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Mode of inheritance for hypotrichosis in families of Sahiwal Division, Punjab, Pakistan

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Abstract

Congenital hypotrichosis is a major genetic disorder of hair-growth that affects millions of people all around the world. In this study, hypotrichosis was studied in the affected families in the district of Sahiwal. A wide survey was conducted in both rural and urban areas of district Sahiwal. For additional investigation and pedigree construction, five families were selected after the survey was completed for further analyses. Verbal consent was taken from the participants to assure them that the information and data was taken with their complete willingness and harmony, without any pressure. During the survey, each family was thoroughly interrogated, and the pedigree was constructed. The pedigree analyses were used to determine the prevalence of hypotrichosis and origin of mutation in each family. A pedigree analyses of hypotrichosis-infected individuals found that the disease was handed down through generations. In each generation of infected families, some people remain unaffected showed that the disease was genetically recessive disorder. Overall prevalence of this genetic disorder was 25.82S % in the selected families. The hypotrichosis affected 55 individuals out of 213 individuals in studied families. In the current study, the prevalence of this disease varied across all reported families. The prevalence rate of the disease in UOA was 17.24%, in UOB was 20.00%, in UOC was 41.94%, in UOD was 23.40% and in UOE was 40.740% of the families. The present study concluded that hypotrichosis in the selected families were persistent for at least three generations and the mode of inheritance was autosomal recessive.

Introduction

Hairs are the extensions of skin, made up of keratin and produced by the hair follicles synthesized during embryogenesis by the interactions between the ectoderm and mesenchyme tissues. Congenital hypotrichosis is a disease in which male become bald. Development of hairs can be altered due to mutation in the governing genes. The hair in the affected areas is normally short, dry, and rough. It can also be tightly curled, lighter in color, and more likely to split. Hypotrichosis is a congenital condition that has been attributed to a number of genetic syndromes. It has been evidenced that it is a genetic disorder. X-linked generalized hypertrichosis has been previously mapped to the Xq24-q27.1 chromosome [1]. This disease occurs alone and also in syndromic forms including Ambras syndrome (AS; OMIM 145701). It is a rare form that affects people who have generalized hypertrichosis that is more pronounced over the upper part of the body, face, and ears, as well as abnormal facial features like a triangular, coarse face and long palpebral fissures. Similarly, hypertrichosis having gingival hyperplasia (OMIM 135400) is also a syndromic form and most commonly inherited as an autosomal dominant pattern. The affected individuals present with generalized hypertrichosis and coarse facial features, including thick lips, wide and flat nasal bridge, large ears, and gingival hyperplasia [2].

Hypotrichosis with recurrent skin vesicles is a condition with an autosomal recessive pattern of inheritance and identified in Pakistani population. Clinically, the symptoms may vary and generally include affected individuals with a sparse scalp, facial, and body hair with fragile hair shafts, as well as recurrent diffuse vesicles involving the scalp and body and non-mucosal surfaces of the body that heal without scarring. The disease was mapped to the *DSG–DSC* cluster on chromosome 18q12.1, and a homozygous nonsense mutation on *DSC3* [3].

Numerous people have been identified for having fewer hair pouches, smaller follicles, and delicate irregular hair [4]. This could happen as a result of a single defect, or as a symptom of an inherited disease, and it usually occurs in combination with other ectodermal disorders.

The objective of current study was to provide information on hypotrichosis in the Sahiwal area of Punjab, Pakistan. The prevalence of such genetic disorders in Pakistan is also an important aspect of the present study.

Material and Method

Study Area

The current study was conducted in Sahiwal previously known as Montgomery a city in Punjab, Pakistan. It is Pakistan's 21st most populous city and the administrative center of both the Sahiwal District and the Sahiwal Division. Sahiwal is located between Lahore and Multan, about 180 Kilometers from the capital Lahore and 100 Kilometers from Faisalabad between the Sutlej and Ravi rivers. Wheat, cotton, tobacco, legumes, potato, and oil seeds are the main crops. Cotton textiles and lacquered woodwork are also the product of Sahiwal.

Sample Collection

Both rural and urban areas of district Sahiwal was visited to find out the families with disorders. After detailed visits, five families were selected for study and to construct the pedigree. The pictures of affected individuals were also taken with the consent of each family. The samples were collected from five different families using simple and direct questions. The university's ethical committee granted permission to conduct the current research (**Table 1**).

Pedigree analyses

Seven families were selected for pedigree analyses. Each family was detailed interviewed, and pedigree was constructed. The prevalence of hypotrichosis among each family and origin of mutation was recorded through pedigree analyses.

Statistical analysis

The third section concerned the history of patients having hypotrichosis. In the final section, some questions about baldness were observed. Data were analyzed by using MS office software, using descriptive statistics to find mean, percentage and prevalence rate of the diseases.

Results

Prevalence of hypotrichosis

The present study was planned to record the mode of inheritance of hypotrichosis in selected families of

Table 1: Sampling sites

Family Number	Name of Villages	Geographical coordinates
UOA	9/sp distteric Pakptan division Sahiwal	30.3930° N, 73.5259° E
UOB	Chak 68/4-r Sahiwal	30.66595, 73.10186
UOC	Toot wala Noorshah	30° 50' 0" North, 73° 12' 0" East
UOD	Urban area of Sahiwal	30° 40' 39.7812" N and 73° 6' 24.5232" E.
UOE	Chak 86/6-r Sahiwal	30.41°N 73.40°E

the Sahiwal Division Punjab Pakistan. Five families with hypotrichosis were selected for the detailed study. The persons having hypotrichosis were identified. The prevalence of this genetic disorder was 25.82 % in the studied families. The prevalence was recorded by number of affected men out of total number of members of the family. Out of 213 members, 55 were affected with hypotrichosis (**Table 2**).

The prevalence of hypotrichosis was different in different families. In family, UOA was observed 17.24%, UOB was 20.00 %, UOC was 41.94 %, UOD was 23.40 %, UOE was 40.740 %, UOF was 46.43 % and UOG was 39.13 % in affected members.

Table 2: Prevalence of hypotrichosis

Sr.#	Family	Affected	Total	Prevalence
1	UOA	10	58	17.24
2	UOB	10	50	20
3	UOC	13	31	41.94
4	UOD	11	47	23.40
5	UOE	11	27	40.74
Total		**55**	**213**	**25.82**

Description of family UOA

The family UOA was visited in a rural area of District Sahiwal which was affected with Hypotrichosis (baldness). There were 58 members in this family and ten members in four generations were affected with the genetic disorder of baldness. Two women were belonging to the family UOB. The 5th generation was not affected. The big factor which affected this genetic disorder was age. At the time of study, 5th generation was not affected because their age was less than 25 years. In the first four generations, baldness started before or at the age of 25 years. Affected individuals showed typical features of baldness for hypotrichosis. The mode of inheritance was autosomal recessive. The pedigree of the family is shown in **Fig. 1**.

Description of family UOB

Family UOB also belongs to district Sahiwal and affected with baldness. In this family, there were 23 males and out of them 10 were affected with a genetic disorder. There were 27 females, and all were normal. The 10 affected members were present in 3 consecutive generations starting from 1st generation and penetrate to 3rd generation. The 4th generation was not affected. All members in the 4th generation were below the age of 25 years. In the first four generations, baldness started at the age of 25 years.

The affected individuals showed typical features of baldness. The nature of inheritance was autosomal receive. The pedigree of this family is shown in **Fig. 2**.

Description of family UOC

This family belongs to Toot Wala Noor Shah, the rural location of district Sahiwal. In this family, 13 members were affected out of 18 male members. The other 13 were the normal female. The affected were present in 4 consecutive generations and transformation was continuous from 1st generation to 4th generation. This starts from the 1st generation including only one affected man. In the 2nd generation, two brothers were affected. In the 3rd generation, 4 brothers were affected. In the last 4th generation, 6 cousins were affected showing typical features of baldness, phenotype of hypotrichosis nature segregating in an autosomal recessive manner. The pedigree of this family is shown **Fig. 3**.

Description of family UOD

In the family UOC, 11 members were affected out of 24 men with this genetic disorder. In this family, 23 normal women were also present. The affected males were present in three consecutive generations transformation of this disorder started from 1st generation to 3rd generation continuously. This starts from the 1st generation including only one affected man. In the 2nd generation, only one man was affected. In the 3rd generation, 9 brothers were affected. These 9 brothers were from two mothers. The 4th generation was not found affected. Affected individuals showed typical features of baldness, phenotype of hypotrichosis and mode of transmission was autosomal recessive. The pedigree of this family

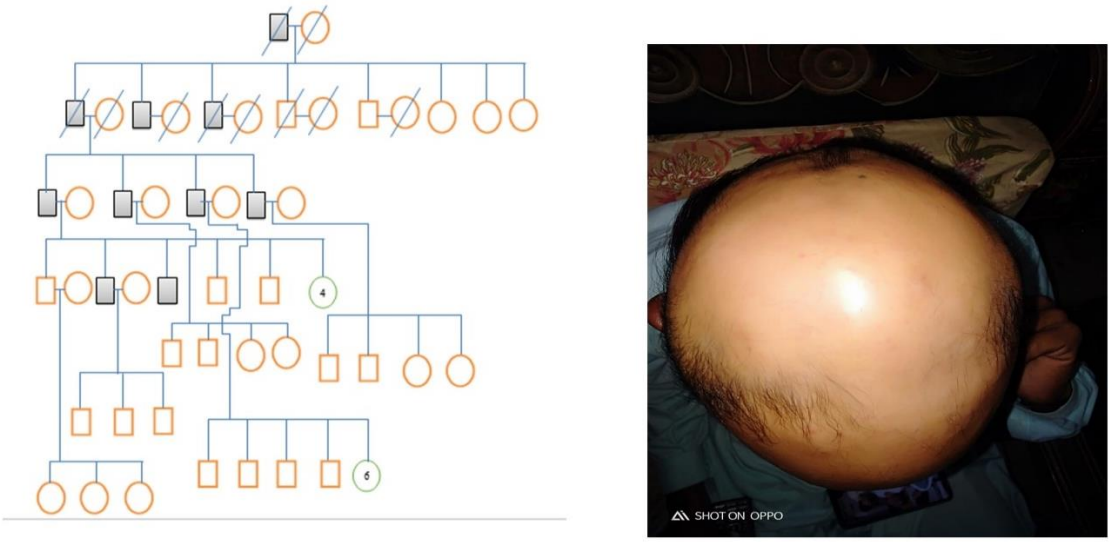

Fig. 1: Pedigree of Family UOA with all affected male

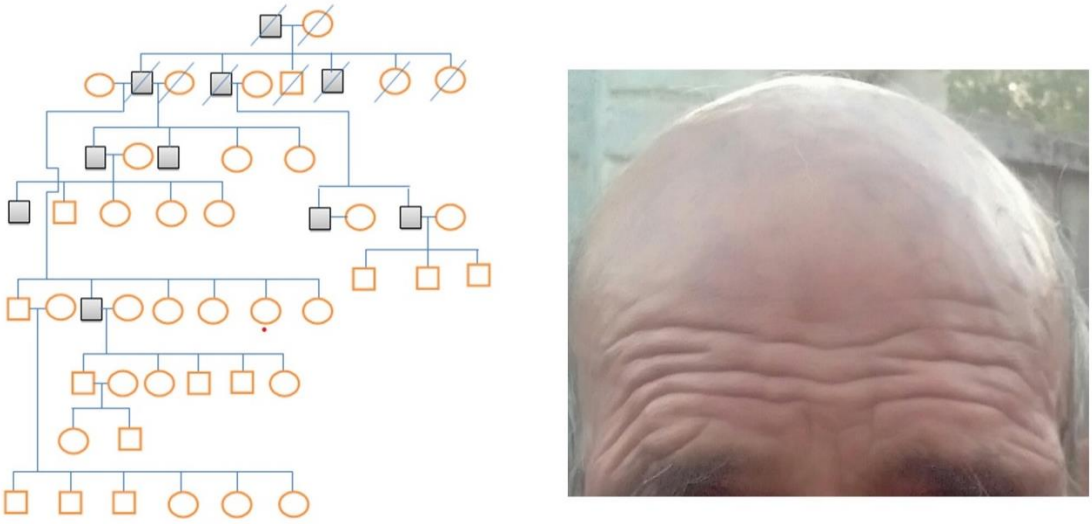

Fig. 2: Pedigree of Family UOB with all affected male

is shown in **Fig. 4**.

Description of family UOE

In family UOE eleven members were affected out of 15 men with this genetic disorder. In this family 12 women were present. Total members were 27. In the present study, about 11 men have been affected in 4 consecutive generations, transformation of this disorder started from 1st generation to 4th generation continuously. This starts from the 1st generation including only one affected man. In the 2nd generation, one man was affected. In the 3rd generation, 3 brothers were affected. In the last 4th generation, six men were affected. The affected individuals showed typical features of baldness, phenotype of hypotrichosis nature, segregating in an autosomal recessive manner. The pedigree of this family is shown in **Fig. 5** (**Table 3**).

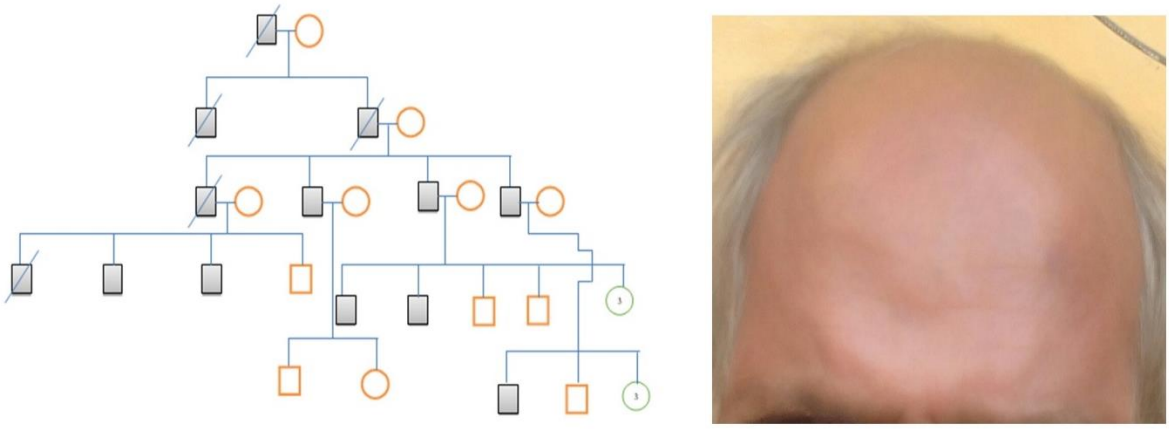

Fig. 3: Pedigree of family UOC with all affected male

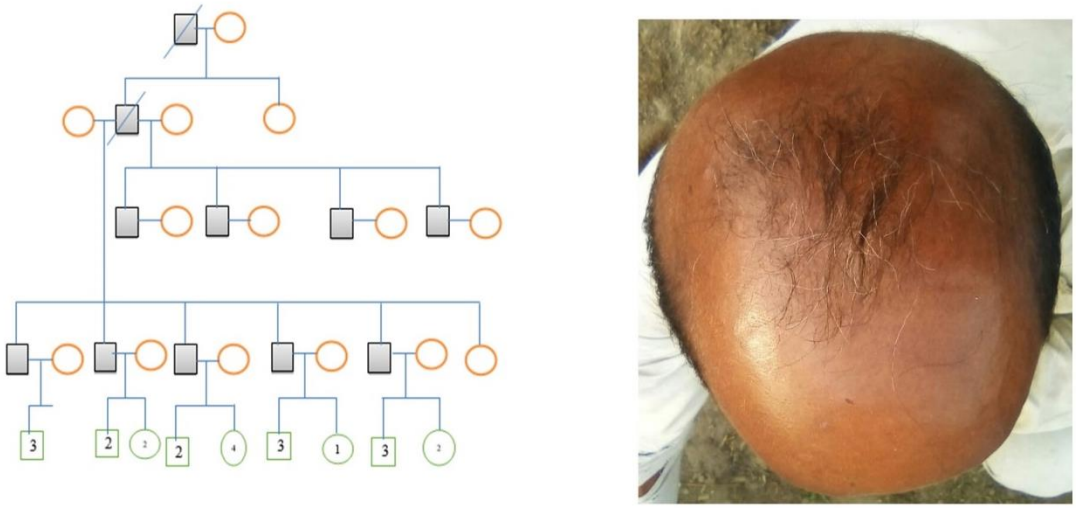

Fig. 4: Pedigree of family UOD with all affected male

Discussion

Congenital hypotrichosis is the most complex hair growth disorders, with several distinctive entities. Hypotrichosis is a condition characterised by a lack of hair in the early stages of life [5]. Autosomal dominant or autosomal recessive hypotrichosis caused by mutations in *LIPH* [6], *LPAR6* or *DSG4* [7] can be inherited in an autosomal dominant or autosomal recessive manner [8] and has a wide genetic diversity [9-12]. The purpose of current study was to document the prevalence of hypotrichosis in some families in the Sahiwal region of Punjab, Pakistan. The results of current study revealed that the overall prevalence of this genetic condition was 25.82 percent (55/213) in the families investigated. However, the prevalence of hypotrichosis was different in families such as UOA 17.24%, in UOB 20.00 %, in UOC 41.94 %, in UOD 23.40 %, in UOE 40.740 %, in UOF 46.43 % and in UOG 39.13 %.

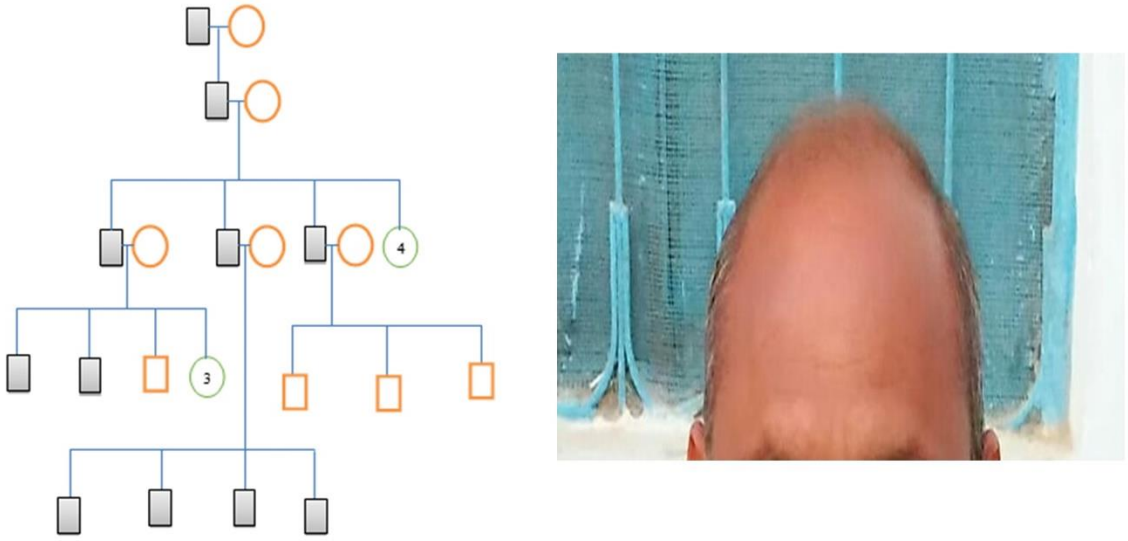

Fig. 5: Pedigree of family UOE with all affected male

Cambiaghi and Barbareschi [13] reported a six-membered family with hypotrichosis while Basit, Wali [14] reported two families affected by hypotrichosis and displayed common symptoms of hereditary hypotrichosis of the scalp. They were either absolutely or partially deafening. Hair on the scalp was missing or thin and grew slowly. They have regular brows, axillary and body hair, and eyelashes. In certain cases, the affected members of the family, eyebrows, and lashes were sparse. In our study, affected members showed common symptoms of inheritance of hypotrichosis and hair fall. Eyebrows were not dispersed.

Bentley-Phillips and Grace [15] observed that the history was same in both male and female patients, with the main difference being the severity of the hypotrichosis. For the pedigree, an arbitrary distinction was made between extreme (those wearing wigs) and partial (those not wearing wigs). Until they were under school age, all of the children had normal hair. Then came a gradual and diffuse hair loss that affected the scalp, brows, and eyelashes, leaving only wispy hairs on the scalp. Body hair grew slowly and scattered. Current study showed no affected person wore the wig till the end of life. Under 25 years they had normal hairs. Eyelashes, eyebrows, and hair of the body except for hair of the head were found normal. Body hair grew slowly but not scattered.

Zlotogorski, Marek [16] observed 12 families with hypotrichosis. The parents of two of the families (3 and 4) were first cousins. Within the first days of life, all of the patients developed early-onset generalized scalp alopecia with the appearance of black dots. Infancy was also marked by follicular scalp hyperkeratotic papules with erythema, scaling, dryness, and pruritus. Hairs were generally small and brittle, could grow up to 10–20 cm in length. Occasionally, two or three hair follicles converged in a single ostium. With nobody's hair, reduced axillary hair, and limited presence of pubic hair, the brows and eyelashes were sparse. 8 families of hypotrichosis were observed. The parents of the family UOA and UOB were first cousins. The black dots of alopecia did not appear in these families. Before the 25-year age, the hair growth was normal. The remaining hairs like eyelashes pubic hair were normal and these hairs were not sparse.

Ali, Chishti [17] described the genotyping of hypotrichosis and to identify the chromosomes. Genotyping with markers linked to four different phenotypes was used to identify the underlying hypotrichosis locus in the family. There were Human hairless (*HR*) genes located on chromosome 8p21.3. Desmoglein Corneodesmosin is encoded by *DSG4*, present on chromosome 18q12.1. The *CDSN* is located at 6q21.33 and the AH locus is located at 3q27.2. The markers were entirely informative, and the three affected family members (IV-1, IV-2, and

IV-5) were homozygous for the markers linked to AH locus (D3S2314, D3S3609, D3S3578, and D3S3583), implying a connection to this area on chromosome 3q27. Phenotypical analyses were performed and autosomal recessive hypotrichosis was observed.

Conclusion

In conclusion, the hypotrichosis prevailed in the families up to generations due to cousin marriages. The age of onset in these families was 25 years or above. Males were affected and most of them with head hairs.

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Conflict of interest

The authors declare no conflict of interest.

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