ARTICLE

Cite This:Int J Cos Derma. 2021, vol 1-1, 1-6

Sciforce

International Journal of Cosmetics and Dermatology

Journal homepage: www.sciforce.org

Vitiligo – Study in View of Familial Occurence

Salim Musa Mulla

Department of Genetics, Immunology and Biochemistry, Maharashtra University of Health Sciences, Nasik, India

ARTICLE INFO

Article history:
Received 20210422
Received in revised form 20210512
Accepted 20210522
Available online 20210610

Keywords:
Vitiligo
Familial occurrence
Genetics
Cause

ABSTRACT

Vitiligo is a chronic skin disease that causes loss of pigment in the skin. It is caused by a combination of auto-immune, genetic, and environmental factors.

This clinical study was carried out to find out the familial tendency in patients of vitiligo. Literary review & clinical study in 60 patients of vitiligo done. The study included the detailed family history with pedigree analysis in patients under study. The conclusion drawn from the study is that the familial occurrence of vitiligo in the studied population is 26.66 % .Younger age group up to 20 Yrs. is predominantly affected.

Genetic variations play a significant role in the aetiology of vitiligo.

*Corresponding author. Tel.: +91 7588627408; e-mail: drsmmulla@hotmail.com

Introduction

Historical background: (Rational of the study)-

Vitiligo or **leukoderma** is a chronic skin disease that causes loss of pigment, resulting in irregular pale patches of skin. It occurs when the melanocytes, the cells responsible for skin pigmentation, die or are unable to function. The precise cause of vitiligo is complex and not fully understood. There is some evidence suggesting it is caused by a combination of auto-immune, genetic, and environmental factors. Vitiligo may also be caused by stress that affects the immune system, leading the body to react and start eliminating skin pigment. It creats a very bad social stigma for the victim, although no other major systemic abnormality is generally present. I have seen number of patients visiting my clinic for the treatment of this problem. So I decided to work on this subject to carry out this clinical study.

Epidemiology:

The population incidence worldwide is considered to be between 1% and 2%., or as many as 65 million people, have vitiligo.[1]

Clinical Presentation:

In most cases, vitiligo develops early in life, between the ages of 10 and 30 years. Ninety-five percent of those affected will develop the disorder before age of 40 years. Both men and women are equally likely to affected by vitiligo. Vitiligo may run in families; those with a family history of vitiligo or premature graying of the hair are at increased risk for the development of vitiligo. Other risk factors that increase one's chances of developing vitiligo include having autoimmune diseases, such as autoimmune thyroid disease (Hashimoto's thyroiditis). However, most people with vitiligo have no other autoimmune disease. Vitiligo is associated with autoimmune and inflammatory diseases, commonly thyroid over-expression and under-expression.

Vitiligo may also be hereditary; that is, it can run in families. Children whose parents have the disorder are more likely to develop vitiligo (not the rule). In fact, number of people with vitiligo has a family member with the disease. However, only 5 to 7 percent of children will get vitiligo even if a parent has it, and most people with vitiligo do not have a family history of the disorder.[9]

Clinical classifications of vitiligo[10]-

The most widely used classification of vitiligo is localized, generalized, and universal

Types and is based on the distribution, as follows:

- Localized
  - Focal: This type is characterized by one or more macules in one area, most commonly in the distribution of the trigeminal nerve.

- Segmental: This type manifests as one or more macules in a dermatomal or quasidermatomal pattern. It occurs most commonly in children. More than half the patients with segmental vitiligo have patches of white hair or poliosis. This type of vitiligo is not associated with thyroid or other autoimmune disorders.
- Mucosal: Mucous membranes alone are affected.
- Generalized
- Acrofacial: Depigmentation occurs on the distal fingers and periorificial areas
- Vulgaris: This is characterized by scattered patches that are widely distributed.

Signs: Half of people with vitiligo develop patches of de-pigmented skin appearing on extremities before their 20s. The patches may grow, shrink, or remain constant in size. Patches often occur symmetrically across both sides on the body. Occasionally small areas may repigment as they are recolonised by melanocytes. The location of vitiligo affected skin changes over time, with some patches re-pigmenting and others becoming affected. Vitiligo on the scalp may affect the color of the hair (though not always), leaving white patches or streaks. It will similarly affect facial and body hair. [14]

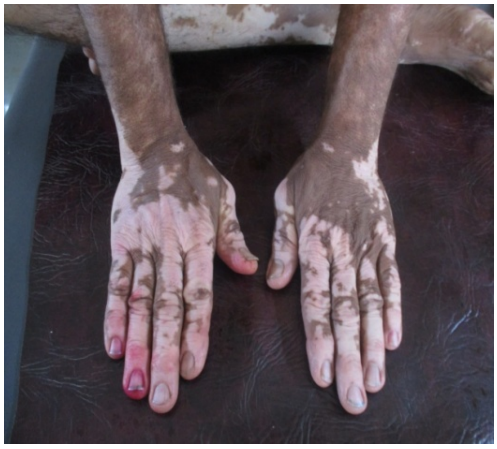
Symptoms: Some symptoms are:

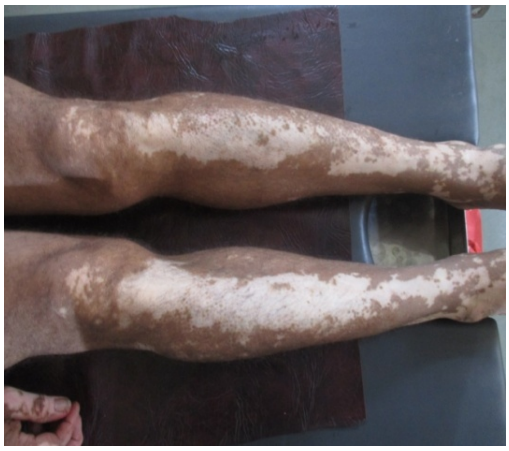
- white patches on the skin, including the face, limbs, trunk, and groin
- purple or golden brown patches on mucous membranes and around the eyes, nostrils, and mouth
- premature graying of hair
- sun sensitivity

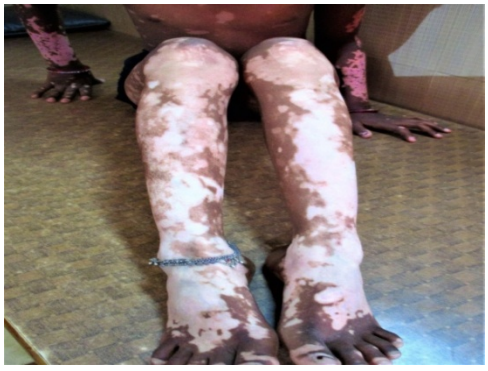
Psychological effects

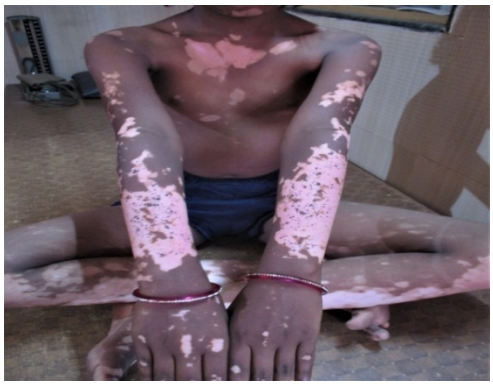
Vitiligo can have a significant effect on the psychological well being of the patient.[8] This is especially true for darker skinned patients as the contrast between pigmented and depigmented skin can be quite drastic. In some cultures there is a stigma attached to having vitiligo. Those affected with the condition are sometimes thought to be evil or diseased and are sometimes shunned by others in the community. People with vitiligo may feel depressed because of this stigma or because their appearance has changed dramatically. Other people with vitiligo experience no negative psychological effects at all.[14]

Clinical Photographs:









Disease mechanism: (pathophysiology)

According to Diseases Database: "A disorder consisting of areas of macular depigmentation, commonly on extensor aspects of extremities, on the face or neck, and in skin folds. Age of onset is often in young adulthood and the condition tends to progress gradually with lesions enlarging and extending until a quiescent state is reached."

In generalized vitiligo melanocytes are not found in the affected skin. Melanocytes contain the pigment melanin which serves a protective action against the harmful effects of sunlight.

Phenylalanine (adrenals) → tyrosine→ dihydroxyphenylalanine(DOPA)→ melanin

Melanin formation in skin is augmented by the hormone melanocyte stimulating hormone(MSH) or intermedion secreted by the pars intermedia of the pituitary gland (post.pituitary). ACTH by ant.pituitary has melanocyte stimulating activity similar to MSH although to a much lesser degree. 25% cases are autoimmune. [11]

Patients with vitiligo have an increased incidence of several autoimmune disorders including hypothyroidism, Graves'disease, pernicious anaemia, Addison's disease, alopecia areata, chronic mucocutaneous candidiasis etc. Diabetis mellitus is also associated in some subjects.

Localized hypopigmentation is also found in chemical leukoderma, Piebaldism (autosomal dominant disorder), post-inflammatory, tinea versicolor etc.[11-12]

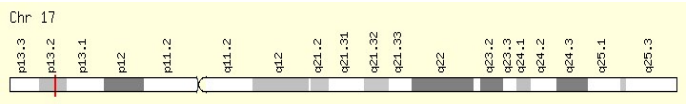
Vitiligo is a multifactorial polygenic disorder with a complex pathogenesis. It is related to both genetic and nongenetic factors. Although several theories have been proposed about the pathogenesis of vitiligo, the precise cause remains unknown. Generally agreed upon principles are an absence of functional melanocytes in vitiligo skin and a loss of histochemically recognized melanocytes, owing to their destruction. However, the destruction is most likely a slow process resulting in a progressive decrease of melanocytes. Theories regarding destruction of melanocytes include autoimmune mechanisms, cytotoxic mechanisms, an intrinsic defect of melanocytes, oxidant-antioxidant mechanisms, and neural mechanisms. [10]

Vitiligo Genetics: Lerner (1959) suggested autosomal dominant inheritance.[15] Genetic variations in NLRP1 are associated with susceptibility to vitiligo [MIM:193200]. Jin in the New England Journal of Medicine reported a study comparing 656 people with and without vitiligo in 114 families, which found several mutations (single-nucleotide polymorphisms) in the NALP1 gene.[2-3] The NALP1 gene, which is on chromosome 17 located at 17p13, is on a cascade that regulates inflammation and cell death, including myeloid and lymphoid cells, which are white cells that are part of the immune response. NALP1 is expressed at high levels in T cells and Langerhan's cells, white cells that are involved in skin autoimmunity.

NLRP1 Gene in genomic location: bands according to Ensembl, locations according to GeneLoc.

The main text must be clearly paragraphed.[5] State the objectives of the work and provide an adequate background, comprehensive insight on the purpose of the study and its significance, avoiding a detailed literature survey or a summary of the results.[6]

Among the inflammatory products of NALP1 are caspase 1 and caspase 5, which activate the inflammatory cytokine interleukin-1β. Interleukin-1β is expressed at high levels in patients with vitiligo. There are compounds which inhibit caspase and interleukin-1β, and so might be useful drugs for



vitiligo and associated autoimmune diseases.

Of the 656 people, 219 had vitiligo only, 70 had vitiligo with autoimmune thyroid disease, and 60 had vitiligo and other autoimmune diseases. Addison's disease (typically an autoimmune destruction of the adrenal glands) may cause vitiligo.

In one of the mutations, the amino acid leucine in the NALP1 protein was replaced by histidine (Leu155->His). The original protein and sequence is highly conserved in evolution, and found in humans, chimpanzes, rhesus monkey, which means that it's an important protein and an alteration is likely to be harmful.[3]

The following is the normal DNA and protein sequence in the NALP1 gene:

TCA	**AC**	**CTC**	**TAC**	**AA**
Ser	**is**	**Leu**	**Tyr**	**Gln**
S		**L**	**Y**	**Q**

TCA	**CTC**	**CTC**	**TAC**	**CAA**
Ser	**Leu**	**Leu**	**Tyr**	**Gln**
S	**L**	**L**	**Y**	**Q**

In some cases of vitiligo the first leucine is altered to histidine, by a Leu155→His mutation:

(Leucine is nonpolar and hydrophobic; histidine is positively charged and hydrophilic, so it is unlikely both serve the same function.)[4,5]

The normal sequence of the DNA code for NALP1 of TCACTCCTCTACCAA is replaced in some of these vitiligo families by the sequence TCACACCTCTACCAA,[6] which respectively code for the amino acid sequence of the normal NALP1 protein SLLYQ being replaced by SHLYQ.[7]

Aims and objectives:

1. To study the familial occurrence of vitiligo.
2. Study of genetics of vitiligo.

Methodology:

The following methodology is adopted to conduct the study.

Literary review: For collecting all the available information about Vitiligo, literary review of available texts & Journals done thoroughly. Available information from internet also taken into consideration.

Clinical study:

A. **Study design**: This is a randomised single blind clinical study in vitiligo patients. The study was carried out on 60 patients. The study included the detailed family history with pedigree analysis in patients under study.

B. **Selection of patients**: The study was carried out on outdoor patients.

Inclusion criteria:

a. Patients complaining of white depigmentation as a main complaint.

b. Patients from all age groups.

c. Selection was irrespective of sex, duration of the disease.

d. Patients with or without family history of hypopigmentation.

Exclusion criteria:

a. Patients not ready for the study.

3. **Statistical Methods**- proper statistical methods applied to find out the results.

Place of work:

1. Dept of Genetics, Immunology and Biochemistry

Maharashtra University of Health Sciences, Pune

2. Mulla Ayurvigyan Hospital, Islampur. Dist.- Sangli.

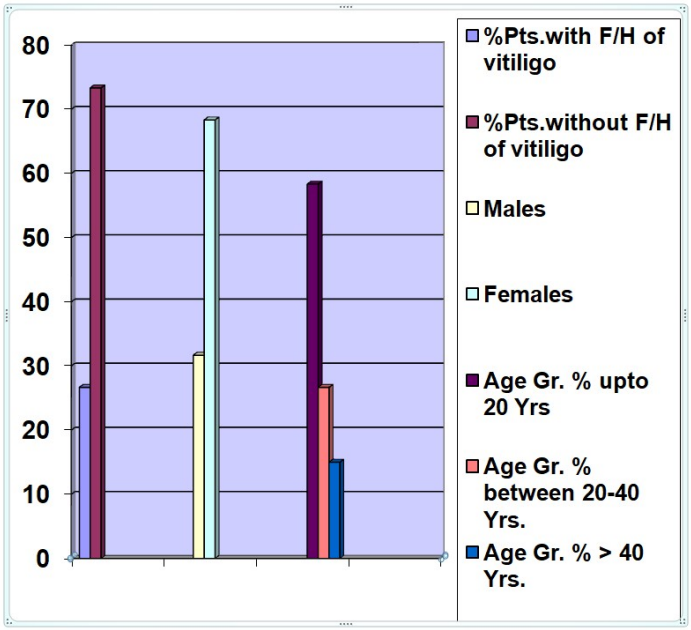
Informed conscent:

Informed conscent taken about nature and purpose of study from each patient.

Observations: observations were made in the following ways,

Patient group	No.of Patients
Total	60
Patients with hereditary history	16
Patients with no hereditary history	44
Males	19
females	41
Age Group upto 20 Yrs.	35
Age Group 20- 40 Yrs	16
Age Group ≥ 40 Yrs	9

Out of total 60 patients observed 16 (26.66 %) patients have family history of vitiligo either paternal or maternal. While 44 patients don't have family history for vitiligo. 41 patients are female & 19 are male. The age group affected more i.e 58.33 % (35 patients) is upto 20 Yrs. 26.66 % (16 Patients) are between the age group 20- 40. Just 15 % (9) patients are ≥ 40 Yrs.



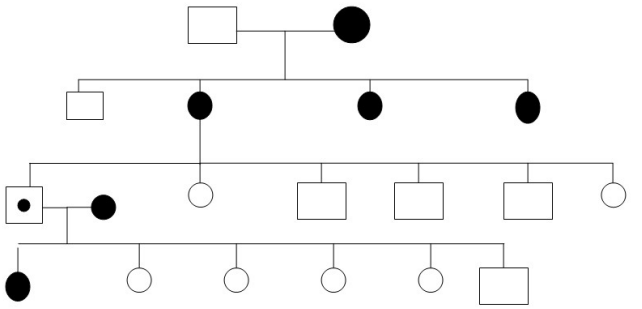
Statistical calculations -

Data is , randomised selected, qualitative. So Chi-square (χ^2) test is applied as a test of "goodness of fit ".[13]to determine if actual frequency found in this study is similar to the expected or theoretical number. The theoretical(expected) number is taken as 30 % frequency of familial tendency in the patients with vitiligo.[9,10]

The calculated (χ^2) value is 0.31. At one degree of freedom the (χ^2) table value is 3.841 at 5% level of significance. The calculated (χ^2) value 0.31 is much lower than the table value. Hence insignificant at probability 0.05. Hence the observed distribution fit to the hypothetical or expected distribution.

Pedigree of Patients observed (for example) –

1. Name of the patient - XXY age – 20 Yrs. sex- Female



Pedigree of four generations shown. Affected female has both paternal & maternal side history of vitiligo. Father may be carrier.

Results

- The above study shows that in the population studied for familial occurrence of vitiligo 26.66 % subjects have past family history of vitiligo.
- Statistically this observed frequency fits to the expected distribution.
- Younger age Group up to 20 Yrs. is predominantly affected.

Conclusion

The following conclusion can be drawn from the present study:

- The familial occurence of vitiligo in the studied population is 26.66 %.
- So genes & mutations play a significant role in the aetiology of vitiligo.
- Younger age Group upto 20 Yrs. is predominantly affected. Also the older patients might have the onset of vitiligo at the younger age.

Suggestions:

- The results from the present study can be verified by taking larger sample size.
- Also further genetic research regarding aetiology & prevention may be of value.
- Research in the field of gene therapy can be of value.

Application of this research:

- By knowing the familial tendency we can predict about aetiology & prognosis of vitiligo in total also & in a particular case also.
- Spread of disease can be prevented by proper pre-marital genetic counseling & carrier detection.
- Gene therapy may be useful in familial cases.

References

1. Ortonne J. Vitiligo and other disorders of Hypopigmentation. In: Bolognia J, Jorizzo J, Rapini R, eds. Dermatology. Vol 1. 2nd. Spain: Elsevier; 2008, 65.
2. Gregersen PK. "Modern genetics, ancient defenses, and potential therapies". *N. Engl. J. Med*. **2007**, 356(12), 1263–1266. doi:10.1056/NEJMe078017.
3. Jin Y.; Mailloux CM.; Gowan K.; Riccardi SL.; LaBerge G.; Bennett DC.; Fain PR.; Spritz RA. "NALP1 in vitiligo-associated multiple autoimmune disease". *N. Engl. J. Med*. **2007**, 356(12), 1216–1225. doi:10.1056/NEJMoa061592.
4. List of Amino Acids and Their Abbreviations.
5. The Genetic Code (DNA).
6. Ensembl Transcript Report Ensembl Transcript ID: NST00000262467.
7. Ensembl Protein Report Ensembl Peptide: ID ENSP00000262467.
8. Mechri A.; Amri M.; Douarika AA.; Ali Hichem BH.; Zouari B, Zili J. "[Psychiatric morbidity and quality of life in Vitiligo: a case controlled study]" (in French). La Tunisie médicale.**2006**, 84(10), 632–635.
9. MedicineNet.com -Vitiligo Symptoms, Causes, Pigmentation Loss Treatment and Diagnosis on MedicineNet.com October 6, 200810.
10. Article By (Medline.Updated: Aug 8, 2008)-Vlada Groysman, MD, Staff Physician, Department of Dermatology, University of Alabama School of Medicine Naveed Sami, MD, FAAD, Assistant Professor Department of Dermatology, University of Alabama School of Medicine.

11. Harrison's Principles of Internal medicine McGraw-Hill 14th edition.
12. Golwalla-Medicine For Students Dr. Golwalla Dr. A. F. Golwalla 17th edition International.
13. Methods in Biostatistics. By B.K. Mahajan 6th edition.
14. Wikipedia, the free encyclopedia
15. Lerner, A. B. Vitiligo. J. Invest. Derm. **1959**, 32, 285-310.
16. UniProtKB/Swiss-Prot Q9C000 (NALP1_HUMAN) Last modified November 25, **2008**. Version 89.