and in addition inside of the ethnic groups, Leghari, and Khosa (X^2=10.87 P<0.001, X^2=47.45 P<0.001 and X^2=03.73 P<0.001 respectively).

4.2.2 Distribution of Marriage sorts in Ethnic gatherings of Tuman Leghari Tribe

Among various marriage sorts, first cousin (FC) were more regular when contrasted with all other marriage sorts, for example, second cousin (SC), directly related (DR) and non-related (NR) with recurrence 38.67%, 26.11%, 21.18% and 14.04% separately. (Table 4.3) first cousin and non related relational unions were most

pervasive in Khosa and when contrasted with other ethnic gatherings. Factual investigation reveal the huge distinction among different sorts of relational unions in Leghari, Khosa and Saraiki other than Baloch (X^2=20.00 P<0.001).

4.3 Inbreeding and Outbreeding Relational Unions

The recurrence of inbreeding relational unions in all out populace was 85.96%. Correspondingly in ethnic gatherings, the frequency of inbreeding relational unions was 44.70%, 36.10% and 19.20% in Saraiki other than Baloch, Leghari and Khosa separately. Table 4.4 demonstrates the correlation of inbreeding and outbreeding relational unions in Leghari, Khosa and Saraiki other than Baloch, which contrasted essentially (X^2=10.87; 0.001 < P<0.005). A huge contrast was seen in Leghari and non-critical distinction saw in Khosa and Saraiki other than Baloch with 10.87, 27.09 and 3.73 Chi values.

4.4 Mean Inbreeding Coefficient (F)

The mean inbreeding coefficient (F) for the aggregate population was ascertained as 0.0287 Moreover, the mean inbreeding coefficients (F) for the Baloch and Saraiki other than Baloch populations were likewise discovered high (Table 4.5). These evaluations demonstrated the higher level of connection in Saraiki other than Baloch and Baloch when contrasted with population.

4.5 Variables Effecting Rate of Inbreeding

There are various variables which have immediate or aberrant effect on the rate of inbreeding. These variables incorporate, yet don't include every, social tie, rank, financial conditions, family structure, instructive level of companions, religion and topography. In the present study, the most critical components have been displayed which incorporates: training (both male and female instruction), male financial status. Instruction is constantly viewed as an essential component in choice of mate in every single cultivated society.

4.5.1 Male Education

With a specific end goal to survey the effect of male instruction on the marriage sorts; the example was separated into three groups in light of male educating years at the season of marriage. Subsequently, in complete examples, speaking to the lower, center and larger amounts of male training included 81 (19.95%), 141 (34.72%) and 184 (45.32%) couples, individually. Male instruction observed to be measurably noteworthy in Saraiki other than Baloch bunch (Table 4.5).

4.5.2 Female Education

To evaluate the effect of male instruction on the marriage sorts, the specimen was partitioned into three groups in light of male educating years at the season of marriage. In absolute specimens, speaking to the lower, center and more elevated amounts of male training contained Leghari 114 (19.95%), Khosa 133 (34.72%) and Saraiki other than Baloch 184 (45.32%) couples, respectively. Female instruction observed to be factually huge in Khosa bunch (Table 4.6).

4.5.3 Socio-economic Status of Male

With a specific end goal to discover the effect of financial status of male on marriage sorts, the example was separated into three gatherings taking into account male financial status at marriage time. The aggregate specimen speaking to the lower, center, and larger amounts contained Leghari 120 (29.56%), Khosa (131 (32.26%) and Saraiki other than Baloch 155 (38.18%). The factual investigation reveals critical results altogether and Leghari ethnic group (Table 4.7).

4.5.4 Socio-economic Status of Female

Keeping in mind the end goal to discover the effect of financial status of female on marriage sorts, the specimen was separated into three gatherings in light of male financial status at marriage time. The aggregate example speaking to the lower, center, and larger amounts involved Leghari 108 (26.60%), Khosa (152 (37.44%) and Saraiki

other than Baloch 146 (35.96%). The factual investigation reveals critical results in all out example, Leghari and Saraiki other than Baloch ethnic groups (Table 4.8).

4.6 Effect of Inbreeding

During the study, 39 concerned couples, having influenced youngsters or one hereditarily influenced tyke with positive history, were distinguished. To contemplate the impact of marriage sorts on particular gathering of hereditary issue, these couples were separated into two gatherings, for example, skin issue, and thalassemia. The quantity of pale skinned person and thalassemia couples were 13 (33.33%) and 26 (66.67%) separately (Table 4.9). Over all the distressed couples with Thalassemia were discovered most pervasive in the example. On ethnic base, 33.33%, 10.26% and 56.41% of aggregate harrowed couples were observed to be connected with the Leghari, Khosa and Saraiki other than Baloch amasses individually. Inbreeding relational unions were discovered endemic in harrowed couples (100%) when contrasted with all inclusive community (00%). In various gatherings of burdened couples taking into account hereditary scatters, inbreeding was discovered 100% in both albino person and thalassemia (Table 4.10).

The recurrence of inbreeding relational unions in the specimen of harassed couples was 100% with mean inbreeding co-effective was observed to be 0.0287. Measurably huge distinction was found in the middle of inbreeding and outbreeding couples in the specimen (X^2=00 P<0.001) (Table 4.11). Information on relational unions in non-affected and affected groups of various ethnic groups was discovered measurably noteworthy in chi-test (X^2=24.42) and in various sorts of relational unions FC (38.92), SC (25.86%), DR (21.18%), and NR (14.04%) were likewise factually huge. If there should be an occurrence of albino person and thalassemia couples, thalassemia was found to exceptionally huge in all marriage sorts (i.e. X^2=11.69) (Tables 4.12, 4.13 and 4.14).

Information on youngsters in Leghari, Khosa and Saraiki other than Baloch were measurably huge in both affected and non-affected (Table 4.15-4.16). If there should arise an occurrence of information on number of youngsters in Leghari, Khosa

and Saraiki other than Baloch in albino person were discovered lesser in number and in thalassemia very huge in chi- test (Table 4.17-4.18).

Mindfulness about albino person, thalassemia and conduct of parents, relatives, society toward albino people and thalassemic were discovered factually huge (Table 4.19 and 4.20).

Table 4.1: Data summary on basis of tribes in Tuman Leghari Dera Ghazi Khan

Ethnicity	**Number**	**Percentage**
Leghari	131	32.26
Khosa	83	20.44
Saraiki Other than Baloch	192	47.00
Total 406		

Table 4.2: Statistical analysis for comparison of inbreeding and out breeding marriages between Leghari, Khosa and Saraiki other than Baloch couples from Tuman Leghari

Samples	**Inbreeding**	**Outbreeding**	**Total**	**X^2**
Leghari	126 (35.10%)	05 (10.64%)	131 (32.26%)	10.87 (P<0.001)
Khosa	67 (18.66%)	16 (34.04%)	83 (20.44%)	47.45 (P<0.001)
Saraiki Other than Baloch	166 (46.24%)	26 (55.32%)	192 (47.00%)	03.73 (P<0.001)
	359 (88.42%)	47 (11.58%)	406	34.05 (P<0.001)

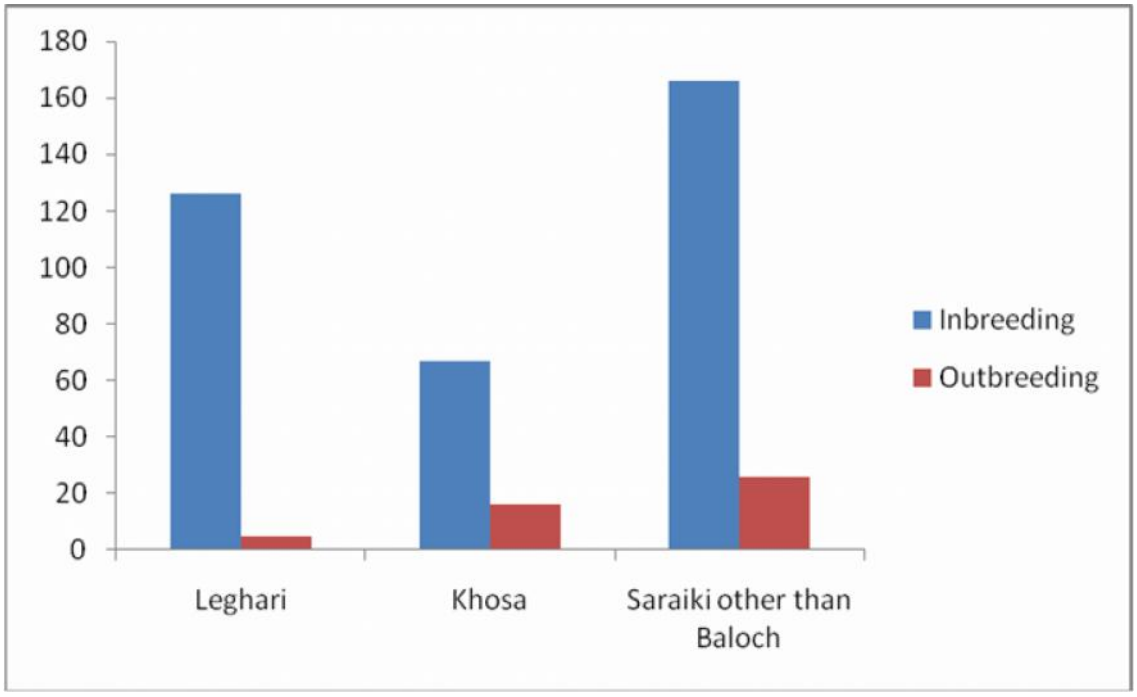


Figure 4.1: Comparison of inbred and out bred marriages between Leghari, Khosa and Saraiki other than Baloch couples from Tuman Leghari

Table 4.3: Distribution of marriage types in ethnic groups of Tuman Leghari Tribe

Types of Marriages	F	Leghari	Khosa	Non Baloch	Total
FC	0.3821	49 (37.40%)	36 (43.37%)	72 (37.50%)	157 (38.67%)
SC	0.1301	37 (28.24%)	16 (19.28%)	53 (27.60%)	106 (26.11%)
DR	0.1085	40 (30.53%)	15 (18.07%)	31 (16.15%)	86 (21.18%)
NR	0	05 (3.83)	16 (19.28%)	36 (18.75%)	57 (14.04%)
Total	0.1354	131 (32.27%)	83 (20.44%)	192 (47.29%)	406

X^2= 20.00 P> 0.001

Table 4.4: Comparison of inbred and outbreed marriages in Leghari, Khosa and Saraiki other than Baloch

Sample	Mean F	IM	OM	Total	X^2
Leghari	0.0301	126 (35.10%)	05 (10.64%)	131 (32.27%)	10.87 P < 0.001
Khosa	0.0256	67 (18.66%)	16 (34.04%)	83 (20.44%)	47.45 P<0.001
Saraiki other than Baloch	0.0303	166 (46.24%)	26 (55.32%)	192 (47.29%)	3.73 P < 0.001
Total	0.0287	359 (88.42%)	47 (11.58%)	406	16.160.001<P<0.005

X^2=16.16; 0.005< P < 0.001

IM= Inbreeding marriages OM= Out breeding marriages

Table 4.5: Inbreeding coefficient (F), inbreeding and outbreeding marriages with respect to husband's education

Population	**Mean F and Inbreeding**	**Husband's education level**			**Total**
		Lower	Middle	Higher	
Mean Inbreeding coefficient (F)		0.0272	0.0292	0.0311	
Leghari	Inbreed	16	27	39	82
	Outbreed	11	17	21	49
	Total	27	44	60	131
	X^2= 0.33 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0291	0.0301	0.0251	
Khosa	Inbreed	10	17	24	51
	Outbreed	07	12	13	32
	Total	17	29	37	83
	X^2= 0.26 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0303	0.0249	0.0310	
Saraiki other than Baloch	Inbreed	22	37	48	107
	Outbreed	15	31	39	85
	Total	27	68	87	192
	X^2= 4.07 P>0.001				
Mean Inbreeding coefficient F		0.0290	0.0249	0.0271	
Total	Inbreed	48	81	111	240
	Outbreed	33	60	73	166
	Total	81	141	184	406
	X^2=0.21 P>0.001				

Table 4.6: Inbreeding coefficient (F), inbreeding and outbreeding marriages with respect to the Female's educational level

Population	**Mean F and Marriage type**	**Female's education level**			**Total**
		Lower	Middle	Higher	
Mean Inbreeding coefficient F		0.0261	0.0279	0.0301	
Leghari	Inbreed	31	18	37	86
	Outbreed	13	11	21	45
	Total	44	29	58	131
	X^2=0.64 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0302	0.0305	0.0307	
Khosa	Inbreed	15	21	14	50
	Outbreed	07	09	17	33
	Total	22	30	31	83
	X^2=40.96 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0280	0.0202	0.0278	
Saraiki other than Baloch	Inbreed	31	43	44	118
	Outbreed	17	31	26	74
	Total	48	74	70	192
	X^2=0.69 P>0.001				
Mean Inbreeding coefficient F		0.0265	0.0271	0.0222	
Total	Inbreed	77	82	95	254
	Outbreed	37	51	64	152
	Total	114	133	159	406
	X^2=2.61 P>0.001				

Table 4.7: Inbreeding coefficient (F), inbreed and outbreed marriages with respect to socioeconomic status of male

Population	**Mean F and Marriage type**	**Male's Socioeconomic status**			**Total**
		Lower	Middle	Higher	
Mean Inbreeding coefficient F		0.0211	0.0256	0.0215	
Leghari	Inbreed	34	21	40	95
	Outbreed	17	13	06	36
	Total	51	34	46	131
	X^2=8.55 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0311	0.0301	0.0305	
Khosa	Inbreed	13	19	17	49
	Outbreed	09	11	14	34
	Total	22	30	31	83
	X^2=1.02 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0256	0.0298	0.0227	
Saraiki other than Baloch	Inbreed	23	37	48	108
	Outbreed	24	30	30	84
	Total	47	67	78	192
	X^2=1.67 P>0.001				
Mean Inbreeding coefficient F		0.0311	0.0305	0.0301	
Total	Inbreed	70	77	105	252
	Outbreed	50	54	50	154
	Total	120 (29.56%)	131 (32.26%)	155 (38.18%)	406
	X^2=8.32 P>0.001				

Table 4.8: Inbreeding coefficient (F), inbreeding and outbreeding marriages with respect to the Female's educational level

Population	**Mean F and Marriage type**	**Female's socioeconomic status**			**Total**
		Lower	Middle	Higher	
Mean Inbreeding coefficient F		0.0231	0.0241	0.0253	
Leghari	Inbreed	27	19	39	85
	Outbreed	16	18	12	46
	Total	43	37	41	131
	X^2=9.05 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0256	0.0271	0.0278	
Khosa	Inbreed	13	23	19	55
	Outbreed	08	11	09	28
	Total	21	34	28	83
	X^2=0.21 0.90 < P<0.75				
Mean Inbreeding coefficient F		0.0311	0.0321	0.0325	
Saraiki other than Baloch	Inbreed	29	45	49	123
	Outbreed	15	36	18	69
	Total	44	71	67	192
	X^2=6.28 P>0.001				
Mean Inbreeding coefficient F		0.0341	0.0361	0.0357	
Total	Inbreed	69	87	107	263
	Outbreed	39	65	39	143
	Total	108 (26.60%)	152 (37.44%)	146 (35.96%)	406
	X^2= 8.4 P>0.001				

Table 4.9: Data collection summary of affected couples

Ethnic Group	Genetic Disorder		Total
	Albino	Thalassaemia	
Leghari	02 (15.38%)	11 (42.31%)	13 (33.33%)
Khosa	00(0%)	04 (15.39%)	04 (10.26%)
Saraiki other non-Baloch	11 (86.62%)	11 (42.30%)	22 (56.41%)
Total	13	26	39

Table 4.10: Distribution of inbreeding and outbreeding marriages among affected couples with respect to the disorder

Marriage Types	Genetic Disorder		Total
	Albino	Thalassaemia	
Inbreeding	13 (100%)	26 (100%)	39 (100%)
Outbreeding	00(0%)	00 (00.00%)	00 (00.00%)
Total	13	26	39

Table 4.11: Distribution of inbred and outbreed marriages and mean (F) values among afflicted couples with respect to the Disorder

Marriage Types	Genetic Disorder		Total
	Albino	Thalassaemia	
F	0.0291	0.0302	---
Inbreeding	13 (100%)	26 (100%)	39 (100%)
Outbreeding	00	00	00
Total	13	26	39
$\mathbf{X^2}$	00	00	00
Significance	Significant		

Table 4.12: Data on marriages in non affected and affected families

Sr.	Tribe	F.C	S.C	D.R	N.R	Total	X^2
1	Leghari	44 (27.85%)	37(35.23%)	32(37.21%)	5(08.77%)	118(29.06%)	11.67
2	Khosa	33(20.88%)	15(14.28%)	15(17.46%)	16(28.07%)	79(19.45%)	03.05
3	Saraiki other than Baloch	60(37.97%)	44(41.90%)	30(34.88%)	36(63.15%)	170(04.18%)	05.70
4	Affected families	21(13.29%)	09(08.57%)	09(10.47%)	00(00.00%)	39(09.60%)	04.00
Total		158(38.91%)	105(25.86%)	86(21.18%)	57(14.04%)	406	24.42

Table 4.13: Data on number of affected albino families

Sr.	Tribe	F.C	S.C	D.R	N.R	Total	X^2
1	Leghari	02 (25%)	-	-	-	02 (15.38%)	0.5
2	Khosa	-	-	-	-	-	00
3	Saraiki	06 (75%)	04 (100%)	01 (100%)	-	11 (84.62%)	0.49
Total		08 (61.53%)	04 (30.77%)	01 (7.69%)	00	13	0.99

F.C = First Cousin S.C = Second Cousin D.R = Distantly related N.R = Non-related

Table 4.14: Data on number of thalassemia affected families

Sr.	Tribe	F.C	S.C	D.R	N.R	Total	X^2
1	Leghari	03 (25%)	-	08 (100%)	-	11 (42.31%)	9.66
2	Khosa	03 (25%)	01 (16.66%)	-	-	04 (15.38%)	050
3	Saraiki other than Baloch	06 (50%)	05 (83.33%)	-	-	11 (42.31%)	1.53
Total		12 (46.15%)	06 (23.08%)	08 (30.77%)	00	26	11.69

Table 4.15: Data on number of children in non affected families

Sr.	Tribe	Number of children in non-affected families								Total	X^2
		1st cousin		2nd cousin		Distantly related		Non-related			
		M	F	M	F	M	F	M	F		
1	Leghari	77(32.35%)	29 (38.16%)	78 (42.39%)	27 (39.13%)	50(31.85%)	34(41.97%)	15(16.48%)	05(08.77%)	315(33.05%)	25.8
2	Khosa	56(23.53%)	13(17.11%)	28 (15.22%)	13(18.84%)	28(17.83%)	08(09.88%)	30(32.96%)	22(38.6%)	198(20.77%)	24.46
3	Saraiki	105(44.12%)	34(44.73%)	78 (42.39%)	29(42.03%)	79(50.32%)	39(48.15%)	46(50.54%)	30(52.63%)	440(46.17%)	2.86
Total		238(24.97%)	76(07.97%)	184(19.30%)	69(07.24%)	157(16.47%)	81(08.5%)	91(09.55%)	57(05.98%)	953	53.12

Table 4.16: Data on number of children of affected families

Sr.	Tribe	Number of children in Affected families								Total	X^2
		1st cousin		2nd cousin		Distantly related		Non-related			
		M	F	M	F	M	F	M	F		
1	Leghari	18(33.96%)	05(17.24%)	-	-	10(45.45%)	09(56.25%)	02(40%)	01(25%)	45(27.11%)	7.13
2	Khosa	16(30.19%)	10(34.48%)	-	-	09(40.91%)	05(31.25%)	01(20%)	01(25%)	42(25.30%)	3.72
3	Saraiki	19(35.85%)	14(48.28%)	21(100%)	16(100%)	03(13.64%)	02(12.5%)	02(40%)	02(50%)	79(47.6%)	30.94
Total		53(31.92%)	29(17.47%)	21(12.65%)	16(09.64%)	22(13.25%)	16(09.64%)	05(03.01%)	04(02.41%)	166	41.79

Table 4.17: Data on children of albino affected families

Sr.	Tribe	Number of children in Albino affected families										Total	X^2
		1st cousin		2nd cousin		Distantly related		Non-related		Alive	Dead		
		M	F	M	F	M	F	M	F				
1	Leghari	01(14.29%)	01(14.67%)	-	-	-	-	-	-	02(08.33%)	-	02(04.34%)	1.31
2	Khosa	-	-	-	-	-	-	-	-	-	-	0	0
3	Saraiki	07(15.91%)	06(85.71%)	07(100%)	01(100%)	01(100%)	-	-	-	22(91.67%)	-	44(95.66%)	0.14
Total		08(17.02%)	07(14.89%)	07(14.89%)	01(02.12%)	01(02.12%)	0	0	0	24 (48.94%)	0	46	1.45

Table 4.18: Data on children of thalassemia affected families

Sr.	Tribe	Number of children in Thalassaemia affected families										Total	X^2
		1st cousin		2nd cousin		Distantly related		Non-related		Alive	Dead		
		M	F	M	F	M	F	M	F				
1	Leghari	02(10.52%)	02(11.76%)	-	-	13(100%)	12(100%)	-	-	29(38.16%)	-	58(37.91%)	28.83
2	Khosa	05(26.32%)	08(47.06%)	-	-	-	-	-	-	13(17.11%)	01(100%)	26(17.00%)	14.03
3	Saraiki	12(63.16%)	07(41.18%)	11(100%)	04(100%)	-	-	-	-	34(44.73%)	-	68(44.44	10.65
Total		19(12.42%)	17(11.11%)	11(07.19%)	04(02.61	13(08.5%)	12(07.84%)	00	00	76(49.67%)	01(0.65%)	153	53.51

Table 4.19: Awareness about albino and thalassemia

Genetic	Treatable	Not treatable	Medicinal effect	Curse	Superstitious	Ignore
290(71.43%)	37 (9.11%)	27 (6.65%)	10 (2.46%)	08(1.97%)	04 (0.99%)	30(7.39%)

Table 4.20: Behavior of the parents, relatives and society

Behavior Type	Parents	Relatives	Society
Good	218 (53.69%)	191 (47.04%)	187 (46.06%)
Bad	43 (10.59%)	71 (17.49%)	72 (17.73%)
Ignore	120 (29.56%)	123 (30.29%)	127 (31.28%)
Mercy	25 (6.16%)	21 (5.17%)	20 (4.93%)
Total	406	406	406

4.7 Clinical Study of Affected Families

The most extreme number of individuals both influenced and in addition typical, of the considerable number of families was physically and clinically analyzed. The subjects were taken to the region head quarter hospital center Dera Ghazi Khan or private facilities for this reason. Clinical studies as indicated by the prerequisite of turmoil were performed on chose people to affirm the hereditary issue. Extraordinary consideration was taken in inspecting the patients so as not to miss any related disorder.

4.7.1 Families Studied

For the study displayed here, thirty nine families are incorporated. In which thirteen families/couples are influenced with albino person and twenty six families/ couples are influenced with thalassemia. Family (A, B) speak to Leghari while (C, D, E, F, G, H, I, J, K, L, M) articulate to Saraiki other than Baloch with albino affected. Twenty six (A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, U, V, W, X, Y, Z) with thalassemia were determined from various union councils of Tuman Leghari of Dera Ghazi Khan District.

4.7.2 Albino Affected Families

4.7.2.1 Leghari

In Leghari Tribe two families/couples were pale skinned person influenced (albino), their clinical perceptions were seen as.

Family A

The family "A" dwells in a town Choti Bala of Tuman Leghari Dera Ghazi Khan and has a place with Leghari Tribe. The relatives usually get within the family due to close kinship, therefore the history of affected person shows, it is by the female having mutant gene controlling the disorder which is transmitted in autosomal recessive pattern. The age of the influenced child is two year.

Family B

The family "B" dwells in Choti Bala of Dera Ghazi Khan and has a place with Leghari tribe. The relatives customarily wed inside of the family, which bring about innate relational unions. The relatives usually get marriage within the family due to close kinship, therefore the history of affected person shows, it is by the female having mutant gene controlling the disorder which is transmitted in autosomal recessive pattern. The age of the influenced child is 15 year.

4.7.2.2 Saraiki other than Baloch

In Saraiki other than Baloch eleven families/couples with pale skinned person influenced were clinically seen as:

Family C

The family "C" lives in a Basti Gud Pur of Dera Ghazi Khan and has a place with Saraiki standing Machii. The relatives customarily wed inside of the family. The family history demonstrates two influenced male and one influenced female. As the sickness controlling quality shows up in both guys and females, influenced people are delivered by typical folks in the wake of avoiding the eras in this way proposing the characteristic is transmitted in the autosomal passive mode.

Family D

The family "D" dwells in a Basti Khosa of Dera Ghazi Khan has a place with rank Machii. The relatives generally wed inside of the family and result in innate marriage. The family history shows one influenced male. The age of the influenced individual is 15 year. As the infection controlling attribute shows up in males and females consequently recommending that the quality is transmitted in the autosomal latent mode.

Family E

The family "E" lives in a town Gubra close Dera Ghazi Khan has a place with Trawni rank. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows two influenced male. The times of the influenced people are 50 and 60 years. As the ailment controlling quality shows up in both males and females, influenced people are delivered by ordinary folks in the wake of skirting the eras in this manner recommending that the attribute is transmitted in the autosomal recessive mode.

Family F

The family "E" lives in Sakhi Sarwar town close Dera Ghazi Khan has a place with Maddati rank. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows one influenced male. The age of the influenced individual is 19 years. As the infected peoples are created by ordinary folks in the wake of avoiding the eras along these lines recommending that the characteristic is transmitted in the autosomal latent mode.

Family G

The family "G" lives in Kot Chutta town close Dera Ghazi Khan fits in with Bhatti standing. The relatives generally wed inside of the family and result in ingrained relational unions. The family history demonstrates one influenced male. The age of the influenced individual is 12 years. As the illness controlling characteristic shows up in males and females, influenced people are created by typical folks subsequent to avoiding the eras in this way proposing the attribute is transmitted in the autosomal passive mode.

Family H

The family "H" dwells in Sakhi Sarwar (Jumma MOR) close Dera Ghazi Khan has a place with Khaliq Dadani position. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history demonstrates one

influenced male. The age of the influenced individual is 35 years. As the illness controlling characteristic shows up in males and females in this manner proposing that the quality is transmitted in the autosomal latent mode.

Family I

The family "I" dwells in a town Rojhani close Sakhi Sarwar town of Dera Ghazi Khan has a place with Malik position. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history demonstrates one influenced male. The age of the influenced individual is 10 years. As the illness controlling characteristic shows up in males and females, influenced people are created by ordinary folks subsequent to skirting the eras in this manner proposing that the quality is transmitted in the autosomal passive mode.

Family J

The family "J" dwells in a town close Choti Road of Dera Ghazi Khan fits in with Bhutta rank. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history demonstrates one influenced male. The age of the influenced individual is 2 years. As the illness controlling characteristic shows up in males and females, influenced people are created by typical folks subsequent to skirting the eras along these lines proposing that the quality is transmitted in the autosomal latent mode.

Family K

The family "K" dwells in Sakhi Sarwar close Dera Ghazi Khan fits in with Gamoli rank. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history demonstrates one influenced male. The age of the influenced individual is 18 years. As the illness controlling characteristic shows up in males and females, influenced people are created by typical folks subsequent to skirting the eras along these lines proposing that the quality is transmitted in the autosomal latent mode.

Family L

The family "L" dwells in Maimori close Dera Ghazi Khan has a place with Bundoani standing. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history shows one influenced male. The age of the influenced individual is 60 years. As the ailment controlling quality shows up in both guys and females, influenced people are created by typical folks in the wake of skirting the eras in this way proposing the characteristic is transmitted in the autosomal latent mode.

Family M

The family "M" lives in Choti Bala close Dera Ghazi Khan has a place with Bhatti position. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history shows 4 influenced male and one influenced female. The periods of the influenced people shift from 11 to 60 years. As the illness controlling quality shows up in both guys and females, influenced people are created by typical folks in the wake of skirting the eras in this way proposing the attribute is transmitted in the autosomal passive mode.

4.7.3 Clinical Features of Albino

Aforementioned pale skinned people families have regular side effects identified with eye capacity was watched like Rapid, automatic forward and backward development of the eyes, Inability of both eyes to stay coordinated at the same indicate or move as one and Sensitivity to light. Eye shading can extend from light blue to chestnut and may change with age.

The absence of shade in the hued part of the eyes (irises) makes them to some degree translucent. This implies the irises can't totally piece light from entering the eye. As a result of this, light-hued eyes may seem red in some lighting. This happens in light of the fact that you're seeing light reflected off the back of the eye and going retreat through the iris again — like the red-eye that happens in a glimmer photograph.

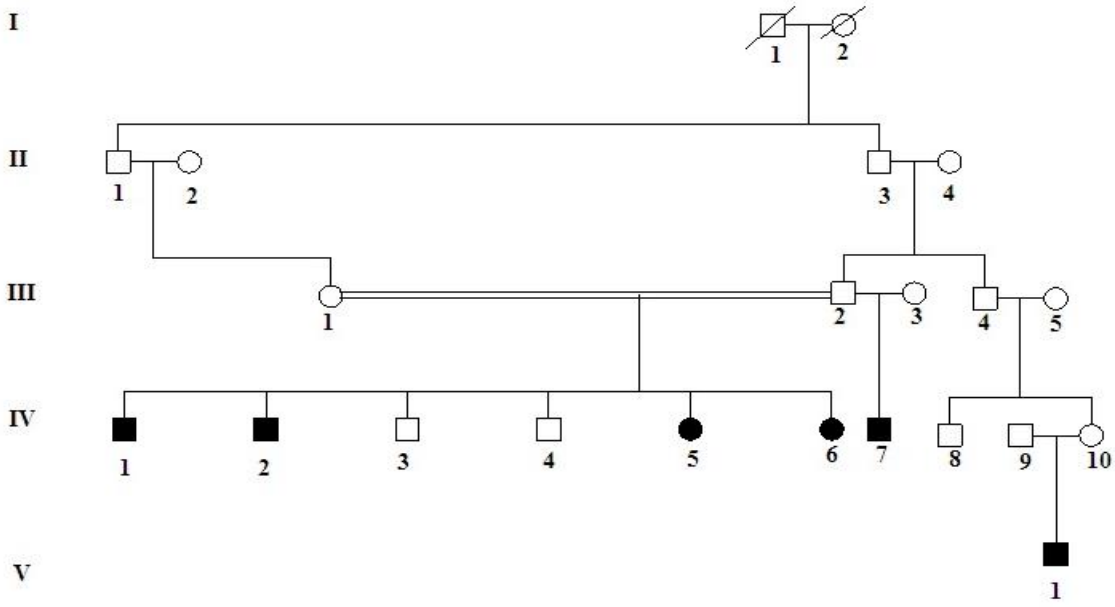


Figure 4.2: Family pedigrees with Albino demonstrating autosomal latent method of inheritance. Circles speak to females, squares speak to guys. Filled circles speak to influenced people. Cross lines at the images show perished people.



Figure 4.3: Some Albino affected individuals in Tuman Leghari

4.8 Thalassemia Affected Families

Twenty six (A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, U, V, W, X, Y, Z) with thalassemia were learned from various union councils of Tuman Leghari of Dera Ghazi Khan District. Eleven Families/couples has a consign with Leghari (A, B, C, D, E, F, G, H, I, J, K, Four to Khosa L, M, N, O and Eleven to Saraiki other than Baloch, P, Q, R, S, T, U, V, W, X, Y, Z).

4.8.1 Leghari

Family A

The family "A" lives in Basti lound close Choti Zareen of Dera Ghazi Khan has a place with Ramdani position. The relatives generally wed inside of the family and result in ingrained relational unions. The family history demonstrates one influenced male. The times of the influenced individual are 9 years. As the sickness controlling characteristic shows up in males and females, influenced people are created by typical folks in the wake of avoiding the eras along these lines recommending that the quality is transmitted in the autosomal latent mode.

Family B

The family "B" dwells in Choti Bala close Dera Ghazi Khan has a place with Bughlani rank. The relatives customarily wed inside of the family and result in ingrained marriages. The family history demonstrates one influenced male and two influenced female. The times of the influenced people differ from 4 to 9 years. As the illness controlling attribute shows up in males and females, influenced people are created by typical folks in the wake of skirting the eras hence recommending that the characteristic is transmitted in the autosomal latent mode.

Family C

The family "C" dwells in Choti Bala close Dera Ghazi Khan has a place with Bughlani rank. The relatives customarily wed inside of the family and result in ingrained relational unions. The family history demonstrates 2 influenced females. As the infection

controlling attribute shows up in males and females, influenced people are delivered by typical folks in the wake of skirting the eras along these lines proposing that the characteristic is transmitted in the autosomal passive mode.

Family D

The family "D" lives in Choti Bala close Dera Ghazi Khan fits in with Bughlani standing. The relatives generally wed inside of the family and result in innate marriages. The family history shows one influenced male. The age of the influenced individual is 5 years. As the infection controlling quality shows up in both guys and females, influenced people are delivered by ordinary folks in the wake of avoiding the eras in this way recommending the characteristic is transmitted in the autosomal passive mode.

Family E

The family "E" dwells in Choti Bala close Dera Ghazi Khan has a place with Bughlani standing. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows one influenced male and one influenced female. The times of the influenced people are from 2 to 3 years. As the malady controlling attribute shows up in guys and females, influenced people are created by typical folks in the wake of avoiding the eras in this way proposing the characteristic is transmitted in the autosomal latent mode.

Family F

The family "F" dwells in Choti Zareen town close Dera Ghazi Khan has a place with Gulliani standing. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows one influenced male and one influenced female. The times of the influenced people shift from 11 to 60 years. As the ailment controlling characteristic shows up in guys and females, influenced people are created by ordinary folks in the wake of avoiding the eras therefore recommending that the attribute is transmitted in the autosomal latent mode.

Family G

The family "G" lives in Choti close Dera Ghazi Khan has a place with Gulliani position. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows one influenced female. The age of the influenced people is 11 years. As the illness controlling quality shows up in both guys and females, influenced people are delivered by ordinary folks in the wake of skirting the eras consequently recommending that the attribute is transmitted in the autosomal passive mode.

Family H

The family "H" lives in Salehon Wala close Dera Ghazi Khan has a place with Jamoani station. The relatives customarily wed inside of the family and result in innate relational unions. The family history demonstrates 1 influenced male. The age of the influenced individual is 1 year. As the illness controlling attribute shows up in guys and females, influenced people are delivered by typical folks in the wake of skirting the eras in this way recommending the quality is transmitted in the autosomal latent mode.

Family I

The family "I" lives in Salehon wala close Dera Ghazi Khan has a place with Jamoani station. The relatives customarily wed inside of the family and result in innate relational unions. The family history demonstrates 1 influenced male. The age of the influenced individual is 5 years. As the illness controlling attribute shows up in males and females, influenced people are delivered by typical folks in the wake of skirting the eras in this way recommending the quality is transmitted in the autosomal latent mode.

Family J

The family "J" lives in Fort Munro close Dear Ghazi Khan has a place with Shahwani standing. The relatives customarily wed inside of the family and result in innate relational unions. The family history demonstrates 1 influenced male. The age of the infected individual 8 years. As the illness controlling attribute shows up in males and females, influenced people are created by ordinary folks in the wake of avoiding

the eras in this manner recommending that the quality is transmitted in the autosomal latent mode.

Family K

The family "K" lives in Choti Bala close Dera Ghazi Khan has a place with Bughlani rank. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows 1 influenced male. The age of the influenced individual is 12 years. As the ailment controlling quality shows up in both guys and females, influenced people are created by ordinary folks subsequent to skirting the eras along these lines proposing that the characteristic is transmitted in the autosomal latent mode.

4.8.2 Khosa

Family L

The family "L" lives in Haiderwala close Dera Ghazi Khan has a place with Khosa rank. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows 1affected male. The age of the influenced singular is 3 years. As the ailment controlling quality shows up in both guys and females, influenced people are created by ordinary folks subsequent to skirting the eras along these lines proposing that the characteristic is transmitted in the autosomal latent mode.

Family M

The family "M" dwells in Qureshi wala close Dera Ghazi Khan has a place with Bundoani rank. The relatives customarily wed inside of the family and result in innate relational unions. The family history demonstrates 1 influenced male. The age of the influenced individual is 1 year. As the ailment controlling characteristic shows up in males and females, influenced people are created by typical folks subsequent to avoiding the eras therefore proposing that the attribute is transmitted in the autosomal latent mode.

Family N

The family "N" dwells in Qureshi wala close Dera Ghazi Khan fits in with Khosa station. The relatives generally wed inside of the family and result in innate relational unions. The family history demonstrates 1 influenced male. The age of the influenced individual is 6 years. As the ailment controlling characteristic shows up in males and females, influenced people are delivered by ordinary folks subsequent to avoiding the eras in this way proposing the quality is transmitted in the autosomal latent mode.

Family O

The family "O" dwells in machiwala close Dera Ghazi Khan fits in with buzdar station. The relatives generally wed inside of the family and result in innate relational unions. The family history demonstrates one influenced female. The age of the influenced individual is 11 years. As the ailment controlling characteristic shows up in males and females, influenced people are delivered by ordinary folks subsequent to avoiding the eras in this way proposing the quality is transmitted in the autosomal latent mode.

4.8.3 Saraiki other than Baloch

Family P

The family "P" dwells in Choti Bala close Dera Ghazi Khan has a place with sohrani position. The relatives customarily wed inside of the family and result in innate relational unions. The family history shows 2 influenced female 1 is kicked the bucket. The age of the influenced individual is 6 years. As the ailment controlling characteristic shows up in males and females, influenced people are created by typical folks in the wake of skirting the eras in this way proposing the attribute is transmitted in the autosomal latent mode.

Family Q

The family "Q" lives in Choti zareen close Dera Ghazi Khan has a place with sanghi rank. The relatives generally wed inside of the family and result in innate relational unions. The family history shows 1 influenced male. The age of the influenced individual is 12 years. As the malady controlling quality shows up in both guys and females, influenced people are delivered by ordinary folks in the wake of skirting the eras subsequently recommending that the characteristic is transmitted in the autosomal latent mode.

Family R

The family "R" lives in mehter colony close Dera Ghazi Khan has a place with jarh rank. The relatives customarily wed inside of the family and result in innate relational unions. The family history exhibited in the pedigree.

Family S

The family ‘S’ resides in doratta near Dera Ghazi Khan belongs to jarh caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1 affected male. The age of the affected individual is 5 years. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family T

The family ‘T’ resides in chak nagar near Dera Ghazi Khan belongs to nangri caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1 affected male. The age of the affected individual is 2 years. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family U

The family ‘U’ resides in Choti Bala near Dera Ghazi Khan belongs to nangri caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 2 affected male and 3 affected female. The ages of the affected individuals vary from 11 to 16 years. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family V

The family ‘V’ resides in shero near kot chutta belongs to Mian caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1 affected male. The age of the affected individual is 10 years. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family W

The family ‘W’ resides in Choti Bala near Dera Ghazi Khan belongs to ghallu caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1 affected male and one affected female. The ages of the affected individuals are 7, 11 years. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family X

The family ‘X’ resides in makoray wala near Dera Ghazi Khan belongs to jarh caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1 affected male. The age of the affected individual is 14 years. As the disease controlling trait appears in both males and females, affected

individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family Y

The family 'Y' resides in Choti Bala near Dera Ghazi Khan belongs to nangri caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1affected male. The age of the affected individual is one year. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

Family Z

The family 'Z' resides in Choti Bala near Dera Ghazi Khan belongs to nangri caste. The family members traditionally marry within the family and result in inbred marriages. The family history indicates 1 affected male. The age of the affected individual is 2 years. As the disease controlling trait appears in both males and females, affected individuals are produced by normal parents after skipping the generations thus suggesting that the trait is transmitted in the autosomal recessive mode.

4.9 Clinical Features of Thalassemia

In above mentioned families affected with Thalassemia the symptoms observed related to growth problems – not putting on weight or growing in height. Anaemia – red blood cell deficiency, leading to tiredness, weakness and shortness of breath. Jaundice – yellowing of the skin and whites of the eyes. Regular transfusion of blood from donors.

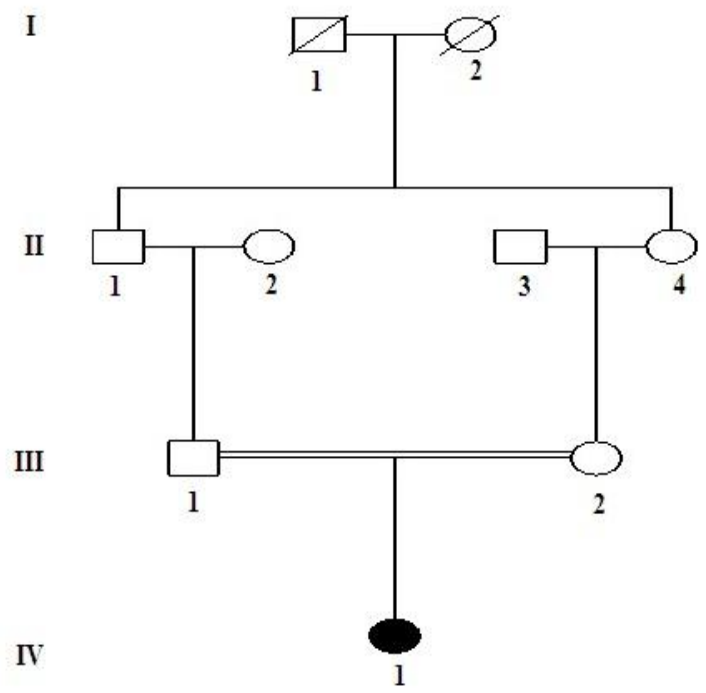


Figure 4.4: Family pedigree with thalassemia demonstrating autosomal suppressed method of legacy. Circles speak to females, squares speak to guys. Filled circles speak to influenced people. Cross lines at the images show perished people.



a) **b)**

Figure 4.5: Some thalassemia affected individuals in Tuman Leghari

DISCUSSION

In this study, a questionnaire was distributed to distinguish different types of marriages, for examples, particularly the inbreeding marriages and to evaluate its effect on the population of Tuman Leghari resident of D.G. Khan District of Punjab Province. The number of inhabitants in Indian sub-continent is stratified into a large number of inbreeding groups and individuals can't wed outside their families as a result of family unit and status ties (Gadgil *et al.,* 1998). In the present study, our outcomes furthermore demonstrated that 70.52% marriages in the overall population and relational unions in all inclusive community respectively 35.10%, 18.66% and 46.24% are inbred (Table 4.2 and 4.3). The preference for inbreeding relational unions is for the most part in light of ethnicity and tribal/group/place association. Inside of the limits of inbreeding characterized by the above parameters, close inbreeding unions are particular because of a coinciding of key elements of groups and individual-level foundation essentials. This study revealed a high rate of inbreeding 88.42% with 0.0201 mean coefficients of inbreeding by and large population (Table 4.4) our outcomes are in accord with the results of a past study aimed at Pakistan level by Hussain (2001); Bittles (1988); Amin (2007).

Some of the possible reasons of high frequency of inbreeding may be:

1) Tribalism is intensely recognized in progress account of population understudy. It is basic imbued human propensity for recognizing oneself as far as gathering of study one's own particular group as by one means or another “unique” and better than other groups and of upsetting communal interaction with individuals from the other groups.

2) High rate of inbreeding alongside the variables like geological conditions, antagonistic method for transportation, destitution, and ignorance that have confined the human developments, came about the population stratification into little common groups where decision of proper companion gets to be constrained outside family.

3) More distant family culture presence in the range expands shot of inbreeding. This study revealed a high rate of inbreeding in ethnic population like Leghari (35.10%). Khosa (18.66%) and Saraiki other than Baloch (46.24%) (Table 4.4). These ethnic gatherings varied essentially from each other regarding inbreeding relational unions.

Shockingly, non-related and inbreeding relational marriages were revealed more invasive in Saraiki other than Baloch when contrasted with other ethnic populations. Conceivable reason of this sudden result may be because of vast specimen number when contrasted with other ethnic groups and long notable relationship of Saraiki's with dominating population of Hindus of north western parts of India where inbreeding relational unions were disallowed (Rao *et al.*, 2002). The social demeanors of population assume part in partiality for various sorts of cousin relational unions (Rao and Reddy, 1978). The transcendence of first cousin relational unions (38.92%) among inbreeding couples and in population under study has as of now been perceived in various Pakistani populations (Table 4.12). These results are in similarity with those of different studies made in Pakistan (Shami, Iqbal and Minhas, 1984; Hussain, 1998). General marriage example of study zone mirrored the patriarchal way of society as expressed by Wahab and Ahmad (1996). The high rate of first cousin relational unions might be because of a conservationist public state of mind engaging in the population in which the key part of the eldest man in a family has a since quite a while ago settled dominancy in every inhabited responsibility.

In this study, we concentrated on the impact of guidance (both male and female), male financial status, and male occupation on predominance of inbreeding. Rate of inbreeding is as a result firmly connected with these components (Table 4.5 and 4.6). The specimen when ordered in various levels/status bunches demonstrated obvious limits in the frequencies of inbreeding relational unions. The inbreeding relational unions were observed to be exceptionally normal in lower level/status, while pattern of inbreeding relational unions diminish with expansion in level/status. This angle of progress was exceptionally noteworthy particularly with female proficiency. Inbreeding relational unions were conversely corresponding to female education. This demonstrated

female education had critical impact on inbreeding. It is obvious that education gives the preference force to female so they get a kick out of the chance to choose or propose a counterpart of corresponding status, when not found in their family and they wanted to get hitched outside the family. Every one of these discoveries related with past studies from various ranges of world (Afzal, 1988; Bittles, 1991). However intriguing circumstance showed up, when we examined the impact of these components in ethnic gatherings. Among Leghari and Khosa, the concentrated on parameters have note-worthy impact in diminishing the inbreeding relational unions however shockingly the relative commitment of every one of these variables stay less unequivocal (obvious) in Saraiki's. The imaginable reasons of this rigorous disposition of Saraiki may be the social standard connected with their inception. These social ties have been set up because of long conjunction with the ruled and powerful population of northern Hindus. Then again, the noteworthy impact of examined components obvious in Leghari and Khosa could be ascribed to a change in social standards/demonstrating a move from tribe to a rustic culture.

Impressive consideration has been paid to the part of inbreeding marriage as a causative component in the pervasiveness of hereditary disorders, (Jain *et al.*, 1993). In the present study, the impact of marriage sorts on particular gathering of hereditary disorder like pale skinned person (albino) and thalassemia was additionally examined. General inbreeding relational unions were discovered altogether most inexhaustible among burdened couples when contrasted with overall public (Table 4.9 and 4.10). Thus, inbreeding relational unions were discovered altogether higher than out breeding relational unions among couples having posterity's burdened with albino and thalassemia.

Information on youngsters were likewise gathered from every single concentrated on families demonstrated obvious confirmation that in inbreeding families the burdened kids commonness were high and measurably huge (Table 4.15 to 4.18). Awareness about the hereditary disorders were requested in the study from every individual from family demonstrates the ailments were considered firmly associate to the deadly hereditary qualities allowed from solid inbreeding among families with rate of 71.43% when contrasted with treatable (9.11%), not treatable (6.65%), Medicinal impact (2.46%),

curse (1.97%), superstitious (0.99%) and overlook (7.39%). Conduct of the folks, relative and society were additionally addressed from families which communicated a higher rate of good conduct with the tormented youngsters 53.69, 47.04 and 46.06 individually. Disregard of influenced youngsters was additionally high in rate among benevolence and terrible demeanors of parents, relatives and society (Table 4.19 and 4.20).

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