

Inheritance of Hypertrichosis Pinnae Auris-A Review of Literature

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ABSTRACT

Hypertrichosis is an excessive growth of hair on a particular area of the body which is abnormal for the age, sex or race of an individual. The presence of the excessive coarse black hair on the auricle of the human ear is referred to as hypertrichosis pinnae auris or hairy ears. The condition is primarily restricted to older men and occasionally observed in females. According to the available literature, hypertrichosis pinnae auris is a Y-linked character. A number of studies have shown that the inheritance of the trait is from father to the son, any exceptions can be attributed to the lack of penetrance of the gene or crossing over from Y to X chromosome. A few researchers have suggested the probability of it being inherited in an autosomal manner. The mode of inheritance of the trait thus, remains controversial as to whether it is Y-linked or autosomal or perhaps both. The present article reviews various available studies on hypertrichosis pinnae auris in different populations of the world. It further deliberates on different aspects of the modes of inheritance of hypertrichosis pinnae auris and discusses the contradictions in its inheritance. The understanding of this area of research is significant for studying morphological variations and their genetic basis, sex differences among individuals and populations together with intergroup differences involving anthropology, anatomy, comparative morphology, personal identification and human genetics.

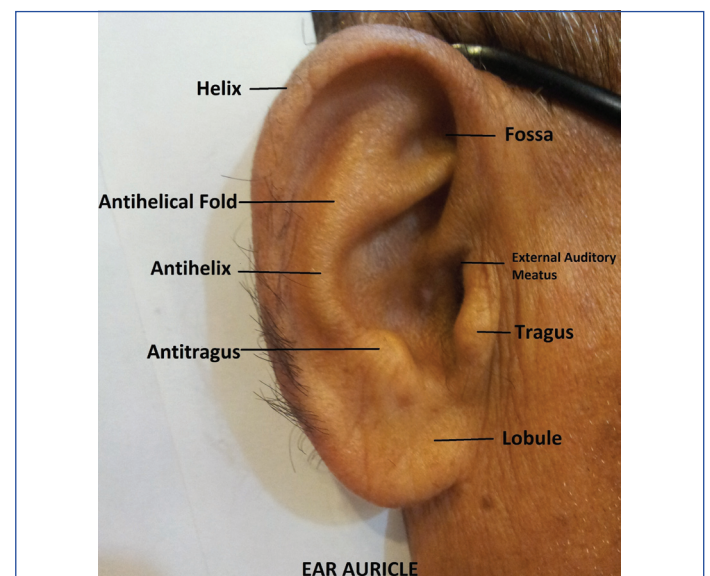
Keywords: Biological anthropology, Hairy ears, Human biology, Human genetics, Pedigree analysis, Penetrance, Population variation, Y-linkage

INTRODUCTION

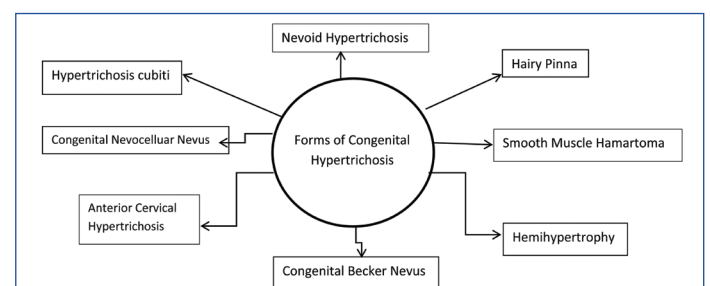
The word 'Hypertrichosis' is derived from 'Hyper' that means over/excess/more than normal and 'trichosis' that refers to any abnormal condition of hair growth. Thus, hypertrichosis is a condition characterised by the excessive growth of hair and its thickness in a particular area of the body which is not considered normal for the age, sex or ethnicity of an individual [1]. It is the presence of excessive hair on the body parts that otherwise lack hair growing normally. Hairs may be present at a single site or may cover the entire body, with the exception of the palms and soles. This type of hair growth is not confined to androgenic areas or bodily surfaces that depend on androgen for hair growth. Thus, hypertrichosis is considered as an androgen independent growth of hair on the body surface. Hypertrichosis should be differentiated from the term 'HIRUSTISM' which is defined as excess androgen sensitive hair growth. It is often diagnosed in women and children who have hair pattern as that of men [2]. Therefore, hypertrichosis pinnae auris, also known as hairy ears is defined as the presence of the excessive hair growth on the outer helix of the pinna of the human ear. This trait is more commonly observed in older men and intermittent in females, the location of the hairs varying from top of the helix to the lateral side of the helix [Table/Fig-1] [3]. Hypertrichosis pinnae auris has been reported in different ethnic groups. In the Online Mendelian Inheritance in Man (OMIM), the molecular catalog of human genes and related disorders, the hypertrichosis pinnae auris is included as hairy ears-139500 or hairy ears, Y-linked-425500 with HEY genetic locus on chromosome Yq [4].

Olsen EA, classified hypertrichotic diseases into congenital and acquired conditions with generalised versus localised hair growth patterns [Table/Fig-2] [5]. The present review details hypertrichosis pinnae auris, a phenotype characterised by the presence of scanty to marked or bushy growth of hair at the helix or the rim of the ear and near the tragus of the ear [Table/Fig-3a,3b]. The condition is often considered to be a congenital/acquired form of hypertrichosis. Basu A, referred to the condition as the presence of hairs that are longer, darker and thicker than lanugo (soft, downy and unpigmented foetal

hairs) hairs on different areas of the pinna [6]. In some individuals, coarse hairs start appearing on the helix of the ear as the age advances, and it is often referred to as hairy pinna or hairy ears. This condition is observed mostly in men; therefore, is proposed to be a Y-linked chromosomal trait [7-10].



[Table/Fig-1]: Figure shows the different areas of the external ear.



[Table/Fig-2]: A figure showing different forms of congenital hypertrichosis.



[Table/Fig-3a]: Photographs showing typical Hypertrichosis pinnae auris condition.



[Table/Fig-3b]: Photographs showing typical Hypertrichosis pinnae auris condition.

Two mechanisms have been proposed for the development of hypertrichosis [3]. The first mechanism deals with the conversion of the vellus (short, fine and light coloured hair) hair to terminal hairs. The increased production of androgen in adolescence causes the follicles in the axillae, groin, and in males, the beard and chest to grow larger and deeper into the dermis and to be converted into terminal hairs. Thus, the body areas devoid of human hair in hypertrichosis often include switching of vellus hair to terminal hairs. Other mechanism is based on the changes occurring in the hair growth cycle. Hair growth cycle involves three phases: anagen, catagen, and telogen. In the anagen phase (growth phase), the hair grows actively and in the catagen phase (transition phase) the hair follicle shrinks and detaches from the dermal papilla, thereby ceasing the growth of the hair followed by the apoptosis. In the telogen phase (resting phase), hairs begin to shed [3]. The hair follicles possess their own intrinsic growth pattern in the whole body, which may be altered by systemic influences, like androgens, thyroid hormone and growth hormone [11]. Hypertrichosis thus, according to the second mechanism results when the hair follicles remain in anagen phase for longer duration than normal, for their location.

The cases which have been reported wherein hypertrichosis results from use of certain drugs/chemical, patients with human immunodeficiency virus infection, infants born to diabetic mothers, in these cases it is often, referred to as the acquired form of hypertrichosis [12,13].

Methodology for Literature Search

A review of the studies was conducted by using a computerised search of articles published in the PubMed database. Various

keywords were employed for the filtering the search involving hypertrichosis pinnae auris such as: hypertrichosis, hypertrichosis pinnae auris, auricular hypertrichosis, hairy pinna, etc. Besides, the articles were identified by exhaustively referring to the reference lists of the already selected articles. All the original research articles published in peer-reviewed English language journals dating from early 20th century till the year 2016 were included in this review. Majority of the studies are based on population residing in particular areas of the world such as Malaya, Japanese, Egyptians, Tribes and different castes of India. As there are few studies conducted on this topic; therefore, the condition remained least explored. The present review of literature is an attempt to highlight the variation in the inheritance pattern of the hypertrichosis pinnae auris as well as its functional role in forensics and anthropology.

A Review of Studies Conducted on Hypertrichosis Pinnae Auris

In earlier works, a few isolated pedigrees of Italian family were being reported by the researchers who proposed that the presence of black coarse hairs on the ear is transmitted from one generation to the other by Y-linked inheritance [14,15]. However, it is not considered to be reliable because the pedigree was constructed on the basis of the information obtained from a single informant. Cockayne EA [16] made an assumption on the basis of the pedigrees analysed by Tommasi C that the transmittance of the hairy pinnae trait from one generation to another is due to the dominant gene present on the Y chromosome [15].

In 1957, Gates RR favoured the inheritance of hairy pinna to be Y linked but much emphasis could not be made due to the small size and limited number of pedigrees [17]. The major work on inheritance of hairy pinna of ears began after 1958 when Penrose LS and Stern C demolished the supposition of 15 other traits as well as hypertrichosis pinnae auris to be Y-linked [18].

Sarkar SS et al., analysed seven pedigrees for this trait and according to him, only one pedigree was in accordance with Y-linked inheritance that does not explain the assumption of being a fully penetrant gene [19]. Gates RR and Bhaduri AR studied the inheritance of hairy pinna by analysing the pedigrees of the 250 individuals in five generations and 30 sibships [20]. They reported the existence of Y-linked inheritance with an exception that the non occurrence of the trait was due to the failure of penetrance of the gene or the X-chromosome in the mother might have been crossed over from Y to X. Besides, there can be a possibility that the presence of few hairs were overlooked by the investigator. The authors however, did not discuss the age of onset for the appearance of the hairy pinna on the ear rims.

Gates RR et al., examined six new pedigrees from different families of Calcutta, West Bengal and observed that the gene responsible for hypertrichosis was not transmitted from the daughters of the affected father [9]. The variations in the amount of hairiness and in the range of age of onset of the trait were reported within the families. The investigators noted a number of associations of the hair in the ear rim with; a) hair in the meatus; b) body hair and; c) amount of chest hair. Thus, they proposed that the inheritance of hairy pinna traits is through Y chromosome with occasional failure of penetrance.

Slatis HM and Apelbaum A investigated the penetrance of hairy pinna of the ear in Israeli population by studying the frequency of hypertrichosis pinnae auris by community of origin and age, and the frequency of affected relatives of propositi by age [21]. They avowed that with the increase in age, the degree of penetrance increases. Stern C and Tokunga C found hairy ear rims in 1 individual out of 261 Japanese males aged between 20 and 91 years residing

in Japan or in California in contrast to the presence of hair in the meatus of the hair [22].

Various studies have been conducted on different families of Indian origin by Chattopadhyay PK, Ali SGM, Bharadwaj VK et al., Garg SK, Ghosh RR and Tyagi D, they stated that the inheritance of the occurrence of hairs on the pinna of the ear is Y-linked [23-27]. The highest average incidence of 53.3% was reported among Kerala population and the hair pattern distribution in Central Indians was similar to Whites population studied by Setty LR [28]. Also, the frequency of tragus-lobular hypertrichosis was found to be 3.84% in the Bhoksa tribe of Dehradun [26].

Another study conducted on 500 individuals with dermatophytosis (fungal infection of skin) from South India [29] showed the presence of the hair on ear rims in 16.6% males and 0.4% females suggesting an autosomal dominant sex linked inheritance of the hypertrichosis pinnae auris. On the other hand, the control group consisting of 1030 patients, the incidence of the trait was reported to be 34.9% among males. The study concluded that the gene could be androgen dependent and similar to the genes for beard hair which are not confined to the Y chromosome. Further, they studied the association between hypertrichosis pinnae auris and diabetes mellitus, whereby nine out of ten diabetic males had hairy ears. Thus, a higher incidence of hairy pinna trait is reported in individuals suffering from diabetes mellitus.

The absence of hairy pinna was observed in eastern Indian populations such as Lepchas, Bhotias, Tibetan Refugees, Khasis and Totos [9]. Only two individuals were found to possess hypertrichosis among Totos (West Bengal) by Chakravarti MR [30]. Besides, a study conducted by Pandey BN et al., of Badhiya Muslims of Purnia District in Bihar reported the absence of hairs on the ears among the 500 unrelated individuals studied [31]. Such a non appearance of hairy pinna in the Badhiyas may indicate its affinity towards these eastern Indian populations, thus, prompting the researchers to pursue research in this direction.

The inheritance of the hairy pinna trait remains unclear. A number of studies have been conducted on individuals belonging to different ethnic groups showing the inheritance of the hairy ear rims to be holandric (father to son transmission). However, to prove the same, strong conclusive evidence involving large population is required. The available research shows that the penetrance of the trait increases with age i.e., most of the time appearance of the hairs on the ear pinna has been observed in the older individuals. Basu A, reported the significant increase in frequency of hair growth at lobe, tragus and antitragus in the individuals showing the presence of hair on the ear rims as observed in Pahira community [6].

Mukherjee DP observed the occurrence of hair on all parts of the ear [32]. He studied the trait in the different sub castes (Bhardwaaj, Sandilya, Sabarna, Vatsa) of Radi Brahmins and observed a frequency of 32.50% in the second series of the population studied. He suggested that the various constitutional factors may be responsible for the expression of the trait gene. He attributed the failure of the manifestation of the condition in older men to the shedding of hair with advancing age. Singh P and Purkait R, observed various somatoscopic characteristics of human auricle in the Thakur caste group in Sagar District of Madhya Pradesh in India and reported the presence of helical, meatal and lobular form of hypertrichosis in 25% of the total males included in their study [33].

Various Scales for Degree of Hairiness

The occurrence of hairy pinnae trait varies from a single hair to the dense bushiness of hair; therefore, recording the presence or

absence of hair. Sarkar SS et al., devised a scale from Grade 0 to Grade 5 viz: 0 Not affected, 1 Very scanty, 2-scanty, 3-Medium, 4-Marked, and 5-Very Marked or bushy [19]. It may be noted that presence of a single hair on either pinnae is considered to be an affected individual denoted as "He". According to Slatish HM and Apelbaum A, the affected individuals are the one having at least several coarse hairs on the top or side of the hair [21]. One more scale of hairiness was given by Gates RR et al., where stage one denotes the most extreme degree and stage six denotes a trace i.e., presence of only 3 or 4 long hairs [9]. Another scale for the intensity of hypertrichosis used by Abbie AA and Rao PD, constituted of two grades only [10]. First grade is slight to moderate (+) involving presence of few long hairs to a distinct, and also a small clump at the scaphoid fossa. Second grade is moderate to extreme in which the hairs are present at the scaphoid fossa spreading further towards the helix as well as the lobe. The location of hairs on ear varies from one ethnic group to other. Gates RR and Vella F, reported the occurrence of hair at the top of the ear in Israeli and Malta populations [34]. On the other hand, in Indian population hair frequently occurs in the sulcus at the side of the ear. The scale given by Sarkar SS et al., is preferred by researchers as it covers the different levels of hairiness [19].

Genetics of Hypertrichosis of the Ear Rims

Many studies in the past reported the inheritance of hairy pinna trait as Y-linked or holandric inheritance. The genes which are present on the differential region of the Y chromosome are commonly referred to as holandric genes. Therefore, the mode of inheritance involving the transmission of such genes from father to son and then to his sons further is called the holandric inheritance. Another characteristic feature of this inheritance is that the females neither transmit the gene nor carry it to the next generation [35].

Tommasi C, in his work on hairy pinna showed that all the male offspring from the affected male had hairy ears in the pedigree analysed by him [15]. On the other hand none of the female descendants had hairy pinna of the ears, thereby suggesting a linked mode of inheritance for the trait. Dronamraju KR [8] after publishing three pedigrees (largest pedigrees consisting seven generation for hypertrichosis inheritance) from Andhra Pradesh interpreted them to be completely Y-linked because of the absence of any evidence for the lack of penetrance and crossing over from Y to X chromosome as hypothesised by Dronamraju KR and Haldane JB [36].

Gates RR, examined about 20 pedigrees showing inheritance of the trait from father to son with different degree of hairiness within the same family [7]. The trait was absent in ten offspring of the normal daughters from affected fathers with exception of the two accounting for the lack of penetrance or likely explanation. Sarkar SS et al., studied seven pedigrees from West Bengal and Orissa and found only one pedigree to be compatible with the Y-linkage of hypertrichosis but unable to prove its rightness [19]. The remaining six pedigrees did not fit in the characteristics of holandric inheritance. In none of the pedigrees observed by Sarkar et al., daughters from affected father had a son with the trait [19]. In another study, Gates RR et al., examined six pedigrees, which showed Y chromosome inheritance with occasional failure of penetrance [9]. The analysis of the data on Israeli population by Slatish HM and Apelbaum A, stated that the data agree with the hypothesis that this trait is determined by a gene on the Y chromosome [21]. The earliest age of onset of the trait is about 20, but penetrance does not appear to be complete until very late in life.

Though there were assumptions by researchers for the trait to be linked through dominant autosomal inheritance but strong evidence in support of this assumption is required. The existence of genetic heterogeneity remains as such for hypertrichosis pinnae auris.

Noted Exceptions to the Y-linked Inheritance

Sarkar SS et al., reported the deviation from the holandric inheritance in six pedigrees; they were non compatible with the Y-linked inheritance of the trait, as the sons from the affected fathers in second and third generation did not show the trait, thereby presenting contradiction to the above mentioned mode of inheritance [19]. However, in absence of any confirmatory evidences such information necessitated additional conformation [36]. Dronamraju KR and Haldane JB, [36] pointed out that Sarkar SS et al., [19] did not examine all the subjects personally and observations in their pedigree was constructed purely on hearsay evidence due to which actual observations may have altered. Subsequently, an exception was observed in Gates RR and Bhaduri AR, pedigree with the presence of four or five hairs in each ear of the son of an unaffected female [20]. Sarkar SS and Ghosh RR, noted the occurrence of short, fine black hairs on the ear lobe and lower part of the pinnae in Bengalee female children aged 10-16 years [37]. Also, the father and brother of one of the affected girls exhibited Grade 4 and 2 hypertrichosis respectively. Stern C et al., reported the dilemma in recording an individual as an affected person because if an affected person is taken as the one who had at least second degree of hairiness then very few individuals are considered to be affected by the trait [38]. Therefore, the assumption that in Y-linkage all the sons from affected fathers are affected appears to be incorrect. Deviation from the Y-linked inheritance assumption was observed by Kamalam A and Thambiah K [29]. They suggested the probability of the trait being autosomal dominant sex limited or incompletely sex linked dominantly inherited trait by the observation of hairy ear pinnae among females of south Indian sample in their study.

The Y-linked heritable trait assumption was then investigated by Lee A et al., in South Indian population [39]. They used 11 Y chromosomal binary markers of 50 unrelated hairy ear males and 50 unrelated unaffected males and found 9 distinct haplogroups in the Y chromosome phylogeny among the affected individuals. They suggested sex limited expression of an autosomal dominant inheritance and hormonal influence for the inheritance of hairy pinna. Their study revealed the non availability of persuasive candidate gene for hypertrichotic phenotypes, thereby, stating the absence of Y linkage for hairs on the ears.

DISCUSSION

There are a number of studies conducted to unravel the inheritance of hairy pinna of the ear- the incidence of the trait, the frequency of hairs in certain regions, the increasing frequency with age, the differences in density among various ethnic groups and its association with the other congenital diseases. The age of appearance of hairs on the ear varies from one ethnic group to the other. Besides, the incidence of the trait is known to show variation, from complete absence to the presence of hair tuft on the ear, and the differences in the site of hypertrichosis as observed in distinct groups [Table/Fig-4].

The mode of inheritance of the trait remains contentious as it remains unclear if the condition is Y-linked or autosomal or perhaps both. The majority of the authors have claimed that the assumption of the hypertrichosis pinnae auris to be completely Y-linked trait is true with exception of lack of penetrance in a few cases [7-9, 20]. The greater number of studies conducted on hairy pinna of the ear assumes, the trait to be completely Y-linked in its mode of inheritance because in the pedigrees analysed it has been observed that it is transmitted from the father to son only with a very little exception of lack of penetrance of the trait or it can be attributed to the crossing over occurring from Y to X chromosome. None of the sons of the daughters of affected fathers showed the condition [7-10,17,35,38]. Kamalam A and Thambiah K, were the first to suggest the probable autosomal-dominant sex limited inheritance of hypertrichosis of the ear [29]. However, the results of such limited pedigrees cannot form the basis of mode of inheritance of the trait. Therefore, more extensive research needs to be conducted to reach a valid conclusion in this regard. Another hindrance in examining the trait is its cosmetic treatment. Young individuals are often concerned about their looks and appearance, resulting in frequent removal of the hair by cutting, shaving, trimming or even laser treatments. Thus, due to the absence of the strong evidence to favour the same, its mode of inheritance is unclear and various large populations are to be studied. Besides, studies have not been conducted to find whether the sons from unaffected fathers, whose maternal

S.No.	Population group studied	N (Sample size) Total affected		Incidence (%)	Surface of the ear	Age of onset (In years)	References
1	Pahira, Bihar	786	268	34	Ear rims	16	Basu A [6]
2	Sinhalese, Ceylon	414	153	37	Whole ear rims	-	Dronamraju KR [8]
3	Andhra Pradesh	345	21	6.08	-	-	Dronamraju KR [8]
4	Calcutta, West Bengal	103	26	25.2	Ear rims	Late puberty	Gates RR et al., [9]
5	Whites	320	-	-	Helical (elevated area)	30	Abbie AA and Rao PD [10]
6	Australian Aborigines	189	37	19.6	Scaphoid fossa	20	Abbie AA and Rao PD [10]
7	Blacks	320	-	-	Helical (elevated area)	29	Abbie AA and Rao PD [10]
8	Israeli	868	88	10.1	Top part of the helix	20	Slatis HM and Apelbaum A [21]
9	Japanese	261	1	0.38	Ear meatus	21	Stern C and Tokunga C [22]
10	Kerala	2105	1123	53.3	Lower part of the helix	20	Ali SG [24]
11	Bhoksa tribe, Dehradun (Uttar Pradesh)	130	5	3.84	Tragus	40	Garg SK [26]
12	Madras	500	85	17	Middle part of the helix	25+	Kamalam A and Thambiah K [29]
13	Badhiya Muslims, Bihar	500	-	-	Absent	-	Pandey BN et al., [31]
14	Thakur Caste, Central India	280	32	11.4	Helix	-	Singh P and Purkait R [33]
15	Nigerian males	100	30	30	-	30	Stern C et al., [40]
16	Egyptians (Alexandria)	197	39	19.79	Helix	20	El Wakil HE et al., [41]
17	Malaya, Malaysian	441	61	13.81	Tragus, antitragus and intertragic incisures	-	Dharap AS and Than M [42]
18	Khatri---	230	12	5.2	Rim cavity lobe	18 and above	Singh L et al., [43]
	Baniyas---- Patiala, Punjab	195	28	14.3	Rim		

[Table/Fig-4]: Site for occurrence of hypertrichosis and its incidence in different ethnic groups.

uncles are found to be affected, carry the trait or not. Moreover, any association of the women affected with virilism (appearance of secondary male characters in females) and appearance of hairy ears may be studied.

Furthermore, the literature shows that the work done on hypertrichosis pinnae auris is mainly based on the pedigree analysis. The information was collected and constructed from the hearsay evidence alone [7]. At times, the subjects were not even examined personally by the researchers, thereby adding subjectivity to the data being collected. There exists a possibility that a few details were overlooked by the examiners. Illegitimacy often considered to be rare in the groups under study cannot be neglected in the population all together. Moreover, the presence of hair on the ear rims of the females was never photographed by any of the researcher attributed with the absence in the literature.

Hairy pinnae can also be considered as an individualising characteristic. The occurrence of hair on the pinnae of the ear could aid in forensic investigations by excluding the criminals in cases of burglary. Sometimes, while listening at the doors of the target house, the burglars inadvertently leave the prints of their ears [44-46]; in such a scenario, the patterns of the hair of the hypertrichotic pinnae may be impressed along with the ear prints which might help in narrowing down the search of the culprits. It is also apparent that sensory hair cells present in the cochlea of the ear are responsible for hearing in humans. Thus, in a recent communication, it has been hypothesised that the presence of hairs at the different surfaces of the ear may be associated with the enhancement in the hearing capacity of humans [47].

CONCLUSION

Much of the progress made to understand the inheritance of the hairy pinna of the ear has been through pedigree analysis, but there remains much to be elucidated. Factors such as constitutional ones and ethnicity differences are held responsible for the expression of the gene. New genetic studies have shown molecular evidence for the absence of Y linkage of the hairy ear trait. Future studies should concentrate on poorly understood aspects of its mode of inheritance by identifying the candidate gene responsible for the same, and to find out the underlying mechanism that forms the transmission of the trait from father to offspring as to explore whether single gene or multiple genes are responsible for the hairy ear trait. It has been clearly highlighted in the review that the inheritance pattern of the hypertrichosis pinnae auris is variable in different populations. The understanding of the mode of inheritance of this area of research is significant for studying morphological variations in different population groups, sex differences and intergroup differences and may be useful in many disciplines such as anthropology, human and comparative morphology, personal identification and human genetics. It is further emphasised in the present review that the hypertrichosis pinnae auris has a functional role which may give a future effect for furthering the research in this field.

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