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ORIGINAL RESEARCH

First Cousin Marriages and the Risk of Childhood-Onset Vitiligo: Exploring the Genetic Background: A Cross-Sectional Study

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Background: Vitiligo, a condition characterized by depigmented skin, has been observed to have a higher incidence in patients with a family history of the disease. This study investigates the relationship between parental consanguinity, family medical history, and the onset of childhood vitiligo, hypothesizing that genetic factors play a significant role.

Methods: A cross-sectional study was conducted involving 382 people diagnosed with vitiligo in Saudi Arabia. The study assessed the prevalence of parental consanguinity and its correlation with the disease's onset, employing statistical analysis to evaluate the data collected through medical records and family history questionnaires.

Results: The findings reveal a significant association between parental consanguinity, particularly among first cousins, and the incidence of childhood-onset vitiligo. Additionally, a notable correlation was found between family medical history and the onset of the condition, with familial vitiligo being more prevalent in patients with adult-onset vitiligo.

Conclusion: This study underscores the critical role of genetic predispositions in the development of childhood-onset vitiligo, highlighting the influence of parental consanguinity. The results advocate for increased awareness and screening in populations with high rates of consanguinity to facilitate early detection and management of vitiligo. Future research should focus on exploring the genetic mechanisms underlying this association to develop targeted interventions.

Keywords: parental consanguinity, childhood-onset vitiligo, genetic factors, familial vitiligo, Saudi Arabia, cross-sectional study

Introduction

Vitiligo manifests through the formation of distinct depigmented white macules and patches on the skin, a result of the targeted destruction of melanocytes within those areas. Accompanying autoimmune disorders, especially those related to the thyroid, are commonly observed alongside vitiligo. With a global prevalence rate of 0.5–2%, vitiligo's appearance is more pronounced on darker skin tones, though it indiscriminately affects all racial and ethnic groups.[1–4]

The condition's prevalence in Saudi Arabia stands at 3.5%, slightly higher among females, attributed possibly to greater cosmetic concern reporting. The onset age in Saudi Arabia does not significantly differ from the global average of approximately 20 years, nor does it vary significantly between genders.[5]

Genetic factors significantly influence the pathogenesis of vitiligo, with about 30% of affected individuals reporting a family history of the condition.[6,7] This prevalence highlights a notable genetic component, underscored by observed patterns of consanguinity linked with particular clinical subtypes of the disease. Notably, a higher incidence of vitiligo is associated with first-cousin consanguinity, particularly in cases of non-segmental and acrofacial vitiligo. The inbreeding coefficient, indicative of genetic closeness within affected families, shows a strong correlation with the prevalence of vitiligo, suggesting a robust genetic predisposition. Genetic analyses suggest that vitiligo likely follows a multifactorial inheritance pattern, involving a combination of polygenic influences and environmental factors, which collectively contribute to its manifestation.[8]

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In Saudi Arabia, consanguineous marriages are common in the population, which increases the prevalence of certain hereditary and rare genetic skin disorders, including vitiligo, compared to other populations.[9]

Vitiligo can develop at any age, but is most frequently seen in individuals aged 10–30 years, with an average onset age of about 24 years. It can appear as early as 3 months of age, and the characteristics of vitiligo can differ between children and adults.[10,11]

There has been limited research differentiating between vitiligo that begins in childhood (before 18 years) and that which starts in adulthood (after 18 years). Studies comparing the clinical aspects of vitiligo in prepubertal children and postpubertal adults are scarce.[12,13] There is an inadequate number of studies comparing various associated clinical factors with both childhood/prepubertal and adulthood/postpubertal vitiligo forms.

This study aims to investigate the relationship between the development of vitiligo in children born from consanguineous marriages and the occurrence of the disease across various age groups. Specifically, it seeks to:

1. Investigate the correlation between parental consanguinity and the age of onset for vitiligo.
2. Assess the impact of a familial vitiligo history on its emergence during childhood as opposed to adulthood.
3. Determine the prevalent types of vitiligo associated with consanguineous marriages and in individuals with a family history of the disease.

Methodology

Study Design and Sample

This retrospective analytical cross-sectional study comprised a total of 382 vitiligo patients, randomly selected from patient records at various hospitals across different regions in Saudi Arabia. All patients are diagnosed with vitiligo utilizing the following criteria: the Vitiligo Area Scoring Index (VASI) score, Wood's lamp examination, which revealed depigmented patches in the form of macules occurring at typical vitiligo sites as per the vitiligo classification. Additionally, other depigmented skin disorders are excluded as part of the diagnostic process. The vitiligo in all patients is categorized according to the revised classification system established by the Vitiligo Global Issues Consensus Conference in 2012,[14] which classifies vitiligo into three primary clinical forms:

1. Non-segmental vitiligo, encompassing generalized vitiligo (formerly known as vulgaris), acrofacial vitiligo with its subtype referred to as "lip-tip" vitiligo, as well as vitiligo universalis.
2. Segmental vitiligo that presents unilaterally as an asymmetric distribution.
3. Unclassified vitiligo, a category reserved for cases that do not progress into either segmental or non-segmental vitiligo within a period of 1–2 years. This category includes focal vitiligo and single mucosal vitiligo, affecting either a genital area or an oral cavity.

The inclusion and exclusion criteria for participation were as follows:

Inclusion Criteria

1. Individuals with a dermatologist-confirmed diagnosis of vitiligo.
2. Patients of any age and gender residing in Saudi Arabia.
3. Willingness to participate in the study and provide informed consent.

Exclusion Criteria

1. Patients with other skin depigmentation disorders that are not vitiligo.
2. Patients with cognitive impairments or conditions that hinder understanding or providing informed consent.

Data Collection

Data were collected through a combination of self-administered questionnaires, direct inquiries by physicians, phone interviews, and review of hospital patient records. The questionnaire was structured into two sections: the first section

collected demographic information (sex, age, nationality), while the second section focused on the family history of vitiligo and parental consanguinity.

Study Variables

Independent Variables

A. Family history of vitiligo: the questionnaire allowed participants to identify if they have relatives with vitiligo, grouping them into three categories. The initial category includes first- and second-degree relatives; the subsequent category covers extended family members, such as third, fourth-degree relatives, and more distant connections; the final category is for those without any family history of vitiligo. The classification of relatives is as follows:

1. First-Degree Relatives: These individuals are directly related and share about half of their genetic material. This group consists of one's parents, siblings, and children.
2. Second-Degree Relatives: Sharing roughly a quarter of their genetic material, this group includes one's grandparents, grandchildren, aunts, uncles, nephews, nieces, and half-siblings.
3. Third-Degree Relatives: Sharing around 12.5% of their genetic material, this includes great-grandparents, great-grandchildren, great-aunts, great-uncles, and first cousins.
4. Fourth-Degree Relatives: These family members share about 6.25% of their genetic material, including great-great-grandparents, great-great-grandchildren, and first cousins once removed.
5. Distant relative: Encompassing relatives beyond the immediate four degrees, these individuals share less than 6.25% of their genetic material, including more distantly related cousins and those related by marriage or adoption without a blood connection.

B. Parental consanguinity: The study asked participants about the consanguinity of their parents, with options ranging from close cousins to those with no blood relation. The levels of consanguinity were divided into four categories:

1. First Cousins: This level indicates that the parents share grandparents, meaning they are the children of siblings.
2. Second Cousins: At this level, parents share great-grandparents, indicating that their grandparents are siblings.
3. Third Cousins: Parents share great-great-grandparents, showing that their great-grandparents are siblings.
4. Fourth Cousins and Beyond: This category includes parents who are fourth cousins or more distantly related, sharing a set of great-great-great-grandparents, or even more distant ancestors.
5. No Consanguinity: This group includes individuals whose parents are not related by blood.

Dependent Variable

Vitiligo onset: classified into two categories, childhood-onset vitiligo (1 to 18 years), and adulthood-onset vitiligo (18 years and older).

Covariates

Nationality was divided into Saudi and non-Saudi, considering the small number of non-Saudi patients. In addition, sex was categorized as male or female.

Data Analysis

Data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 29. Descriptive statistics were utilized to summarize the demographic characteristics of the study population. Chi-square tests and logistic regression analyses were conducted to explore associations between the independent variables and vitiligo onset, adjusting for Covariates such as, gender, nationality, parental consanguinity, and family history of vitiligo. A *P*-value of less than 0.05 was considered indicative of statistical significance.

Results

The study included 382 vitiligo patients, with 191 (31.2%) diagnosed in childhood and 263 (68.8%) having adult-onset vitiligo. Childhood-onset cases had a higher proportion of females (56.3%) compared to adulthood cases (46.4%), although this difference was not statistically significant (P=0.07). Both groups showed a high proportion of Saudi nationals, with 88.2% in childhood-onset and 89% in adulthood-onset vitiligo patients (P=0.83). A notable difference emerged regarding parental consanguinity, with 74.8% of childhood-onset cases reporting consanguineous parents compared to 59.7% in adulthood-onset cases, indicating a significant association between early-onset vitiligo and parental consanguinity (P=0.004). The analysis detailed the degrees of consanguinity, showing 25.2% of childhood-onset cases were from first cousins parents, compared to 11% in adulthood-onset cases (P<0.001). Second and third cousins parents accounted for 33.6% in childhood-onset and 30.8% in adulthood-onset cases, while other or distant cousins parents were 16% and 17.9%, respectively. Furthermore, adulthood-onset cases were more likely to report a family history of vitiligo (51%) compared to childhood-onset cases (42%), although this difference did not reach statistical significance (P=0.11), as shown in (Table 1). Illustrated in (Figure 1).

Acrofacial vitiligo, identified in almost half of the cases (49.2%), was observed in 35.1% of childhood onset cases, and 64.9% in the adult age group, as detailed in (Table 2). The influence of consanguinity was evident, with 28.7% of Acrofacial vitiligo patients having no reported consanguinity; however, a significant portion reported first cousins parents (14.4%), second/third cousins (36.2%), and other cousins parents (20.7%). Focal vitiligo, representing 23.3% of the cases, showed a higher incidence among childhood onset vitiligo patients (44.9%) compared to other vitiligo types, with males less affected (39.3%) compared to females (60.7%). In addition, parental consanguinity in focal vitiligo patients came from first cousins parents (24.7%), second/third cousins (24.7%), and other cousins parents (12.4%). Vulgaris vitiligo (18.8%) showed a lower representation in the younger age group (15.3%) and a higher prevalence in the older age group (84.7%), with parental consanguinity patterns similar to other vitiligo types, with 36.1% having no consanguinity, and contributions from first cousins (12.5%), second/third cousins (33.3%), and other cousins (18.1%), as indicated in (Table 2) and (Figure 2).

Table 1 Comparative Analysis of Childhood-Onset vs Adulthood-Onset Vitiligo: Demographic and Genetic Factors

Variables		Total	Age Group		P-value
			Childhood-Onset	Adulthood-Onset	
		N (%) 382 (100)	N (%) 191 (31.2)	N (%) 263 (68.8)	
Gender	Male	193 (50.5)	52 (43.7)	141 (53.6)	0.073
	Female	189 (49.5)	67 (56.3)	122 (46.4)	
Nationality	Saudi	339 (88.7)	105 (88.2)	234 (89)	0.83
	Non-Saudi	43 (11.3)	14 (11.8)	29 (11)	
Parental Consanguinity	Yes	246 (64.4)	89 (74.8)	157 (59.7)	0.004
	No	136 (35.6)	30 (25.2)	106 (40.3)	
Consanguinity Degrees	1st Cousins	59 (15.4)	30 (25.2)	29 (11)	<0.001
	2nd/3rd Cousins	121 (31.7)	40 (33.6)	81 (30.8)	
	Other / Distant Cousins	66 (17.3)	19 (16)	47 (17.9)	
Family History of Vitiligo	Yes	184 (48.2)	50 (42)	134 (51)	0.11
	No	198 (51.8)	69 (58)	129 (49)	
Family History Degrees	1st/2nd degree relatives	77 (20.2)	18 (15.1)	59 (22.4)	0.17
	Other degrees / Distant relatives	107 (28)	32 (26.9)	75 (28.5)	

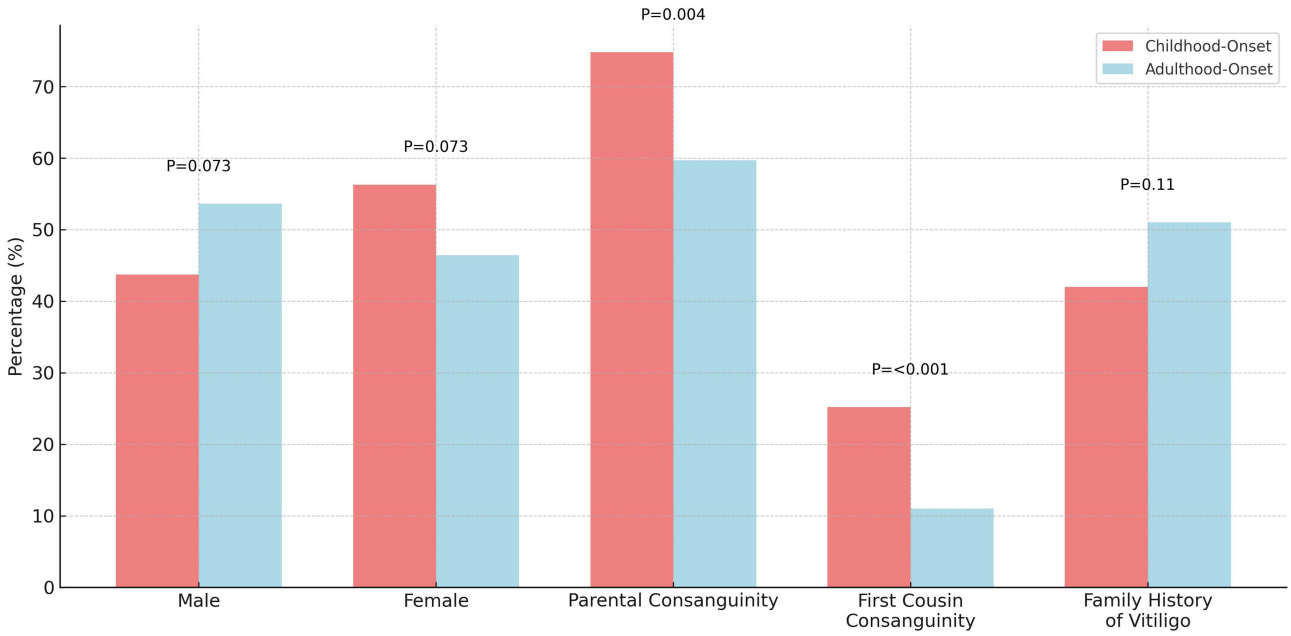

Figure 1 Comparative Analysis of Childhood-Onset versus Adulthood-Onset Vitiligo by Gender, Parental Consanguinity, First Cousin Consanguinity, and Family History of Vitiligo. These visual comparisons underscore the potential influences of genetic and familial predispositions on vitiligo onset age.

Children with consanguineous parents exhibit a significantly increased risk of developing early-onset vitiligo, with an adjusted odds ratio (aOR) of 2.17 (95% CI: 1.32–3.54, *P*=0.002). The risk escalates notably for children whose parents are first cousins, with an aOR of 4.1 (95% CI: 2.1–8.02, *P*<0.001). A more moderate increase in risk is observed for

Table 2 Classification of Vitiligo Types by Demographic and Familial Variables

Variables		Vitiligo Classification						
		Acrofacial N (%)	Vulgaris N (%)	Universalis N (%)	Segmental N (%)	Focal N (%)	Genital N (%)	Total N (%)
Age Group	1–18 Y.O	66 (35.1)	11 (15.3)	0 (0)	1 (11.1)	40 (44.9)	1 (7.1)	119 (31.2)
	19–80 Y.O	122 (64.9)	61 (84.7)	10 (100)	8 (88.9)	49 (55.1)	13 (92.9)	263 (68.8)
Gender	Male	100 (53.2)	39 (54.2)	3 (30)	3 (33.3)	35 (39.3)	13 (92.9)	193 (50.5)
	Female	88 (46.8)	33 (45.8)	7 (70)	6 (66.7)	54 (60.7)	1 (7.1)	189 (49.5)
Nationality	Saudi	166 (88.3)	67 (93.1)	10 (100)	8 (88.9)	76 (85.4)	12 (85.7)	339 (88.7)
	Non-Saudi	22 (11.7)	5 (6.9)	0 (0)	1 (11.1)	13 (14.6)	2 (14.3)	43 (11.3)
Parental Consanguinity	No consanguinity	54 (28.7)	26 (36.1)	3 (30)	8 (88.9)	34 (38.2)	11 (78.6)	136 (35.6)
	1st Cousins	27 (14.4)	9 (12.5)	1 (10)	0 (0)	22 (24.7)	0 (0)	59 (50.4)
	2nd / 3rd Cousins	68 (36.2)	24 (33.3)	3 (30)	1 (11.1)	22 (24.7)	3 (21.4)	121 (31.7)
	Other / Distant Cousins	39 (20.7)	13 (18.1)	3 (30)	0 (0)	11 (12.4)	0 (0)	66 (17.3)
Family History of Vitiligo	No Family History	95 (50.5)	37 (51.4)	4 (40)	3 (33.3)	51 (57.3)	8 (57.1)	198 (51.8)
	1st / 2nd degree relatives	42 (22.3)	17 (23.6)	4 (40)	2 (22.2)	9 (10.1)	3 (21.4)	77 (20.2)
	Other degrees / Distant relatives	51 (27.1)	18 (25)	2 (20)	4 (44.4)	29 (32.6)	3 (21.4)	107 (28)
Total		188 (49.2)	72 (18.8)	10 (2.6)	9 (2.4)	89 (23.3)	14 (3.7)	382 (100)

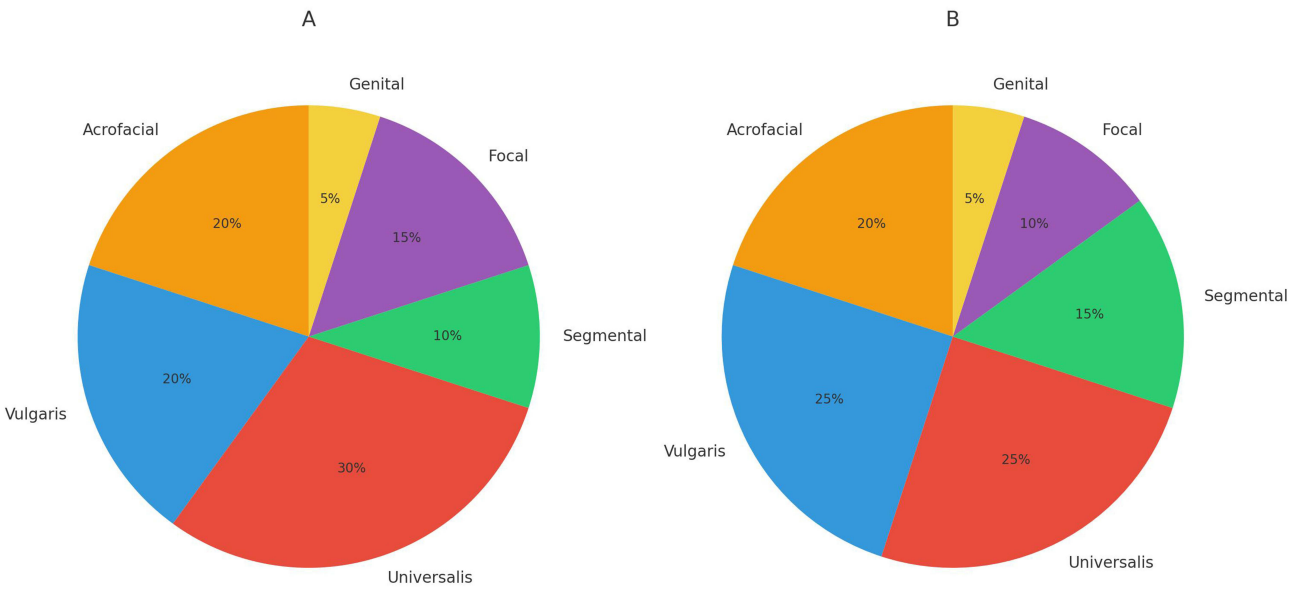

Figure 2 The figure presents two pie charts illustrating the classification of vitiligo types based on familial variables. The left pie chart (**A**) represents the distribution of vitiligo types (Acrofacial, Vulgaris, Universalis, Segmental, Focal, and Genital) in relation to the presence of parental consanguinity. The right pie chart (**B**) displays the distribution of these vitiligo types based on the presence of a family history of vitiligo.

children of second or third cousins, with an aOR of 1.92 (95% CI: 1.08–3.39), suggesting a graded relationship between the degree of consanguinity and early onset vitiligo. The association becomes insignificant for children of more distantly related parents, with an aOR of 1.51 (95% CI: 0.6–2.97). An inverse relationship is observed for familial vitiligo, where a family history of vitiligo was a predictor of adulthood onset vitiligo (aOR=0.63, 95% CI: 0.4–0.99, *P*=0.05), as presented in (Table 3). See (Figure 3) for visual illustration.

Table 3 Logistic Regression Analysis of Parental Consanguinity and Familial Vitiligo History on the Risk of Childhood-Onset Vitiligo

Variables		**aOR[a] (95% CI)**	**P-value**
Parental Consanguinity	No	1	
	Yes	2.17 (1.32–3.54)	0.002
Consanguinity Degrees	No consanguinity	1	
	1st Cousins	4.1 (2.1–8.02)	<0.001
	2nd / 3rd Cousins	1.92 (1.08–3.39)	0.025
	Other / Distant Cousins	1.51 (0.6–2.97)	0.24
Family History of Vitiligo	No	1	
	Yes	0.63 (0.4–0.99)	0.05
Family History Degrees	No Family History	1	
	1st / 2nd degree relatives	0.48 (0.26–0.91)	0.024
	Other degrees / Distant relatives	0.73 (0.43–1.25)	0.25

Note: [a]aOR was calculated by including gender, nationality, parental consanguinity and family history in the final regression model.

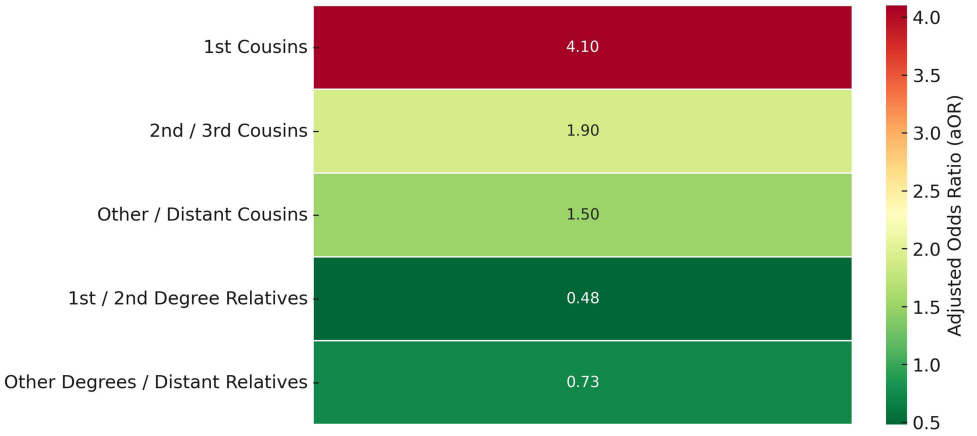

Figure 3 This heat map delineates the adjusted odds ratios (aOR) for varying degrees of consanguinity and family history as they relate to the risk of developing childhood-onset vitiligo. The color intensity correlates with the strength of the association: dark red signifies the highest risk factors, with decreasing risk reflected by progressively lighter shades of red. The light green indicates the lowest risk levels.

Discussion

The study illustrates a significant correlation between parental consanguinity, especially among first cousins, and the onset of vitiligo in children, aligning with our study objectives. It also notes a higher prevalence of familial vitiligo in cases with adult onset, suggesting genetic factors inherited from closely related parents play a pivotal role in the onset of vitiligo.

This research is strengthened by its comprehensive Methodology, large sample size, and the specificity of its focus on a population with high rates of consanguinity, providing valuable insights into the genetic underpinnings of vitiligo.[15] While the study's design allows for significant observations, limitations include potential biases arising from its retrospective nature and the reliance on self-reported family medical history. The magnitude of bias, though not quantifiable, could influence the observed association between consanguinity and vitiligo onset.

With regard to the study's objectives, findings, and limitations, our analysis cautiously supports the hypothesis of a genetic predisposition to vitiligo among children of closely related parents. This interpretation aligns with findings from similar studies, such as those by Alzolibani (2009) and Alenizi (2014),[8,16] which also highlight the significant role of consanguinity in the prevalence and heritability of vitiligo in the Saudi Arabian population. Alzolibani's study focused on the Qassim region and found a high prevalence of vitiligo among individuals with consanguineous parents, particularly first cousins, supporting the notion that genetic factors are crucial in the disease's onset. Similarly, Alenizi's research in Arar demonstrated a significant association between consanguinity and vitiligo, emphasizing the genetic mechanisms that may contribute to the disease's heritability. These studies, along with our findings, underscore the potential genetic mechanisms at play, particularly in populations with high rates of consanguineous marriages. Moreover, while our analysis is robust, it acknowledges the potential for confounding variables and the possibility of analysis multiplicity affecting the outcomes, emphasizing the need for cautious interpretation and validation through further studies.[17]

However, the Results, while indicative of the studied population, should be cautiously applied to other groups. The unique social and genetic makeup of the Saudi Arabian population may limit the generalizability of the findings to broader contexts.

Future studies should aim to further elucidate the genetic mechanisms at play, potentially through longitudinal studies or genetic mapping, to better understand the causal relationships and to explore the effectiveness of targeted treatments for early onset vitiligo.

Conclusion

Our study conclusively demonstrates a significant correlation between parental consanguinity, particularly among first cousins, and the risk of childhood-onset vitiligo, affirming the hypothesis that genetic factors play a pivotal role in the disease's development. The findings also underscore the prevalence of familial vitiligo in cases with adult onset, suggesting a genetic predisposition. These insights pave the way for future genetic studies and the exploration of

targeted interventions for early detection and management of vitiligo. The research fills a critical gap in understanding the etiological factors of vitiligo, offering a foundation for further investigation into genetic contributions and potential therapeutic strategies.

Data Sharing Statement

The data that support the findings of this research are available from the corresponding author upon reasonable request. Due to legal and ethical considerations, the data cannot be made publicly available. Requests for data access should be directed to Amr Molla at amolla@taibahu.edu.sa.

Ethical Considerations

This study was conducted in strict accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee Board of the College of Medicine at Taibah University, registered under reference number [TU-24-15] on 7/2/2024. All procedures involving human participants were performed with the highest ethical standards. Informed consent was meticulously obtained from all participants. For participants under the age of 18, consent was obtained from a parent or legal guardian, ensuring adherence to ethical guidelines for research involving minors. The confidentiality and privacy of all study participants were rigorously protected throughout the research process, reflecting our commitment to ethical research practices and the protection of participant rights.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wolff K, Goldsmith LA. *Fitzpatrick's Dermatology in General Medicine*. McGraw-Hill New York; 2008.
2. James WD, Elston D, Berger T. *Andrew's Diseases of the Skin E-Book: Clinical Dermatology*. Elsevier Health Sciences; 2011.
3. Bolognia J. *Dermatology*. 2nd. Elsevier Health Sciences; 2008.
4. van Geel N, Speeckaert R, Taïeb A, et al. Worldwide expert recommendations for the diagnosis and management of vitiligo: position statement from the international vitiligo task force Part 1: towards a new management algorithm. *J Eur Acad Dermatol Venereol*. 2023;37(11):2173–2184. doi:10.1111/jdv.19451
5. Modeer MA. Journal Homepage. Available from: www.journalijar.com. Accessed June 19, 2024.
6. Ezzedine K, Eleftheriadou V, Whitton M, et al. Vitiligo. *Lancet*. 2015;386(9988):74–84. doi:10.1016/S0140-6736(14)60763-7
7. Sarma N, Chakraborty S, Poojary S, et al. A Nationwide, Multicentric Case-Control Study on Vitiligo (MEDEC-V) to elicit the magnitude and correlates. *Indian J Dermatol*. 2020;65(6):473–482. doi:10.4103/ijd.IJD_822_19
8. Alzolibani A. Genetic epidemiology and heritability of vitiligo in the Qassim region of Saudi Arabia. *Acta Dermatovenerol Alp Pannonica Adriat*. 2009;18(3):119–125.
9. Middle I, Al-Salloum AA, Al-Herbish AS, Qurachi MM, Al-Omar AA. Regional variations in the prevalence of consanguinity in Saudi Arabia. *Saudi Med J*. 2007;28(12):1881–1884.
10. Handa S, Dogra S. Epidemiology of childhood vitiligo: a study of 625 patients from north India. *Pediatr Dermatol*. 2003;20(3):207–210. doi:10.1046/j.1525-1470.2003.20304.x
11. Hu Z, Liu J-B, Ma -S-S, et al. Profile of childhood vitiligo in China: an analysis of 541 patients. *Pediatr Dermatol*. 2006;23(2):114–116. doi:10.1111/j.1525-1470.2006.00192.x

12. Halder RM, Grimes PE, Cowan CA, et al. Childhood vitiligo. *J Am Acad Dermatol*. 1987;16(Pt 1):948–954. doi:10.1016/S0190-9622(87)70119-4
13. Nicolaidou E, Antoniou C, Miniati A, et al. Childhood- and later-onset vitiligo have diverse epidemiologic and clinical characteristics. *J Am Acad Dermatol*. 2012;66(6):954–958. doi:10.1016/j.jaad.2011.07.010
14. Ezzedine K, Lim HW, Suzuki T, et al. Revised classification/nomenclature of vitiligo and related issues: the vitiligo global issues consensus conference. *Pigm Cell Mel Res*. 2012;25(3):E1–E13. doi:10.1111/j.1755-148X.2012.00997.x
15. Said-Fernandez SL, Sanchez-Domínguez C, Salinas-Santander M, et al. Novel immunological and genetic factors associated with vitiligo: a review. *Exp Ther Med*. 2021;21(4):312. doi:10.3892/etm.2021.9743
16. Alenizi DA. Consanguinity pattern and heritability of Vitiligo in Arar, Saudi Arabia. *J Family Commu Med*. 2014;21(1):13–16. doi:10.4103/2230-8229.128767
17. Pajvani U, Ahmad N, Wiley A, et al. The relationship between family medical history and childhood vitiligo. *J Am Acad Dermatol*. 2006;55(2):238–244. doi:10.1016/j.jaad.2006.02.027