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EPIDEMIOLOGY OF VITILIGO AND ASSOCIATED AUTOIMMUNE DISEASES AMONG PATIENTS ATTENDING DERMATOLOGY CLINICS IN AL-MADINA 2016 -2017

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ABSTRACT

Background: Vitiligo is a common skin disorder that affects 1% of the whole world population, little is known about vitiligo prevalence and it is subtypes in Al Madinah, Saudi Arabia. **Objective: T**o estimate the prevalence of vitiligo among patients attending dermatology clinics in Al-Madina, and to identify the distribution of autoimmune diseases among subtypes of vitiligo in patients, besides detecting the association between subtype of vitiligo and other variables. **Methodology:** it is a descriptive cross-sectional hospital based study among vitiligo patients who have an appointment in dermatology clinics at Al Madinah Al Monawarh, the study was conducted in the period from December 2016 to June 2017. **Results:** The overall prevalence of vitiligo was 11% from the total number of patient visiting the dermatology clinics. The most predominant subtype of vitiligo was valgaris type (49.6%). family history of vitiligo was significant in 31.2% of patient. Diabetes and thyroidal disease is the most associated autoimmune disease with vitiligo. **Recommendations:** Consanguinity in marriage may increase the incidence of vitiligo, therefore, genetic counseling and education should be applied to vitiligo patient. Physician should be aware of relatively high prevalence of thyroid and diabetes so, they should request proper screening test when clinically suspected.

KEYWORDS: Vitiligo, AL Madinah Al Monawara, Saudi Arabia, and autoimmune disease.

1-INTRODUCTION

Vitiligo is a common skin disorder that affects 1% of the whole world population.[1] It's characterized by defect of melanocytes which cause depigmentation of skin over different areas of the body including mucous membranes in mouth or eyes, hands, forearms, feet, face, trunk and even may affect the hair. These affected areas are macule and patched with characteristic white dyspigmented lesions ranging from mm to cm in size surrounded by well demarcated borders. Microscopic examination of these lesions shows lymphatic infiltration at margins and epidermal pigmentation loss plus melanocytes absence. Due to clinical variants of vitiligo, the disease course may vary from one patient to another regarding it site, size, shape, duration and areas involved.

Although many theories were conducted regarding the pathophysiology of vitiligo, destruction of skin melanocytes is the generally approved as a precise and the exact cause remains anonymous. caused by different mechanisms such as autoimmune process, where melanocytes become a target and destructed by immune system produced antibodies.[2] Intrinsic mechanism also has been detected to play role in cell destruction pathogenesis due to receptors defects and early apoptosis.[3] Injuries caused by free radicals and oxidants as for example sunburn or chemical burning can play role in triggering vitiligo.[4]

Vitiligo can be localized, generalized and universal. Localized type could be classified as focal macules over only one area of the body. If they're following a specific course of some nerves as the trigeminal nerve for example so, it is called segmental vitiligo. Distribution of these macules When only mucous membranes are affected, then it's called mucous.

Generally vitiligo maybe present with three pictures. First one called acrofacial which appear as losing skin pigment on the fingers and toes. Second one, scattered patches of depigmentation of skin called vulgaris. The last picture called mixed, which comes in combination with types mentioned previously. Finally, The universal type, which presents with complete depigmentation of skin. Family history and genetic relations of Vitiligo is characterized by incomplete penetrance, multiple susceptibility loci and genetic heterogeneity.[5]

2-Rational

It is an area of interest and it is a common disease. despite its popularity, no study was done locally about it. So, we will estimate the prevalence of vitiligo and associated autoimmune

disease among patients attending Al-Madina Al-Monawerah Dermatology Clinics in general, private and military hospitals.

The researcher noticed vitiligo is commonly seen at Al-Madina Al-Monawerah citizen and it is more clustered in certain families. Which usually affect the patient life style. leading to social isolation from the patient community.

3-RESEARCH OBJECTIVES

3-1 General objectives

To estimate the prevalence of vitiligo among patients attending dermatology clinics in Al-Madina and to identify the role of factors associated with vitiligo.

3-2 Specific objectives

1. To explore the sociodemographic status of the participants.
2. Todetermine the relationship between vitiligo and the demographic data (age, sex, and duration) in Al-Madina.
3. To detect socioeconomic status implicated in vitiligo development.
4. Toidentifythe relationship between family history of vitiligo and its subgroups.
5. Toidentify the distribution of autoimmune diseases among subtypes of vitiligo in patients.

4-Literature review

A study was done at Makkah region, Saudi Arabia on 135 vitiligo patients medical records seen at Heraa General Hospital, Makkah, Saudi Arabia between Jan 2010 and June 2013 the result showed that it is more common in female, with 25% positive family history, and the thyroidal disorder was the most prevalent autoimmune disease.[6]

A clinic-epidemiological study was done in King Khalid Hospital, Najran region, Saudi Arabia over a period of 6 month between January 2012 till July 2012, on 101 vitiligo cases and the study revealed a male predominance (57.4%), 28.7% was belong to the age group 31-40 years with a localized type of vitiligo being the most common type in Najran region (49%), 83% showed no associated autoimmune disease, 7% association with diabetes mellitus.[7]

A study include 69 Saudi vitiligo patient, selected from the experience specialist dermatology center in Arar, from April 2011 to 2012, showed high rate of vitiligo in Consanguinity marriage. So, genetic counseling should be conducted to lower the prevalence of vitiligo.[8]

Study was done at Qassim University Referral Center, Qassim region, Saudi Arabia on 111 vitiligo patient during 2008, it found that genetic factors contribute to vitiligo popularity in some Saudi families discouraging high consanguinity rate.[9]

A retrospective study was carried on Saudi nationals with a confirmed diagnosis of vitiligo presenting to the National Center for Vitiligo and Psoriasis, Riyadh, Saudi Arabia, from August 2002 to August 2006 on 4134 patients, and conclusion was that majority of the cases with a female predominance, The mean age of onset of vitiligo was 17.4 years, 90.5% has no associated autoimmune disease, The family history was positive in 42.8%. vitiligo vulgaris was the commonest type (42.3%).[10]

Another study was conducted to assess the quality of life (QOL) in Saudi vitiligo patients and their family at National Center for Vitiligo and Psoriasis, Saudi Arabia at 2011. The overall score of QOL in vitiligo was high, women affected more than men.[11]

Study conducted on 1873 patients with vitiligo seen between January 2002 and October 2012 at the Henry Ford Health System in Detroit, and showed high number of associated autoimmune disease., nearly 20% had at least 1 comorbid autoimmune disease. Compared with the general US population, the result came with a higher prevalence of thyroid disease (12.9%), alopecia areata (3.8%), inflammatory bowel disease (0.9%), pernicious anemia (0.5%), systemic lupus erythematosus (0.3%), Guillain-Barre syndrome (0.3%), discoid lupus (0.2%), linear morphea (0.2%), myasthenia gravis (0.2%), and Sjögren syndrome (0.2%).[12]

5-METHODOLOGY

5-1 Study design

Descriptive cross-sectional hospital based study among vitiligo patients who have an appointment in dermatology clinic.

5-2 Study area

Madinah a city in the Hejaz, and the capital of the AL-Madina Region of Saudi Arabia. The city contains al-Masjid an-Nabawi [" the Prophet's Mosque"], which is the burial place of the Islamic prophet Muhammad, and is the second-holiest city in Islam after Mecca.[13]

AL-Madina Al Munawarah is located at Eastern Part of Al Hijaz Region in the Kingdom of Saudi Arabia.[13] Madina is located in the north-western part of the Kingdom, to the east of

the Red Sea, which lies only 250 km (155 miles) away from it.[13] As of 2013, the city of Medina has a population of about 1.180.770 million.[14]

5-3 Study Period

This study will be conducted for 2 years 2016 / 2017.

5-4 Study Population

There are 26 dermatology clinic in Al-Medina city, in the private hospital there are 18 dermatology clinics, 5 in general hospital and 3 in military hospital.[15] The study will carried among all vitiligo patients of different ages for follow-up.

5-4-1-Inclusion criteria

1- follow up patients only with vitiligo.

2- patients who speak Arabic or English only.

3- All nationality.

5-4-2 Exclusion criteria

1- new patients and walk in patients

2- patients doesn't speak Arabic or English.

5-5 Sampling method

5-5-1 Sample Size

- Population size is 2922.
- Expected frequency is 50%.
- Confidence level is 95%.
- Sample size is 340.
- The calculated sample size by using Epi info.

5-5-2 Technique

A multiple stages sampling technique will be implant in this study.

– Stage 1: stratifying the city of Al-Medina into four sectors [north, south, east and west].

– Stage 2: simple random sampling to select two hospitals from each sector.

– Stage 3: stratified sampling to select one dermatological clinic from each hospital at selected hospital.

- Stage 4: systemic random sampling to include the sample size from the attending patient who have appointment to each dermatological clinic.

The researcher will enroll every third vitiligo patient that comes to dermatology clinic, the number of subjected enrolled in the study will be proportional to the total number of patients attending each dermatology clinic in the last month for follow up.

6-Dada management

6-1 Data collection method

The researcher will distribute the questionnaire to every vitiligo patient who have an appointment.

6-2 Data collection tools

The questionnaire has been taken from Dr. A. Alzolibani, his research was published at 2009 entitled "genetic epidemiology and heritability of vitiligo in the Qassim region of Saudi Arabia".[16] Where we kept the English version to be distributed to the English speakers, and translated to Arabic to be distributed to Arabic speakers. The translation in to Arabic was done by an English native speaker, then the translated version undergoes a second stage review and approved by 3 dermatology consultants.

The questionnaire consists of seven demographic questions (age, gender, nationality, job, educational level, social standard, and social status), 2 questions related to duration & type of the disease, 1 question related to the association of disease e.g. (Thyroid disease, DM, Lupus erythematosus, Pernicious anemia, Rheumatoid arthritis, Ulcerative colitis, Celiac disease, Psoriasis, Down syndrome, Immunodeficiency). 1 question related to treatment (systemic or topical treatment), 1 question related to response to treatment, 3questions related to family history (Family of Vitiligo, Family of autoimmune disease, Family of atopy) and 1 question related to Parental Consanguinity.

6-3 Data analysis

Data will be entered to a personal computer by the researcher and will be analyzed by SPSS version 22 (THE STATISTICAL PACKAGE OF THE SOCIAL SCIENCES). Data will be presented using tables and figures, mean and standard deviation will be used for summarizing quantitative data and percentage for the qualitative data, again t-test and qui square test will be used for the quantitative and qualitative data consecutive.

P value of 0.05 will be used as cut off point for the significance of the results.

7-Pilot Study

The questionnaire well be administrated by researcher to 10 cases in different dermatology clinic to test for applicability and feasibility of the questionnaire, time taken to finish and to test for process of conducting the study.

The data collected from those subjects will not be included in the main study.

8- Study variables

The questionnaire contains the following groups of variables:

1. Demographic information.
2. Types of vitiligo for patients.
3. Autoimmune disease related to vitiligo.
4. Family history of vitiligo and its distribution.

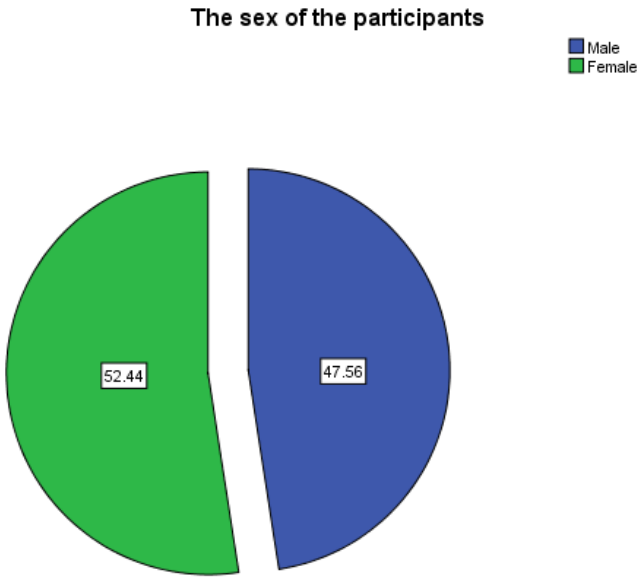
9-Limitation of the study

- Time.
- Response from the patient.

10-Ethical consideration

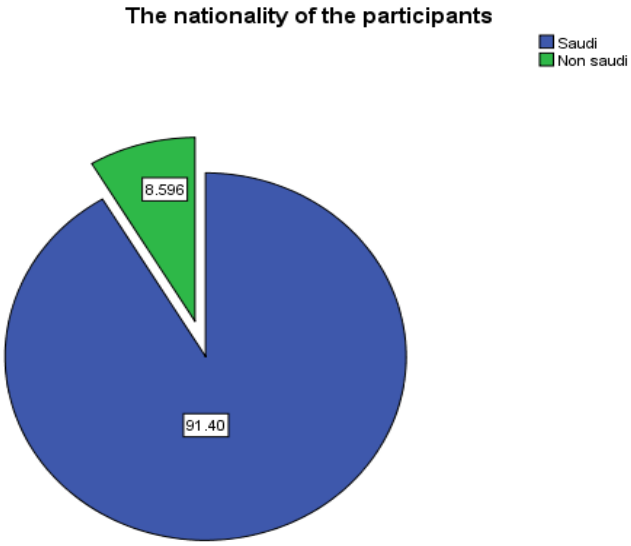
- Ethical approval from the research ethical committee will be taken before starting the study.
- Verbal Consent will be obtained from every subject who will participate in the study.
- All data from the study will be confidential.

11-RESULTS



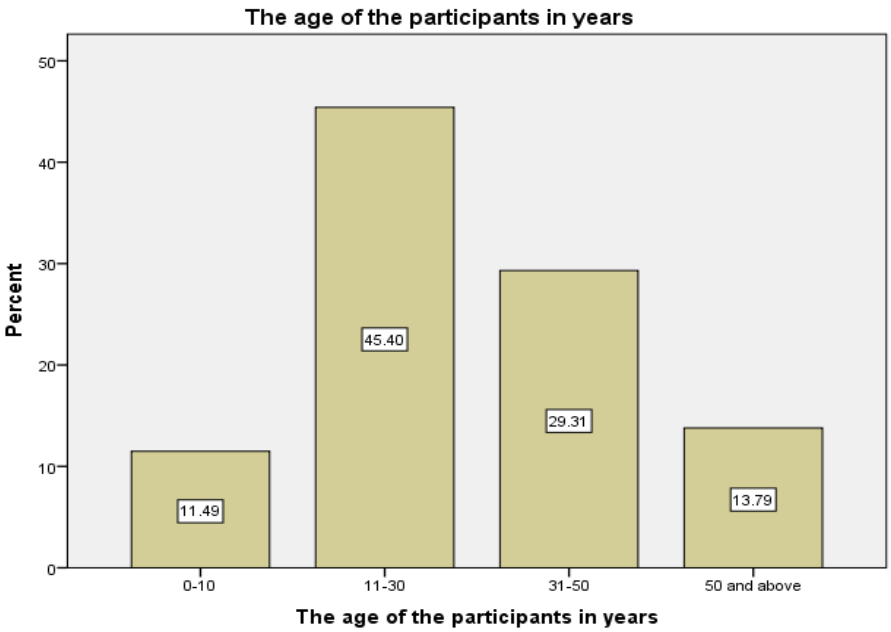
Almost the sex is equally distributed.

Figure (1) shows the sex of the participants (n=349).



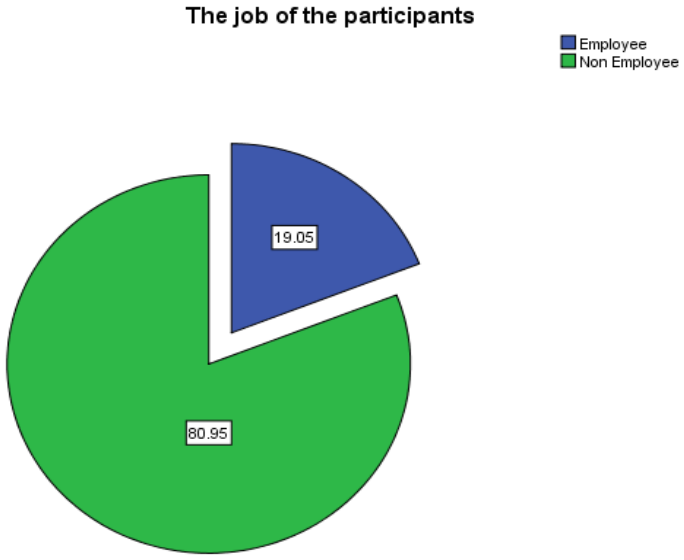
The majority are Saudi.

Figure (2) shows the nationality of the participants (n=349)



Near fifty percent are in the age group of 11-30 years.

Figure (3) shows the age grouping of the participants (n=349).



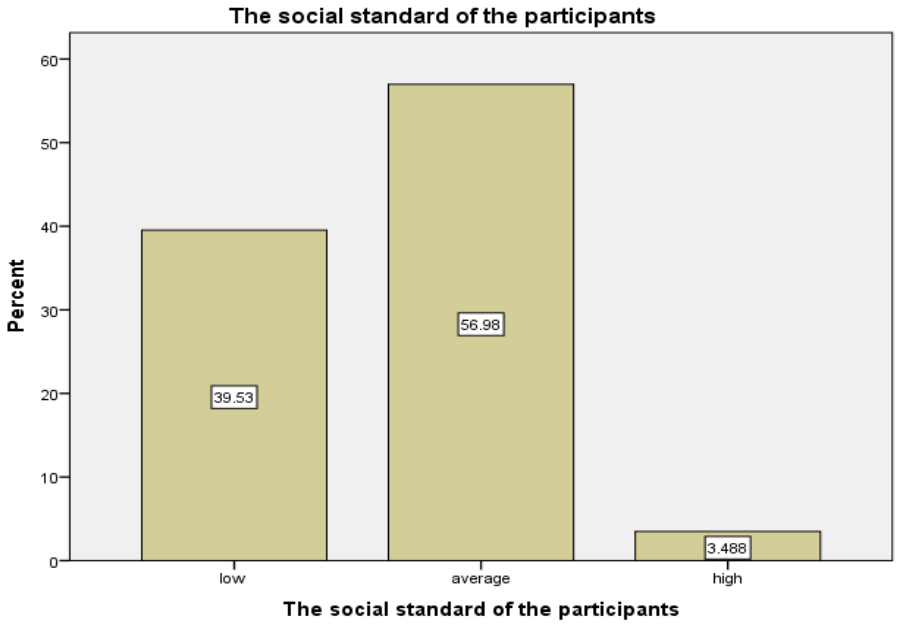
Eighty percent of the participants are non-employed

Figure (4) shows the job of the participants (n=349).

Table (1) shows the level of education of the participants come from (n=349)

The level of education of the participants					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	less than secondary	150	43.0	43.0	43.0
	secondary	87	24.9	24.9	67.9
	university	112	32.1	32.1	100.0
	Total	349	100.0	100.0	

Almost fifty percent are less than secondary



More than fifty percent are of average standard.

Figure (5) shows the social standard of the participants (n=349).

Table (2) shows the marital status of the participants come from (n=349).

The marital status of the participants					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Single	179	51.3	51.9	51.9
	Married	154	44.1	44.6	96.5
	Divorced	12	3.4	3.5	100.0
	Total	345	98.9	100.0	
Missing	System	4	1.1		
Total		349	100.0		

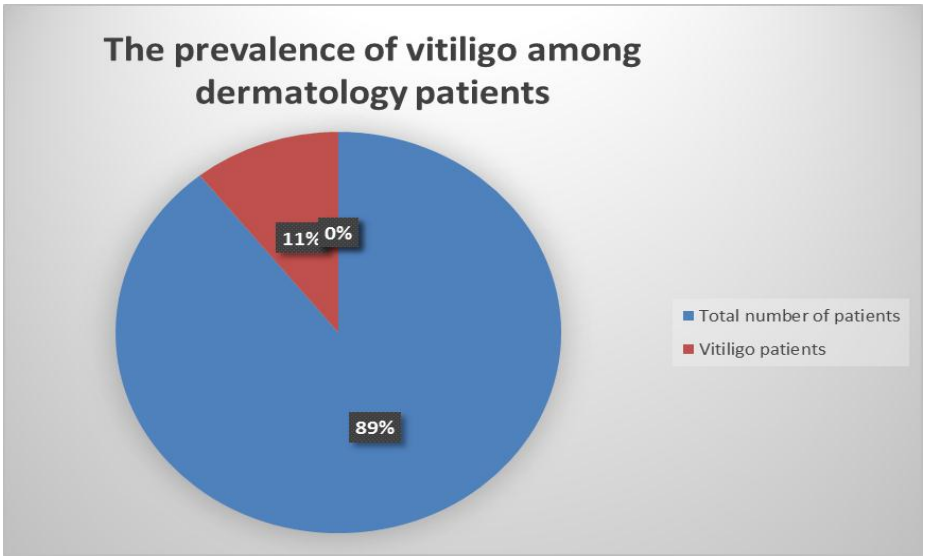


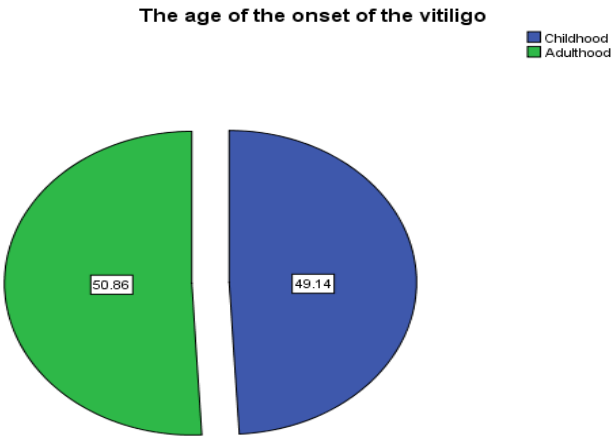
Figure (6) shows the overall prevalence of Vitiligo.

Total number of patients	2922
Vitiligo patients	349

Table (3) shows the types of vitiligo.

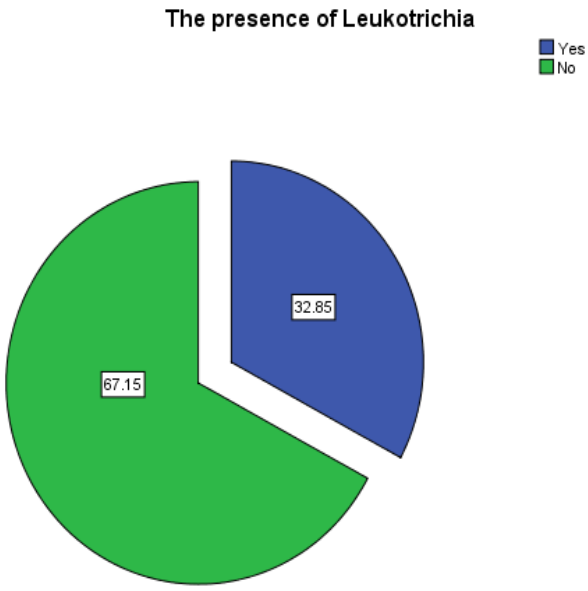
The types of vitiligo					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Focal	12	3.4	3.4	3.4
	Vulgaris	173	49.6	49.6	53.0
	Universal	75	21.5	21.5	74.5
	Acrofacial	84	24.1	24.1	98.6
	Segmental	5	1.4	1.4	100.0
	Total	349	100.0	100.0	

Fifty percent are of vulgaris type



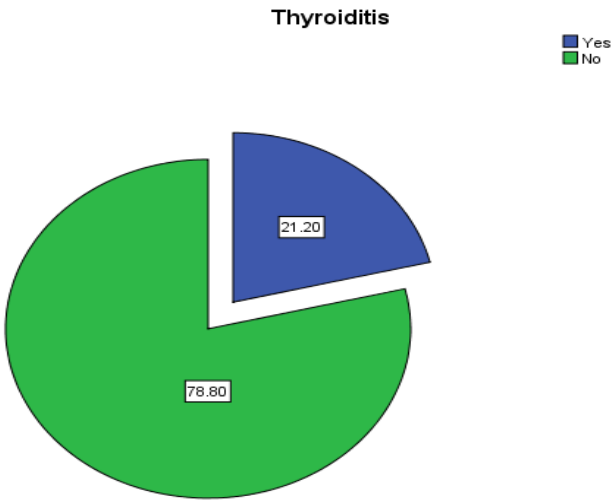
Nearly the same age of onset.

Figure (7) shows the age onset of Vitiligo.



Leukotrichia is present in the third of the participants.

Figure (8) presence of Leukotrichia.



Almost quarter of the participants have thyroidal problem.

Figure (9) shows the presence of thyroiditis

Table (4) shows the presence or absence of diabetes mellitus

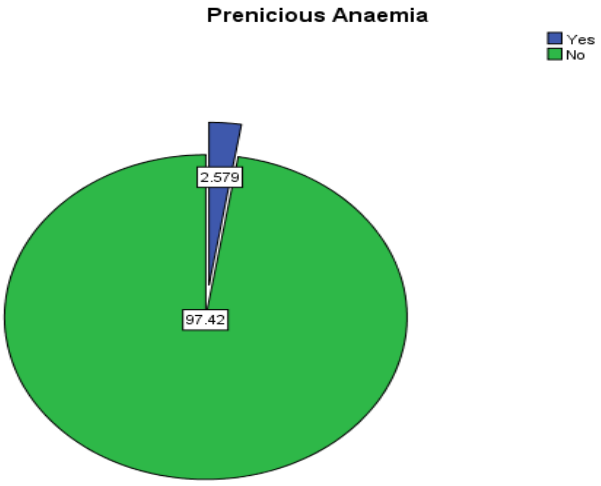
diabetes Mellitus					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Yes	46	13.2	13.2	13.2
	No	303	86.8	86.8	100.0
	Total	349	100.0	100.0	

13% have diabetes mellitus

Table (5): presence or absence of lupus erythematosus.

Lupus Erythematous					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	9	2.6	2.6	2.6
	No	340	97.4	97.4	100.0
	Total	349	100.0	100.0	

Almost all the patients have no Lupus erythematosus



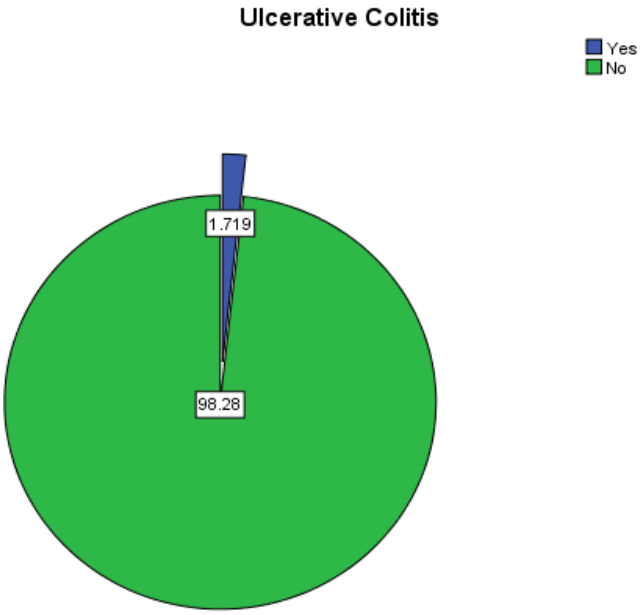
Minority of patients have pernicious anemia.

Figure (9) shows the association of vitiligo with pernicious anemia.

Table (6) shows the association with rheumatoid arthritis.

Rheumatoid Arthritis					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Yes	10	2.9	2.9	2.9
	No	339	97.1	97.1	100.0
	Total	349	100.0	100.0	

Minority of the patients have Rheumatoid arthritis



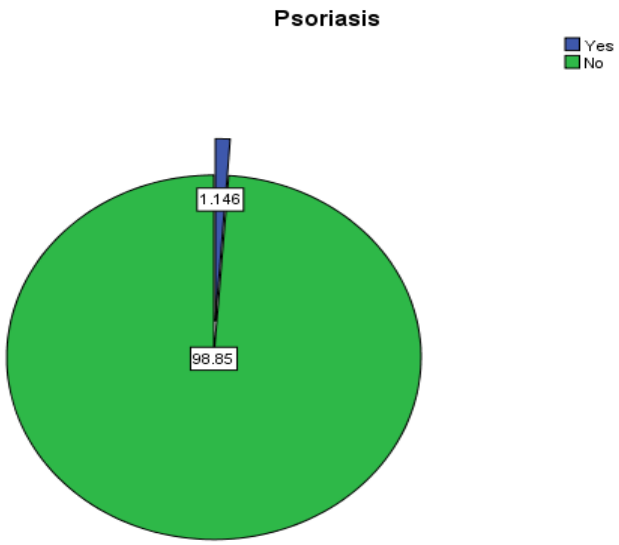
Minority have ulcerative colitis

Figure (10) shows the association of vitiligo and ulcerative colitis.

Table (7) shows the association between vitiligo and celiac disease.

Celiac Disease					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	No	349	100.0	100.0	100.0

No single patient has celiac disease.



Just % of vitiligo patient has psoriasis.

Figure (11) shows the associationbetween vitiligo and psoriasis.

Table (8) shows the association between vitiligo and Down syndrome.

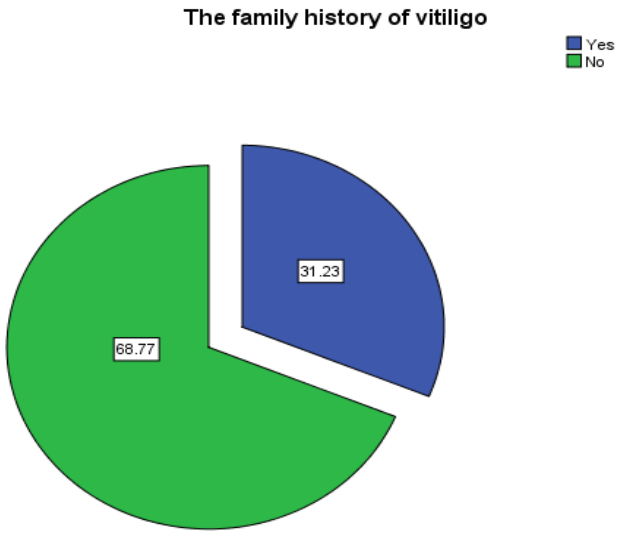
Down Syndrome					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Yes	1	.3	.3	.3
	No	348	99.7	99.7	100.0
	Total	349	100.0	100.0	

1 person of vitiligo hasDown syndrome.

Table (9) shows the type of treatment of vitiligo patient.

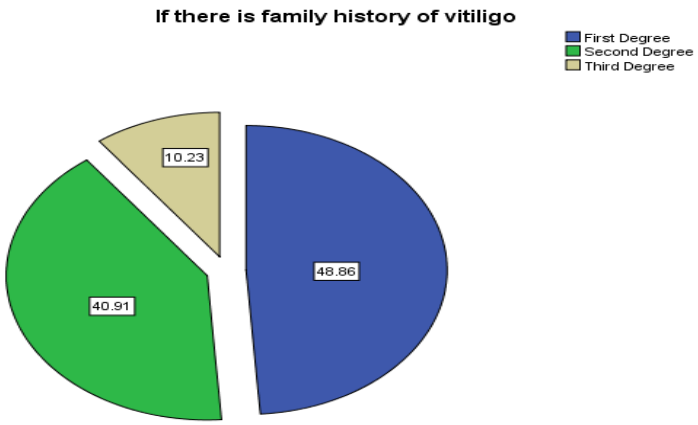
The current treatment					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Topical	225	64.5	64.5	64.5
	Systematic	6	1.7	1.7	66.2
	Other	118	33.8	33.8	100.0
	Total	349	100.0	100.0	

Majority of the patient on topical treatment



More than 30% showed positive family history of vitiligo.

Figure (12) shows the family history of vitiligo.



Almost half of the patient report 1st degree family history of vitiligo.

Figure (13) shows the degree of family history

Table (10) shows the family history of autoimmune disease

family history of autoimmune disease					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Yes	58	16.6	16.6	16.6
	No	291	83.4	83.4	100.0
	Total	349	100.0	100.0	

16% showed family history of autoimmune disease.

Table (11) shows the parental consanguinity.

The parentalConsanguinity.					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Yes	216	61.9	61.9	61.9
	No	133	38.1	38.1	100.0
	Total	349	100.0	100.0	

Almost 62% showed parental consanguinity.

Table (12) shows the relationship between sex of the participants and the types of vitiligo.

Gender/types of vitiligo	**Focal**	**Vulgaris**	**Universal**	**Acrofacial**	**Segmental**	**Total**
Male	6 3.6%	83 50.0%	28 16.9%	45 27.1%	4 2.4%	166 100.0%
Female	6 3.3%	90 49.2%	47 25.7%	39 21.3%	1 0.5%	183 100.0%
Total	12 3.4%	173 49.6%	75 21.5%	84 24.1%	5 1.4%	349 100%

P value = 0.16

There is no significant relationship between sex of the participants and the subtypes of vitiligo.

Table (13) shows the relationship between the age of the onset of the vitiligo and the types of vitiligo Cross tabulation.

age of the onset /types of vitiligo	Focal	Vulgaris	Universal	Acrofacial	Segmental	Total
Childhood	5 2.9%	98 57.3%	36 21.1%	30 17.5%	2 1.2%	171 100.0%
Adulthood	7 4.0%	75 42.4%	38 21.5%	54 30.5%	3 1.7%	177 100.0%
Total	12 3.4%	173 49.7%	74 21.3%	84 24.1%	5 1.4%	348 100%

P value = 0.03

There is a significant relationship between the age of the onset of the vitiligo and the types of vitiligo Cross tabulation.

Table (14): shows the relationship between The Paternal Consanguinity and the types of vitiligo Cross tabulation.

The Paternal Consanguinity /types of vitiligo	Focal	Vulgaris	Universal	Acrofacial	Segmental	Total
Yes	4 1.9%	105 48.6%	50 23.1%	54 25.0%	3 1.4%	216 100.0%
No	8 6.0%	68 51.1%	25 18.8%	30 22.6%	2 1.5%	133 100.0%
Total	12 3.4%	173 49.6%	75 21.5%	84 24.1%	5 1.4%	349 100%

P value = 0.2

There is no significant relationship between the paternal Consanguinity and the types of vitiligo.

Table 15: shows the relationship between family history of vitiligo and the types of vitiligo Cross tabulation.

family history of vitiligo /types of vitiligo	Focal	Vulgaris	Universal	Acrofacial	Segmental	Total
Yes	1 0.9%	45 41.3%	36 33.0%	25 22.9%	2 1.8%	109 100.0%
No	11 4.6%	128 53.3%	39 16.3%	59 24.6%	3 1.3%	240 100.0%
Total	12 3.4%	173 49.6%	75 21.5%	84 24.1%	5 1.4%	349 100%

P value = 0.004

There is a highly significant relationship between the family history of vitiligo and the types of vitiligo.

Table (16) shows the relationship between the presence of Leukotrichiaand the types of vitiligo Cross tabulation.

The presence of Leukotrichia /types of vitiligo	Focal	Vulgaris	Universal	Acrofacial	Segmental	Total
Yes	3 2.6%	51 44.7%	36 31.6%	22 19.3%	2 1.8%	114 100.0%
No	9 3.9%	120 51.5%	39 16.7%	62 26.6%	3 1.3%	233 100.0%
Total	12 3.5%	171 49.3%	75 21.6%	84 24.2%	5 1.4%	347 100%

P value = 0.03

There is a significant relationship between the presence of Leukotrichia and the types of vitiligo.

12-DISCUSSION

This is a descriptive cross-sectional hospital based study conducted among vitiligo patients who have an appointment in the dermatology clinic in Al-Madinah Al-Munawara –Saudi Arabia.

The overall prevalence of vitiligo in our study was found to be 11% from the total number of patient visiting dermatology clinics, which is higher than the 2.8% that found in a study conducted in Lagos Nigeria (Nigeria-2009). And this is could be due to high consanguinity between the parents in our study which was almost 62 % and may be due to the difference in race from Africa to Asia. Studies conducted in Saudi Arabia estimated the incidence rather than prevalence of vitiligo so were difficult to compare. Most of the nationality were Saudi (91.4%) and it is the same as the other studies conducted in Saudi Arabia. Female were more than male patients 52.4%, which is like a study reported in Makkah region (67.4%) and to a study conducted at national center of psoriasis and vitiligo center at al -Riyadh region (53.5%). And this female preference in our study could be explained by the cosmetic concern of the female patients. (Makkah-2014).

Most of the participant of our study were in the age group of 11-30 years (45.3%).And there was 50.8% of the vitiligo onset is in the adulthood,while paternal consanguinity was higher (61.9%) in our study than a study conducted in Qasim region (32.4%) (Qassim-2009).

Family history in our study is positive in 31.2%. compared to 26% at Makkah Region, and 56.8% at Qassim Region.

As has previously been pointed out, our study confirms that vitiligo occurs more frequently in patients with a first-degree family history of this condition (49%).

In our study the patients' social standard (39 %) and level of education (42 %) were below average beside they were non employed (77%) and this could be explained by that they were seeking social insurance so they were enthusiastic to attend the clinics.

Almost third of the participants were single (31.3 %) and this may reflect the social stigma of vitiligo by avoiding get engaged with the community.

Among the different types of vitiligo, the most common type reported in our study was the vulgaris type (49.6%), which is like study conducted at Al-Riyadh (42.3%) although a study conducted in Makkah and Najran showed the focal type is the commonest with 60% and 48.5 respectively.

As other authors have previously pointed out, thyroidal disease and Diabetes mellitus is the most common autoimmune disease associated with vitiligo, our study confirmed the same finding with a percentage of 21.2% for thyroid and 13.2% for Diabetes mellitus.

No predominant subtype of vitiligo can be isolated with positive paternal consanguinity. This contrasts with study conducted at Qassim region which showed the universal subtype was most commonly observed type to be associated with paternal consanguinity.

The affected patient with positive family history is predominantly having the valgaris subtype (41.3%) followed by universal (33%) then Acrofacial (22.9%), a similar result was yielded at Qassim region with the valgaris was the most commonly type with a positive family (80%).

Leukotrichia observed most commonly with valgaris subtype.

Our study showed statistically no significant relationship between the gender of the participant and the subtypes of vitiligo.[17]

13-CONCLUSION

1-Our study showed almost same results as compared to other studies conducted in Saudi Arabia.

2-Over all prevalence of vitiligo is 11%. Female were slightly higher than male (52.4%). most of the participant were in 11- 30 years of age.

3-Parental consanguinity was high, with 49% first degree relative. The most common type of vitiligo was the vulgaris type (49.6%).

4-Thyroidal disease and diabetes mellitus is the most autoimmune disease associated with vitiligo.

14- Recommendations

1-Consanguinity in marriage may increase the incidence of vitiligo, therefore, genetic counseling and education should be applied to vitiligo patient.

2-Our study was lacking the psychosocial burden of vitiligo on the affected patient. So, we encourage the future investigator to research about it at Al Madinah Al Munawara region.

3-Physician should be aware of relatively high prevalence of thyroid and diabetes so, they should request proper screening test when clinically suspected.

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