

# Chronic diseases among vitiligo patients

## A case control study

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### ABSTRACT

**الأهداف:** معرفة وتحديد الأمراض المزمنة التي تصيب مرضى البهاق بمستشفى مركزي بالرياض.

**الطريقة:** دراسة لحالات إفرادية مقترنة بحالات أخرى ضابطة تضم 61 مريضاً بالبهاق كحالات إفرادية و61 حالات ضابطة أخرى ليست مصابة بأي مرض جلدي في مدينة الملك عبدالعزيز الطبية بالرياض، المملكة العربية السعودية في الفترة الممتدة بين 20 يناير 2016 إلى 29 سبتمبر 2016. جُمعت المعلومات عن طريق سحب ملفات المرضى للحصول على أعمارهم وجنسهم والأمراض المزمنة المصاحبين بها المتمثلة بالضغط والسكري والدهون الزائدة والسمنة وخمول الغدة الدرقية. تم استخدام النسبة والمتوسط لعرض بيانات البحث فيما استخدمت النسبة الغربية لشرح العلاقة بين المخرجات.

**النتائج:** العينة النهائية تكونت من 122 مشاركاً (34 ذكر و88 أنثى) موزعين بشكل متساوٍ إلى حالات إفرادية وأخرى ضابطة. متوسط الأعمار هو  $45 \pm 19$  سنة للحالات الإفرادية و  $40 \pm 17$  سنة للحالات الضابطة. نسبة مرضى البهاق المصابين بالسكري (51%) كانت أعلى من نسبة المشاركين الضابطين (33%) (القيمة الاحتمالية = 0.04)، وكانت نسبة مرضى البهاق المصابين بالدهون الزائدة (67%) أعلى من نسبة المشاركين الضابطين (48%) (القيمة الاحتمالية = 0.03). بالإضافة إلى ذلك كانت نسبة مرضى البهاق المصابين بخمول الغدة الدرقية (48%) أعلى من نسبة المشاركين الضابطين (26%) (القيمة الاحتمالية = 0.03).

**الخلاصة:** الدراسة البحثية تتلخص في أن هنالك زيادة بنسبة الأمراض المزمنة لدى مرضى البهاق وتتمثل هذه الأمراض في السكري والدهون الزائدة وخمول الغدة الدرقية ومشاكل الكلى والسمنة. ولذلك يتطلب عمل دراسات بحثية أوسع لتوضيح هذه العلاقة بشكل أكبر.

**Objectives:** To identify the proportion and risk of chronic diseases in vitiligo patients in a tertiary hospital in Riyadh, Kingdom of Saudi Arabia (KSA).

**Methods:** A retrospective case-control study included 61 vitiligo patients and 61 normal non-dermatology controls in King Abdulaziz Medical City, Riyadh, KSA between January and September 2016. Age, gender and co-morbid diseases including hypertension, diabetes,

dyslipidemia, obesity and hypothyroidism were retrieved from participants' charts and medical records. Proportion and mean were used to describe the variables, and odds ratio (OR) was used to test the data.

**Results:** A total of 122 participants (34 males, 88 females) equally divided in cases and controls. The mean age was  $45 \pm 19$  years for the case and  $40 \pm 17$  years for the control group. The proportion of diabetes (51%) was higher in the case group than the control (33%) (OR: 0.47; 95% confidence interval [CI]: 0.23-0.98;  $p=0.04$ ). Dyslipidemia was significantly associated with vitiligo (67%) compared with the control group (48%) (OR: 0.44; 95% CI: 0.21-0.92;  $p=0.03$ ). Vitiligo participants had a significantly increased risk of having hypothyroidism (26%) compared with the control group (10%) (OR: 0.31; 95% CI: 0.11-0.85;  $p=0.02$ ).

**Conclusion:** There is an increased risk of chronic diseases among vitiligo patients including diabetes, dyslipidemia, hypothyroidism, renal injuries, and obesity.

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Vitiligo is an acquired skin pigmentation disorder, which can affect any part of the skin, hair, eyes, and mucus membrane. It is an autoimmune process, which causes the destruction of melanocytes leading to depigmentation of the skin. The rate and extent are variable and unpredictable.<sup>1</sup> It is a multifactorial polygenic disease and its exact cause remains unknown.

Many theories have been developed to explain the mechanisms of melanocytes destruction. These theories include autoimmune mechanisms in the humoral and cellular immunity, cytotoxic, intrinsic, oxidant, and neural mechanisms.<sup>2</sup> The prevalence of vitiligo is estimated to be 0.06-2.28% worldwide.<sup>3</sup> Family history is present in 30% of the cases. The prevalence is higher in females and the mean age of onset is 20 years old.<sup>2</sup> Vitiligo can be segmental or non-segmental, and is described as well-demarcated patches and macules of depigmented lesions.<sup>4</sup> Lesions can be linear, oval, or round, and the most frequent sites involved the face, scalp, and neck.<sup>5</sup> It is diagnosed clinically, and the diagnosis is confirmed by biopsy.<sup>6-7</sup> Recently, the dermoscope has been introduced and used for the diagnosis of evolving vitiligo.<sup>8</sup> There is no cure for vitiligo, yet there are some combined therapies can be used, most importantly topical steroids and phototherapy.<sup>9</sup> The disorder has been associated with other autoimmune diseases such as diabetes mellitus, thyroid diseases, Addison's disease, and pernicious anemia.<sup>10</sup> A study conducted in the United States (US) reported that 58% of the vitiligo patients were females with 42% males and 23% had comorbidities including thyroid conditions, rheumatoid arthritis, and diabetes.<sup>11</sup> In addition, vitiligo was found to be associated with mental health problems. Major depressive disorder was found in 57% of vitiligo patients, and suicide ideation in 28%.<sup>12</sup> In an academic medical center in the US, hypothyroidism was found to be the most common co-morbidity associated with vitiligo. Anti-thyroid peroxidase (37%) and anti-thyroglobulin antibodies (18%) were found in and of vitiligo patients.<sup>13</sup> In another study, vitiligo was also associated with medical co-morbidities including vitamin B12 deficiency (30%), elevated absolute eosinophil count (16%), hypothyroidism (11%), hypoacusis (10%) and retinal changes (9%).<sup>14</sup> In another study,<sup>15</sup> increased frequencies of systemic lupus erythematosus (4%) and inflammatory bowel disease (2%) were found among vitiligo patients. In a Chinese study, vitiligo patients were more likely to have rheumatoid arthritis, ichthyosis, chronic urticaria, or alopecia areata ( $p < 0.01$ ).<sup>16</sup> Sleep disturbance was found to be the most common complaint of psychiatric

illnesses among 20% of the vitiligo patients.<sup>17</sup> A Korean study reported that vitiligo was associated with increased relative risk of autoimmune co-morbid diseases such as thyroiditis and insulin-dependent diabetes and non-autoimmune diseases like anemia.<sup>18</sup> Locally, a study was conducted in Riyadh, Kingdom of Saudi Arabia (KSA) to assess the quality of life among vitiligo patients by 2 validated questionnaires, the Dermatology Life Quality Index<sup>19</sup> and the Family Dermatology Life Quality Index.<sup>20</sup> It was found that family member's quality of life was affected in 129 (91%) of the subjects.<sup>21</sup> In a study conducted in Arar, the mean age of vitiligo patients was found to be  $34.5 \pm 11.8$  with a median of 23 years. A family history was positive in 65% of patients.<sup>22</sup> Another study from Riyadh showed that 56% of vitiligo patients were males while 44% were females.<sup>23</sup> So, vitiligo was investigated and associated with many autoimmune and non-autoimmune disorders in the literature review as mentioned earlier. However, there is a lack of statistics regarding the association and the risk of developing chronic cardiovascular co-morbid illnesses, specifically hypertension, diabetes, dyslipidemia and obesity among vitiligo patients. Therefore, the objective of this study is to explore the risk of these chronic diseases in vitiligo patients at King Abdulaziz Medical City (KAMC) in Riyadh.

**Methods.** This was a retrospective case control study in KAMC between January 2016 and September 2016. It included vitiligo and non-dermatological patients from both genders and different ages for case and control groups. Participants without a follow-up within the last 10 years were excluded. The study was conducted as per the principles and guidelines of Helsinki Declaration, and by the Institutional Review Board of King Abdullah International Medical Research Center. Participants' charts and medical records were retrieved and reviewed. The data included demographic information (age and gender) and co-morbid diseases (hypertension, diabetes, dyslipidemia, hypothyroidism, liver diseases, and renal injuries). If patients did not have a confirmed diagnosis of a chronic diseases, abnormal laboratory tests and investigations were used for the diagnosis. For example, if there was no diagnosis for hypertension (either high or low), blood pressure measurements were used. The same method was used for the other disorders. A fasting blood glucose level were used to diagnose diabetes, dyslipidemia by low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol levels, hypothyroidism by the thyroid-stimulating hormone

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level, liver diseases by the alkaline phosphatase level, and renal injuries by the creatinine level. Data collection was carried out using a structured data collection form. The expected sample size was 54 for each group based on 95% confidence level and 80% power according to the estimated prevalence of hypothyroidism in vitiligo, which was 28% versus 6% for controls.<sup>24</sup> The Statistical Package for the Social Sciences (IBM Corp., NY, USA) Version 22 was used to analyze the data. Proportion was used for descriptive categorical variables and mean was used for descriptive numerical variables. In the

inferential statistics, odds ratio was used to analyze the data and to identify the risk.

**Results.** The sample included 122 patients (61 participants in each group). The gender distribution between cases and controls was equal (males were 28% and females were 72% for each group). The mean age was  $45 \pm 19$  years for cases and it was  $40 \pm 17$  years for controls (Table 1). The percentage of hypertensive patients (32%) was equal in both genders with diabetes, dyslipidemia, and hypothyroidism higher among female

**Table 1** - Age distribution for vitiligo cases and controls (n=122).

| Age range (years) | Case (n=61)<br>n (%) | Control (n=61)<br>n (%) |
|-------------------|----------------------|-------------------------|
| <30               | 11 (18)              | 20 (33)                 |
| 30-39             | 14 (23)              | 15 (24)                 |
| 40-49             | 9 (15)               | 9 (15)                  |
| 50-59             | 13 (21)              | 7 (11)                  |
| 60-69             | 6 (10)               | 6 (10)                  |
| >70               | 8 (13)               | 4 (7)                   |
| Mean $\pm$ SD     | $45 \pm 19$          | $40 \pm 17$             |
| Median            | 47                   | 37                      |

**Table 2** - Frequency of chronic diseases among the participants based on gender (n=122)

| Variables         | Gender                |                         |
|-------------------|-----------------------|-------------------------|
|                   | Males (n=34)<br>n (%) | Females (n=88)<br>n (%) |
| Hypertension      | 11 (32)               | 28 (32)                 |
| Diabetes Mellitus | 14 (41)               | 37 (42)                 |
| Dyslipidemia      | 18 (53)               | 52 (59)                 |
| Hypothyroidism    | 5 (15)                | 17 (19)                 |
| Liver Diseases    | 3 (9)                 | 7 (8)                   |
| Renal Diseases    | 3 (9)                 | 7 (8)                   |
| Overweight        | 9 (27)                | 25 (28)                 |
| Obesity           | 10 (29)               | 45 (51)                 |

**Table 3** - Comparing odds ratio (OR) between vitiligo cases and controls (n=122).

| Variables      | Case/Control         |                         | OR (95% CI)      | p-value |
|----------------|----------------------|-------------------------|------------------|---------|
|                | Case (n=61)<br>n (%) | Control (n=61)<br>n (%) |                  |         |
| Age            |                      |                         |                  |         |
| Mean $\pm$ SD  | $45 \pm 19$          | $40 \pm 17$             | 0.98 (0.96-1.01) | 0.13    |
| Median         | 47                   | 37                      |                  |         |
| Gender         |                      |                         |                  |         |
| Male           | 17 (28)              | 17 (28)                 | 1.00 (0.45-2.21) | 1       |
| Female         | 44 (72)              | 44 (72)                 |                  |         |
| Hypertension   | 19 (31)              | 20 (33)                 | 1.08 (0.50-2.31) | 0.85    |
| Diabetes       | 31 (51)              | 20 (33)                 | 0.47 (0.23-0.98) | 0.04*   |
| Dyslipidemia   | 41 (67)              | 29 (48)                 | 0.44 (0.21-0.92) | 0.03*   |
| Hypothyroidism | 16 (26)              | 6 (10)                  | 0.31 (0.11-0.85) | 0.02*   |
| Liver Diseases | 8 (13)               | 2 (3)                   | 0.23 (0.05-1.11) | 0.05    |
| Renal Diseases | 9 (15)               | 1 (2)                   | 0.10 (0.01-0.79) | 0.01*   |
| Overweight     | 16 (26)              | 18 (30)                 | 1.18 (0.53-2.60) | 0.69    |
| Obesity        | 33 (54)              | 22 (36)                 | 0.48 (0.23-0.99) | 0.045*  |

\* Statistically significant at  $p < 0.05$ , CI - Confidence interval

participants (Table 2). A third of both the vitiligo group (31%) and the control group (33%) was hypertensive. Diabetes, dyslipidemia, hypothyroidism, liver and kidney disease, and obesity were diagnosed more in the vitiligo group compared to the control group. (Table 3) Table 3 shows the odds ratio (OR) for the 2 groups. Diabetes, dyslipidemia, hypothyroidism, renal disease and obesity were significantly associated with vitiligo.

**Discussion.** The study describes the frequencies and proportions of co-morbid disorders among vitiligo patients and a control group. Cardiovascular co-morbidities including hypertension, diabetes, dyslipidemia, and obesity along with hypothyroidism, liver diseases, and renal injuries have been investigated in both groups.

In the present study, most of vitiligo patients were females (72%). A study in the US by Sheth et al<sup>11</sup> supported the higher frequency of females though the difference between females (58%) and males (42%) were less than what was shown in this study. Proportions of co-morbidities among cases in this study were 31% hypertensive, 51% diabetetic, 67% dyslipidemic, 26% overweight and 26% having hypothyroidism. An Indian study by Shankar et al<sup>14</sup> presented the proportions of co-morbidities among vitiligo patients with one condition, hypothyroidism (11%), related to this research.

In the current study, the risk of hypothyroidism was significantly increased among vitiligo patients in comparison with the control group. A case control study in India by Biswas et al<sup>24</sup> (100 age and gender matched participants for each group) reported that the proportion of hypothyroidism was significantly higher among cases (28%) than controls (6%) ( $p < 0.05$ ), which was similar to this study. Goyal et al<sup>25</sup> included 150 vitiligo cases and 100 non-vitiligo dermatology controls (age and gender matched) in another case control study in India. Hypothyroidism was diagnosed among 20% of the case group compared with 2% in the control group ( $p = 0.004$ ).

In addition, a significant increased risk of diabetes and dyslipidemia in the vitiligo group of this study was established. In the Indian case-control study by Goyal et al<sup>25</sup> a significantly higher proportion of diabetes was reported in the case group (16%) than the control group (5%) ( $p = 0.006$ ). A case control study from Poland by Pietrzak et al<sup>26</sup> found that lipid abnormalities were more prevalent among vitiligo cases than controls (participants were 7-15 years old). It has showed that the

concentration of the LDL/HDL ratio was significantly higher among the case group than the control group, which was similar to the significant relation found in this study between vitiligo and dyslipidemia. Other co-morbidities including obesity and kidney injuries were found to have a significant association with vitiligo. It was found that vitiligo patients had an increased risk of developing obesity and renal diseases in comparison with the control group.

There are several strengths and limitations of this study. One of the strengths is that many chronic diseases were studied for both groups. In addition, data collection relied on test results and not on participant recall nor responses. A limiting factor worth mentioning is that due to the charts review methodology, some data including the percentage of body surface affected by vitiligo, psychosocial effects, quality of life, medications used, and family history were missing.

In conclusion, the study concluded that there is an increased risk of developing co-morbid chronic disorders among vitiligo patients including diabetes, dyslipidemia, hypothyroidism, renal injuries and obesity. The findings mandate further research, and the importance of monitoring these disorders among vitiligo patients.

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