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Consanguinity and Occurrence of Genetic Disorders in District Attock

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Consanguineous marriages are the marriages between blood relatives; nevertheless, it can also be referred as unions between second cousins or closer by the geneticists. Consanguinity increases the risk of congenital anomalies and autosomal recessive diseases; the closer the relationship, the higher the risk. Consanguinity is a common and preferable custom of marriage in different global communities. Consanguineous marriages have been practiced since the start of human culture. Consanguinity is major cause of occurrence of various genetic disorders in human population. It is common problem in Pakistan. The purpose of this research was to identify the families with Mendelian disorders specifically in Attock. The purpose of this research was to identify the families with Mendelian disorders specifically in Attock. Various areas of Attock have been surveyed for identification of families and most prevalent disorders were identified. Common disorders in Attock included NDM (Neuromuscular Disorder), MR (Mental Retardation), Blindness, Hearing Impairment, Microcephaly, Epilepsy, Diabetes, Familial Cancer, Albinism and one of rarely found disorder, i.e., Ichthyosis. Families were identified using some local resources and by visiting special education institutions located in Attock. Pedigrees were drawn by the help of elder family members. The most common disorder found in the area was Blindness, secondly the Deafness and also NMD, then Microcephaly. Out of 60 families contacted about 25 families (42%) were having Blindness disorder, about nine (15%) were of microcephaly. Survey had been done to collect the samples of different Mendelian Phenotypes. The information collected for analysis include: Pedigree, Diagnosis, and Clinical Reports and contact information of family. The study will highlight the consequences of consanguineous marriages and will create awareness and might secure the future generations.

Keywords: Consanguinity, NDM (Neuromuscular Disorder), MR (Mental Retardation), Microcephaly, Epilepsy, Ichthyosis

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Introduction

Controversies always exist on consanguineous marriage in western societies. Asian and African immigrant populations are especially being focused in this regard. However, in Pakistan, effects of hereditary population stratification are not focused much particularly in Biraderi system in which male members govern choice of partner and thus the transfer of mutated genes also. Caste, Quom, and Zat are preferred in such societies over health (Bittles & Small, 2016).

Round about 66% marriages in Pakistan are among blood relatives. The most important reason behind the consanguineous marriages is that the parents are only allowed to decide the future bonds of their children, i.e., both son and daughter. Moreover, this preference depends upon social and cultural priorities. In rural areas the percentage goes further high due to preference of preserving social setup related to tribal association (Hussain, 2005).

Pakistan Genetic Mutation Database (PGMD) is the public database that gives information about various syndromic as well non-syndromic disorders. Thousand different mutations are registered and 130 genetic disorders are being reported in it (Qasim et al., 2018).

Number of grandparents for genetic contribution is less in consanguineous marriages as compared to non-consanguineous marriages. Inbreeding coefficients for first and second cousin marriages are $F = 0.0625$ and $F = 0.0156$ respectively. In case of double first cousin marriages, this value goes up to $F = 0.125$ (Hamamy et al., 2011). Inbreeding coefficient increases further in more complex consanguineous families.

Materials and Methodology

Methodology involved the conduction of survey to identify the consanguineous families. Various areas of Attock tehsil (33.7660 ° N, 72.3609 °) including Village Mirza, Village Shakardara, DhokFateh, and Sanjwal Cantt were being visited for the purpose. Families were then contacted directly or by the help of reference person. Special Education Centers were also visited to identify the patients with various genetic disorders. Consent of the families was considered as top priority. Questionnaires were especially designed to investigate the families. Various medical reports were also used to confirm the disorder. Questionnaire included the following details:

Table 1

Symptoms (Clinical Information)

	Yes	No
Mentally retarded		
Dumb		
Deaf		
Physically impaired		
No. of patients		
Disorder		

Table 2

Basic Details of a Patient

	Name	Age	Father's name	Mother's name	No. of normal siblings of patient	Address	Phone No.	Family history, pedigree	Relationship among the parents of patient	Onset of disorder (by birth/later in life)
Patient No. 1										
Patient No. 2										

The survey was conducted keeping the ethics of humanity under special consideration. Pictures of the patients were also captured with the consent of the family.

Results

Various disorders had been identified after survey these disorders included Blindness, Microcephaly, Familial Cancer, Diabetes, Heart Attack, Epilepsy, Deafness, Hypertension, Day Blindness, Hypertension, Neuromuscular Disorders, Mental Retardation, Asthma, Infertility, Albinism, and one of the rare disorders Ichthyosis. Ichthyosis patients were characterized by dry and scaly skin. Occurrence of this wide variety in high percentage indicated high consanguinity in the area. Out of all families contacted about 25 families (37%) were having Blindness disorder, 12 (18%) with Mental Retardation, about 9 (15%) of Microcephaly. Blindness, Mental Retardation, and Microcephaly were in highest percentage. Day Blindness was also identified in the area. These results indicated that Blindness had highest prevalence in the area, second being the Mental Retardation. Patients of blindness with varied disease symptoms were found during survey. Major conditions of the eyes included glaucoma, cataracts, and retinitis pigmentosa. Primary Microcephaly followed by small head circumference, also common according to ratio of its occurrence rate (1/20,000). Many families had multiple patients of same disorder and many of the families were also having different patients with different disorders in the same family. In Attock people from different areas settled and continuous in-breeding resulted in high proportion of genetic disorders. Patients of Mental Retardation, Microcephaly, Neuromuscular Disorders were in poor health condition and they were totally dependent on their families. However, patients of other disorders were somehow in better condition. Some of them were students and some were also doing jobs according to their physical condition.

Figure 1. Case of Blindness (Amna Bibi) (right); case of Day Blindness (Rida Ahsan) (left).

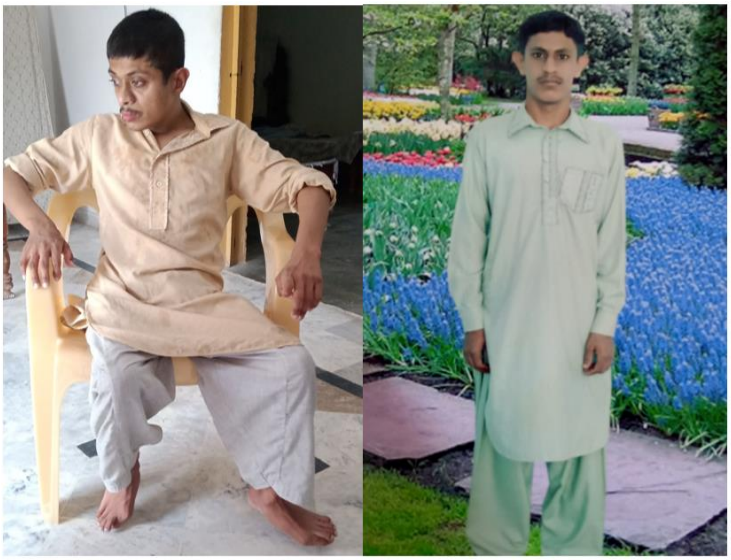

Figure 2. Muhammad Tayyab (left) and Muhammad Awais (right)—cases of Neuromuscular disorder.

Figure 3. Haris Ali (left) and Fakhar Hayat (right)—cases of Primary Microcephaly.

Figure 4. Ayesha—case of Albinism.

Table 3

Summary Report of Survey

Sr. No.	Disorder	No. of cases/families	City/area	Family relationship
1.	Microcephaly	9	Attock	Some are siblings; others are 1st cousins
2.	Deafness	5	Attock	Some are siblings; others are 1st cousins
3.	Blindness	25	Attock	Some are siblings; others are 1st cousins
4.	Hypertension/High B. P	7	Attock	Siblings and cousins
5.	Day blindness	2	Attock	Relationship from mother side
6.	Familial cancer	2	Attock	Niece and aunt
7.	Thalassemia major	2	Attock	Siblings
8.	Neuromuscular disorder	5	Attock	Siblings
9.	Mental retardation	12	Attock	Some are siblings; others are 1st cousins
10.	Infertility	2	Attock	Cousins
11.	Asthma	4	Attock	Siblings and cousins
12.	Albinism	2	Attock	Siblings

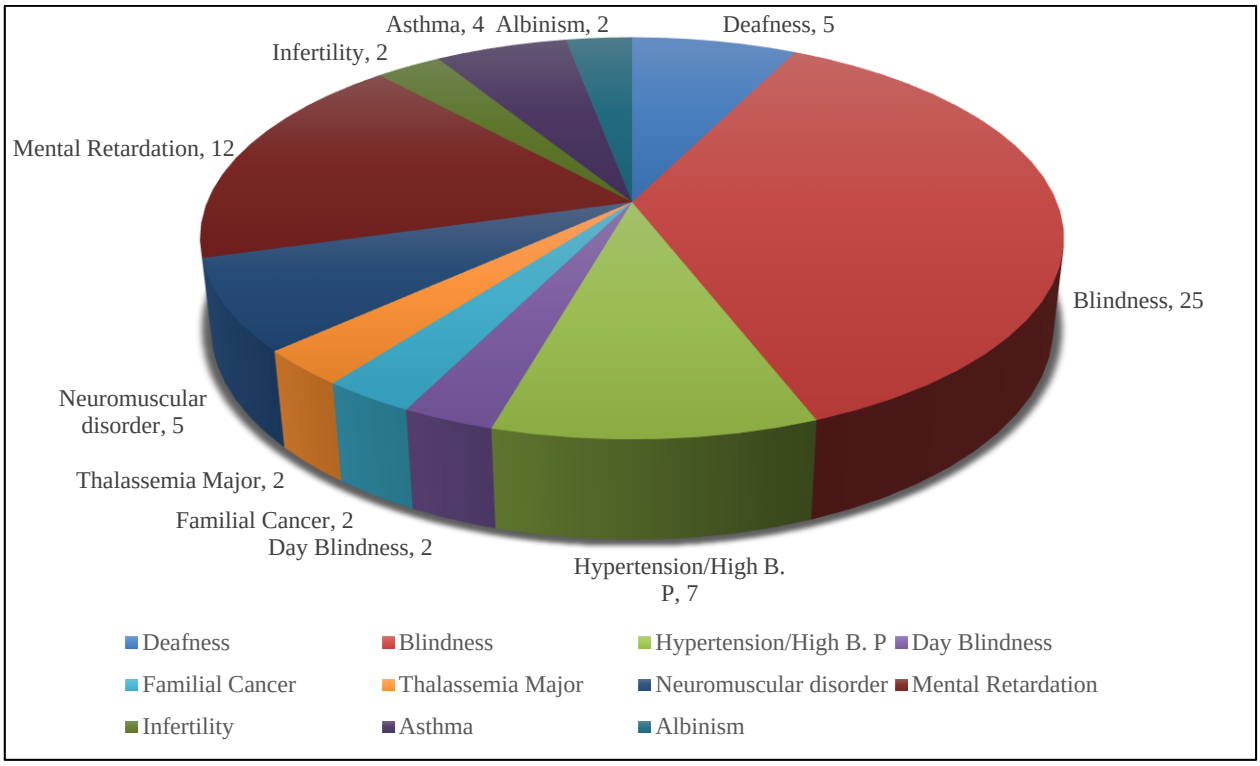

Figure 5. Pie graph indicating the relative occurrence of various disorders.

Statistical analysis was done using SPSS software and frequency was calculated for various disorders. SPSS calculated valid percent and cumulative percent and results were obtained in tabular as well as graphical form.

Table 4

Indicating Valid and Cumulative Percent Calculated by SPSS Software

		Frequency	Percent	Valid percent	Cumulative percent
Valid	4.00	1	8.3	8.3	8.3
	7.00	1	8.3	8.3	16.7
	9.00	1	8.3	8.3	25.0
	12.00	1	8.3	8.3	33.3
	25.00	1	8.3	8.3	41.7
	5.00	2	16.7	16.7	58.3
	2.00	5	41.7	41.7	100.0
	Total	12	100.0	100.0	

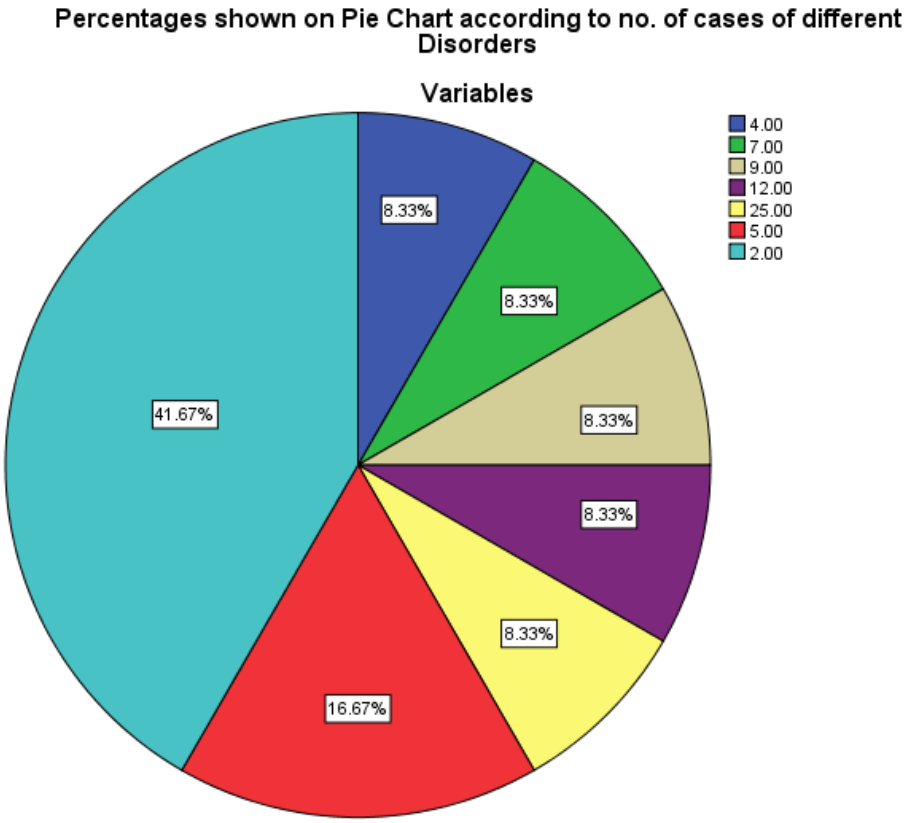

Figure 6. Pie graph drawn using SPSS tool indicating valid percent of various disorders. Various colors are used to indicate the disorders. Blindness (yellow), Microcephaly (grey), Mental Retardation (purple), Asthma (dark blue), Hypertension (green), Deafness (red), Familial Cancer, Day Blindness and Thalassemia Major (light blue).

Cumulative percentage expresses frequency distribution. Cumulative percentage calculated the percentage of the cumulative frequency in each interval. Valid percent is indicating non-missing cases.

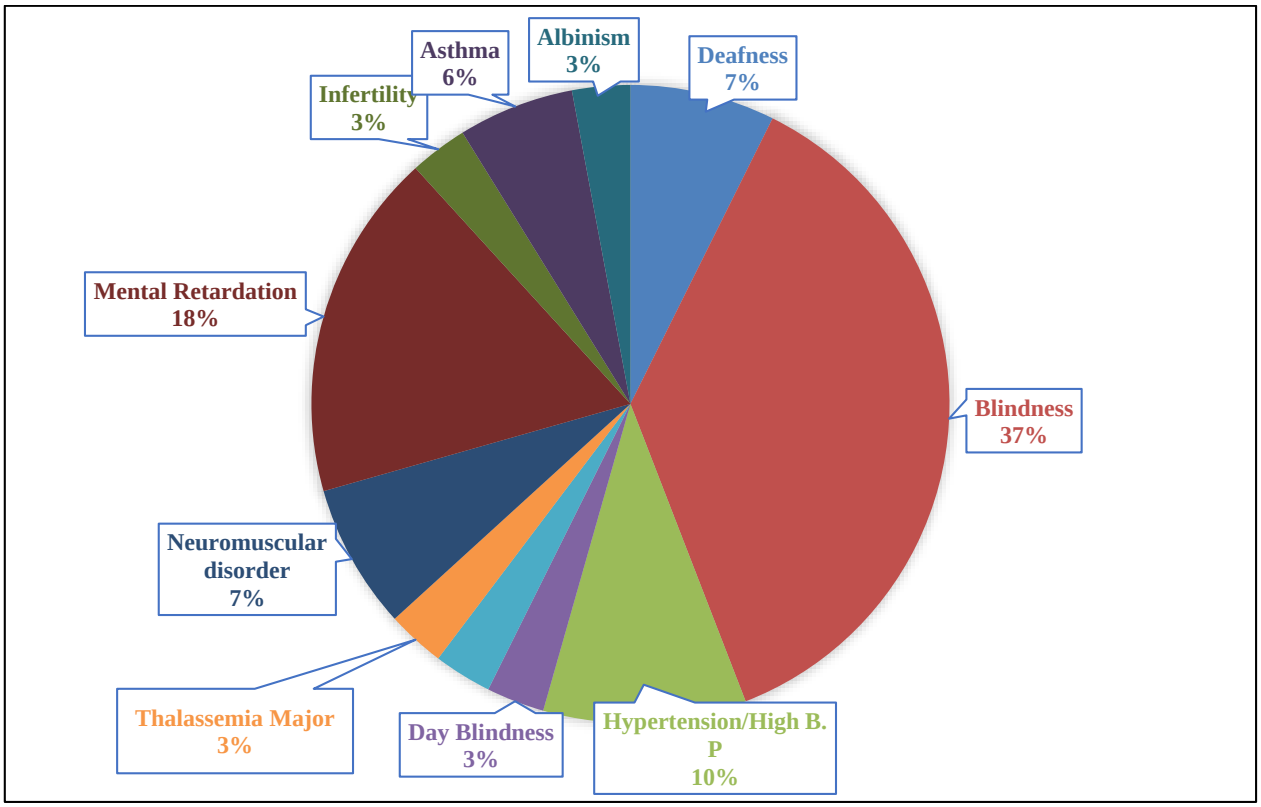

Figure 7. Pie chart showing percentages of various disorders.

Discussion

Consanguinity is more common in illiterate societies with weak economy and lack of awareness. Homozygosity increases as a result of consanguineous marriages and results in high chances of inherited disorders. However, this also limits the disease-causing allele only in affected families. Most of the patients do not live up to reproductive age and thus exclude the disease-causing alleles from the population. If non-consanguineous marriages are being followed in a population, the disease allele will go into whole population and number of carriers increase in a population. These populations can give diseased individuals in upcoming generations. Majority of disorders do not have any proper treatment; these disorders have high rate of occurrence and thus become an unfeasible option.

Education of women has greatest effect on consanguinity as with increase in level of education of women, rate of consanguineous marriages decreases (Bhasin & Kapoor, 2015).

There are three times more chances of consanguineous marriages when women are illiterate as compared to highly educated women. Economic status including wealth and property is also the major reason behind consanguineous marriages (Akbayram et al., 2009).

Ten families were tested for Primary Microcephaly from South Waziristan and two from rural areas of Punjab, mutation in ASPM segregated 10 out of 12 families indicating that one of the ASPM mutation is the founder mutation for this area and this also confirmed that the mutation is most commonly occurring mutation in Pashtun culture residing in Pakistan and Afghanistan (Khan et al., 2021). This confirms the high percentage of Primary Microcephaly in the area.

Attock has collection of people from many surrounding areas, where comparatively smaller tribal groups stay and prefer marriages within families; especially Pashtun families have high percentage of inbreeds. This consanguinity resulted in high prevalence of genetic disorders in Attock as compared to other areas. Though the literature does not have much data of this area in context of genetic disorders, many studies reveal the serious outcomes of the consanguinity in this area.

It is considered that when women contribute in financial matters, they are given more freedom of deciding their marriages. The literacy rate is improving in the area day by day. However, decision of marriages is still in the hand of elder family members, to whom rituals and customs are more important than family health.

Conclusion and Suggestions

Consanguinity is not good for economic status of any country. Pakistan is already facing serious economic pressures. Therefore, consanguinity can never be the affordable option. Genetic counselling is very important to avoid any serious circumstances. Women should be educated and government should create awareness among public either through seminars or social media. Premarital testing should be suggested for those disorders which are fixed to particular population, for example Primary Microcephaly.

Health care staff including doctors should be taught to focus on diseases associated with consanguinity, for example, Thalassemia, Blindness, Mental Retardation, Microcephaly, Epilepsy, Hearing Loss, etc. Counselling should be arranged for those families who are at major risk. Testing centers should also be established and religious reference should be given to get the trust of the families. Though the advantages of marrying to close relatives cannot be neglected, the severity of harmful consequences cannot be ignored. Therefore, criteria should be developed to avoid the serious and uncurable health issues.

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