Evaluation of thyroid hormones in Alopecia Areata in Iraqi patients

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Abstract- Alopecia is a general term for hair loss. Alopecia areata is a common cause of non-scarring hair loss that can occur at any age. It usually causes small, coin-sized, round patches of baldness on the scalp, although hair elsewhere such as the beard, eyebrows, eyelashes, body and limbs can be affected. In some people larger areas are affected and occasionally it can involve the whole scalp (alopecia totalis) or even the entire body and scalp (alopecia universalis).

It is not possible to predict how much hair will be lost. Regrowth of hair in typical alopecia areata is usual over a period of months or sometimes years, but cannot be guaranteed. The chances of the hair regrowing are better if less hair is lost at the beginning.

Most people, with only a few small patches get full regrowth within a year. If more than half the hair is lost then the chances of a full recovery are not good. The hair sometimes regrows white, at least in the first instance. Most people get further attacks of alopecia areata. In alopecia totalis and alopecia universalis, the likelihood of total regrowth is less.

Hair is lost because it is affected by inflammation with main cause of this inflammation is unknown but it is believed that the immune system may attack growing hair. The disease of alopecia areata is considered more affected by autoimmune diseases such as thyroid disease, although the risk of developing these disorders is still very low.

In present study aimed to identify the correlation between thyroid function in alopecia areata patients and compare it with healthy control. And determined the prevalence of alopecia areata according to gender.

A Case control study carried out at the outpatient clinic of dermatology department in Salah Aldeen general hospitals during the period from 1st of October 2018 to 30th of April 2019. We selected 100 patients included 50 patients with alopecia areata as a cases and compared with 50 normal person. Then thyroid function test of cases was compared with that of equal number of age and sex matched healthy controls.

The result of study revealed a total of 100 patients were enrolled in both case and control groups. Mean age of case and control groups were 24.30±6.80 the most prevalent age group was <18 years 39%. The prevalence of thyroid disorder was significantly higher in alopecia areata group (34%) as compared to the control group (14%) (P=0.001).

The Conclusion of this study found a significant association between alopecia areata and thyroid dysfunction.

I. INTRODUCTION

Alopecia areata (AA) is a chronic autoimmune disease of the Pilar follicles and sometimes affected nails. It is characterized by no scarring alopecia and can affect any hair-bearing area of the body. The loss of scalp and body hair by interruption of their synthesis, though without destruction or atrophy of the follicles and consequently can be reversible. The onset may be at any age and there is no unknown race or sex preponderance.

The affected skin that may be slightly reddened but otherwise appears normal. Short broken hairs (exclamation mark hairs) are frequently seen around the margins of expanding patches of alopecia areata.

The most common pattern is a small annular or patchy bald lesion (patchy alopecia areata), usually on the scalp, that can progress to total loss of scalp hair only (alopecia totalis), and total loss of all body hair (alopecia universalis). This skin disease can begin at any time of life and the peak of incidence between 20 and 50 years of age, and other articles affirm 60% of the patients present the first episode of the disease before 20 years of age.2 and according
to several study found more than 70% of the cases occurred between 10 and 25 years., although it has been observed that with relation to the severe forms, 63% occur in men and 36% in women.4

Alopecia areata accounts for 2% of the first dermatological consultations in the United Kingdom and United States. as documented by several large epidemiological studies from Europe, North America, and Asia, the prevalence of alopecia areata in the early 1970s was reported to be between 0.1% to 0.2% with a life time incidence of 1.7%-5.3. A follow-up study of this population form 1990–2009 found that the cumulative incidence increased almost linearly with age and that the lifetime incidence of alopecia areata was 2.1%. 6

Some studies show that the prevalence seems to shift to women in patients >45 years of age1. And another no sexual dichotomy. Most studies report no significant differences in the age of onset, duration, or type of alopecia areata by sex or ethnicity.7
The aim of study:
Identify the correlation between thyroid function test and alopecia areata and compare it with healthy control.

Objective
1.Evaluate the serum thyroid hormones (throxine) (T4), triiodothyronoine (T3) and thyroid stimulating hormone (TSH) level in both study groups (alopecia areata ) and control group.
2.Identify the prevalence of alopecia areata according to gender.

II. PATIENTS AND METHODS

Ethical consideration
• Agreement of MOH-Iraq, and Salah Alden directorate of health.
The collection of data was kept confidential and not be divulged except for the purpose of the study.
The Participant’s agreement will be considered and they will be informed that the participation is voluntary and they can withdraw from the study after having agreed to participate
A written informed consent from each participant was obtained after explaining the study objectives and prior to the start of data collection.

Study Design, Study setting and Study population
Hospital based case control study was conducted in Salah Alden general hospitals during the period from 1st of October 2018 to 30th of April 2019. The researcher visited the hospitals 5 times a week from 8:30 a.m. to 1:30 p.m. for four months .Target population in this study was the people who lived in Salah Alden governorate with different aged.

Data collection tools
The data were collected by the researcher using the following tools :

Questionnaire
The questionnaire was prepared by the researcher. The data requested included: age, sex, and level of education, residency, occupational history, and family history of disease, history of systemic diseases (hypertension, DM, coronary artery disease (CAD), and AF, duration of disease and history of thyroid disorders.
About the past medical history regarding the systematic disease, the patient was regarded as positive history if the condition had been previously diagnosed by specialist physician, or if he was receiving medicine specified to the disease.

Physical examination
Physical examination was performed by the researcher for each patient .

Inclusion criteria
Cases:
Patients with (a alopecia areata) diagnosed by the consultant dermatology or dermatologists in dermatology department of Salah Alden general hospital.
Controls
Patients attending to the same hospital of the cases and without previous history of alopecia areata. Those participants matches the alopecia’s cases in gender and age (± 5 years)

Exclusion criteria
Cases
a) Patients not residing in Salah Alden governorate .
b) Secondary type’s alopecia areata
c) Patients with any chronic diseases (like asthma, diabetes mellitus) or on chronic medication (like cortisone )
d) Any Psychotic patients

Those patients of chronic and critical disease were not include by the researcher for two reasons, ethically and scientifically. Ethically because those patients are tired and psychologically disturbed .
Laboratory investigations
A- Thyroid function test
This is done by measuring thyroid hormones level in blood that included
- thyroxine (T4)
- triiodothyronine (T3)
- thyroid stimulating hormone (TSH) level

Collection of Blood Sampling
The patients in the ward should be overnight fasting 12 hours then a sample of venous blood was drawn from the anticubital vein using disposable syringes by expert paramedical staff and taken 5 ml of blood from patients. The blood samples were coded and sent to the lab of the hospital for testing the samples, then the results registered on the laboratory form to the patients’ case sheet.

Methods
Principal and procedure: after taken blood sample from patient, we separation blood serum by centrifuge and taken 0.75 ml by specific tube (small green tube) and added it to specific material in yellow tube after that mixed the material with serum and shaking it for 10 time, and put 0.75 ml from mixture on white slide, enter the slide to advice for 8 min for T3 and T4 but TSH 12 min. at temperature 20c. We calculated that by specific device and record the reading.

Statistical Analysis
The data were reviewed, cleaned with double check entry into the computer using Statistical Package for Social Sciences (SPSS) version 20; then, it was coded by the researcher under supervision of the academic supervisor and statistician.
- The data presented as frequency and percentages tables, pie and bar charts were used also.
- A chi – square test was performed to assess relations between categorical variables.
- T-test was used for testing significance of difference between different numerical variables.
- A level of p – value equal to or less than 0.05 was considered significant, while odds ratio (OR) with its 95% confidence interval (CI) was calculated.then had their blood tested for S. cholesterol, S.TG, and other lipid profiles tests and A1c. After completion of all anthropometric measures and blood tests. Subjects completed the demographic questionnaire.

III. RESULTS
The current study included 100 patients, 50 of them were suffering from alopecia areata to be compared with 50 normal individual. Out of total sample 55% were females and 45% were male. (Figure 1)

The age of study sample included three category, the most prevalent age group was <18 years 39% and 34% at age 18-35 years, while the least was more than 35 years (27%) (figure 2).

Figure 1: Distribution of study sample according to gender. N=100
Table 1: Distribution of study sample according to sociodemographic characteristic

<table>
<thead>
<tr>
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<th>Control</th>
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<tr>
<td>&lt;18 years</td>
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<tr>
<td>18-35 years</td>
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Pearson Chi-Square 8.460 df=2 p=0.634

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<td>Male</td>
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<td>21</td>
<td>45</td>
</tr>
<tr>
<td>Female</td>
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Pearson Chi-Square 0.364 df=1 p=0.546

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<tr>
<td>Educated</td>
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<td>13</td>
<td>31</td>
</tr>
<tr>
<td>Non-Educated</td>
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<td>37</td>
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Pearson Chi-Square 1.169 df=1 p=0.280

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<td>Yes</td>
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<td>23</td>
<td>54</td>
</tr>
<tr>
<td>No</td>
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<td>27</td>
<td>46</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Pearson Chi-Square 2.576 df=1 p=0.108

Figure 2: Distribution of study sample according to age. N=100

The current study also showed a difference in family history among cases groups; as the positive family history of cases’ was 28% and 72% negative family history. While the duration of disease among patients of alopecia were 62% for less than one years and 38% with history of duration to more than years.

Regarding to severity of disease the study showed 68% have sever disease and 32% have mild to moderate disease. But the types of alopecia was most prevalent multilocularis (46%).as shown in table 2
In a comparison of thyroid function test (TSH,T4,T3) between the study groups; the result of study showed increase abnormal level of TSH more in case group than among control group without significantly associated with alopecia areata (p<0.211) and OR= 0.506 (0.157-1.63), while abnormal T3 level was found in the case group more than those who did not have alopecia areata so the chance of alopecia areata is among the case groups more than control group with a statically significant association (p=0.001) and OR=0.316 (0.117-0.851).

Regarding to abnormal T4 level was found in the case group more than those who did not have alopecia (normal group) but without any a statistically significantly associated (p=0.211) and OR=0.352 (0.114-1.088).
Table 3: Relation between thyroid function test and groups (case and control)

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<thead>
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<th></th>
<th>Total</th>
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</thead>
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</tr>
<tr>
<td>TSH</td>
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<tr>
<td>normal</td>
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<td>86</td>
</tr>
<tr>
<td>abnormal</td>
<td>0</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Fisher’s Exact Test = 1.202 df= 1 p value = 0.211 OR= 0.506 (0.157-1.63)</td>
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Table 4: Relation between TSH and characteristic of disease. N=50

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<td>abnormal</td>
</tr>
<tr>
<td>Types</td>
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</tr>
<tr>
<td>unilocularis</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>multilocularis</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>totals</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>universals</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>9</td>
</tr>
<tr>
<td>Pearson Chi-Square 7.975 df=3 p=0.047</td>
<td></td>
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<table>
<thead>
<tr>
<th></th>
<th>TSH</th>
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<td>abnormal</td>
</tr>
<tr>
<td>severity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>m</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>s</td>
<td>30</td>
<td>4</td>
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<tr>
<td>Total</td>
<td>41</td>
<td>9</td>
</tr>
<tr>
<td>Pearson Chi-Square 2.799 df=1 p=0.094</td>
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<table>
<thead>
<tr>
<th></th>
<th>TSH</th>
<th>Total</th>
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<tr>
<td></td>
<td>normal</td>
<td>abnormal</td>
</tr>
<tr>
<td>duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1year</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>&gt;1years</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>9</td>
</tr>
<tr>
<td>Fisher’s Exact Test 0.101a df=1 p=0.750</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Regarding to relation of TSH with classification of alopecia, the result of study found significant association between abnormal result of TSH with specific types of alopecia (p= 0.047). While the relation to relation of TSH with severity of alopecia, the result of study showed no any significant association between abnormal result of TSH and severity of alopecia (p= 0.094).

Also the relation of TSH with duration of alopecia, the result of study found no any statically difference between abnormal result of TSH with duration of alopecia (p= 0.750).
Regarding to relation of T3 with classification of alopecia, the result of study found no any significant association between abnormal result of T3 with specific types of alopecia (p= 0.101).

While the relation to relation of T3 with severity of alopecia, the result of study showed a significant association between abnormal result of T3 and severity of alopecia (p= 0.004).

Also the relation of T3 with duration of alopecia, the result of study found a statically difference between abnormal result of T3 with duration of alopecia, more than one years in duration (p= 0.029).

Table 5: Relation between T3 and characteristic of disease. N=50

<table>
<thead>
<tr>
<th></th>
<th>T3 Total</th>
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<tr>
<td></td>
<td>normal</td>
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<td></td>
</tr>
<tr>
<td>types</td>
<td></td>
<td></td>
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<tr>
<td>unilocular</td>
<td>10</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>multilocular</td>
<td>14</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>totalis</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>universalis</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>17</td>
<td>50</td>
</tr>
<tr>
<td>Pearson Chi-Square</td>
<td>6.236a</td>
<td>df=3</td>
<td>p=0.101</td>
</tr>
</tbody>
</table>

Regarding to relation of T4 with classification of alopecia, the result of study found no any significant association between abnormal result of T4 with specific types of alopecia (p= 0.099).

While the relation to relation of T4 with severity of alopecia, the result of study showed no any significant association between abnormal result of T4 and severity of alopecia (p= 0.192).

Also the relation of T4 with duration of alopecia, the result of study found no any statically difference between abnormal result of T4 with duration of alopecia, (p= 0.081).

study also found a significantly higher HbA1c level among acanthosis nigricans patients in comparison to controls (p<0.001). This finding is similar to results of Rafalson et al 1 study in USA which stated that acanthosis nigricans is accompanied by 50-100% risk of developing diabetes mellitus and poor glycemic control. Studying demographic characteristics of AN patients in present study showed that mean age of AN patients was 39.4 years. This finding is similar to results of Sharquie et al 8 study in Iraq which found that mean age of AN patients in Baghdad was 39 years.
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**IV. DISCUSSION**

Alopecia areata is a disfiguring health problem. Most studies conducted in this area were to determine the prevalence of AA and they used the cross sectional design.

The aim of the present study was to identify the effect of thyroid dysfunction on alopecia areata by the case control design was used. The risk factors and causes of alopecia areata was very complex and include factors related to individual autoimmunity, families and society and it depends on cultural patterns in each society.

However, the present study has described the different patterns of alopecia seen among cases of alopecia patients and their relation to thyroid dysfunction, age, sex, and associated conditions. And comparison with a normal population.

**Gender factor**

In current study gender variable was female more than male, as they consist 55% and 45% respectively from the total sample. Female had higher prevalence of alopecia areata than male as 52% and 48% of total cases (50 patients), but this different it not a

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**Table 6: Relation between T4 and characteristic of disease. N=50**

<table>
<thead>
<tr>
<th>Types</th>
<th>Total</th>
<th>Abnormal</th>
<th>Normal</th>
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</thead>
<tbody>
<tr>
<td>Unilocularis</td>
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<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Multilocularis</td>
<td>18</td>
<td>5</td>
<td>23</td>
</tr>
<tr>
<td>Totalis</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Universalis</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>38</td>
<td>12</td>
<td>50</td>
</tr>
</tbody>
</table>

Pearson Chi-Square 6.285 df=1 p=0.099

<table>
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<th>Severity</th>
<th>Total</th>
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<td>M</td>
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<td>16</td>
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<tr>
<td>S</td>
<td>24</td>
<td>10</td>
<td>34</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>38</td>
<td>12</td>
<td>50</td>
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Pearson Chi-Square 1.740 df=1 p=0.192

<table>
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<th>Normal</th>
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</thead>
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<td>&lt;1year</td>
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<tr>
<td>&gt;1years</td>
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<td>2</td>
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</tr>
<tr>
<td><strong>Total</strong></td>
<td>38</td>
<td>12</td>
<td>50</td>
</tr>
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</table>

Pearson Chi-Square 3.051 df=1 p=0.081

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**Figure 7: Relation between T4 and characteristic of disease.**
statistically significant level. This result similar to study conducted for 158 adult Chinese patients diagnosed as AA in clinic of dermatology of Jinshan Hospital (2017).

But this result disagree with another study conducted in Nepal (2018).86 Male and female in the AA group were 40 (53.3%) and 35 (46.7%) with male: female ratio being 1.14:1. Similarly, male and female in the control group were 39 (49.4%) and 36 (50.7%) with male and female ratio of 1.08 (P=0.870).

These variations might be attributed to the difference in settings of these studies, study design as a cross sectional study. 85

**Thyroid function test**

The current study shown the prevalence of abnormal thyroid function was double in AA group compared to the control group. This result Similar to study conducted in Nepal (2018)86 and another study from India87 also observed that the thyroid disorder was the systemic disease with highest frequency in AA patients. Likewise, a recent Australian study also reported that almost one fourth (24%) of AA patients had thyroid abnormalities.88 Thyroid dysfunction was also found in AA patients in a study done in Pakistan but its prevalence was half (8.9%) as compared to our study.89

It has been observed that thyroid disease is the most common chronic disease in AA patients, including hypothyroidism, thyroiditis, Hashimoto's disease, Graves’ disease, and simple thyroid gland.90

Previous studies have shown the incidence of thyroid disease ranged from 8% to 28% in AA patients. In China91, thyroid disease occurs in AA patients are rarely reported and the only available data was based on non-controlled studies.

In the current study concentrations of T3, T4 and TSH were detected to evaluate thyroid function for AA patients and normal controls.

We did not find statistically significant differences in concentrations of T4 and TSH between AA patients and natural controls, suggesting no obvious damage. However, there were differences with statistical evidence in T3 concentration indicating a relationship between thyroid function in AA patients (p=0.034) and OR=0.316 (0.851-0.117)

Some researchers found many skin disorders such as AA can see in patients with autoimmune thyroid disease, independently of thyroid function. Most of the time, there is no relationship between cause and effect, but the link may be part of the same weakness of immunity.92

**Duration of disease**

In present study, duration of disease (alopecia areata) among selected cases only was 62% less than one years while 38% more than one years. This result similar to study conducted in Korea (2017).56 it was retrospective study for 1137 cases of alopecia areata. That found 68% of cases have duration of disease less than one years while 32% more than one years.

Also another study conducted in Department of Dermatology, Jinshan Hospital of Fudan University in china that found 77% of cases have duration of disease less than one years while 23% more than one years.

In current study showed no any correlation between (TSH level, T4 level) and duration of disease (p=0.750, p=0.081 respectively) regarding to relation between T3 level and duration of disease the result of study show the level of T3 more abnormal with increase duration of disease more than one year. With significant association (p=0.024) with OR =3.5. However the duration of disease as a risk factors by increase the level of T3 three times more than normal. This result similar to case control study conducted in china 85. (2017)

**Severity of disease**

In present study we found more than 68% of total cases have sever types of disease and 32% have moderate disease.

In current study showed no any correlation between (abnormal TSH level) and severity of disease (p=0.094) also the relation of abnormal T4 level and severity of disease was not significant (p=0.192) in spite of the level of T4 was more in sever disease cases 48% than those have mild to moderate disease was 28%.

But the relation of T3 level with severity of disease was more level of abnormal T3 among moderate disease with significant association p=0.004 (OR=1.56). This result agree to study conducted in Nepal (2018)86 that found the relation between thyroid test and AA Severity: abnormal thyroid function test was increased once the AA disease severity grade was increased but they were statistically not significant (p=0.021). Earlier report suggested that the frequency of thyroid hormone has no clinical correlation with AA severity 93. Seraslan et al. also did not find the correlation between AA disease severity and personal and family history of autoimmune disease 94. Kasumagic et al. compared the frequency of thyroid autoantibodies (TgAb, TPOAb) in 70 AA patients and 30 healthy volunteers. Thyroid functional abnormalities were found in 8 (11.4%) AA patients and positive autoimmune antibodies were associated with AA in 18 (25.7%) patients, with no significant association between the disease severity and presence of these antibodies 95. However, the possible explanation for this different could be the difference in sample size and study setting.

**Types of alopecia areata**

The present study show 22% of cases have unilocularis alopecia areata, and the most prevalence was multilocularis 46% and (20%, 12% were totalis and universalis respectively). This result similar to study conducted by by Emina Kasumagic - (2008)95. That found the most prevalence was also multilocularis 53% and 19% was unilocularis type while the totalis and universalis were (17% and 11% respectively).
Regarding to relation of TSH with classification of alopecia, the result of study found significant association between abnormal result of TSH with specific types of alopecia (p= 0.047) the result reveled that abnormal TSH level was more in multilocualris type of alopecia areata while there are no any significant association between classification of alopecia areata and T3,T4 level (p=0.101 and p=0.099 respectively).

**Limitation**

The present study has its limitations. Screening for thyroid was based on TSH and T3,T4 which are good markers for the purpose. It was not followed-up with additional tests as many of the patients could not afford the cost. Acanthosis nigricans patients in our study were commonly urban residents. Consistently, Dassanayake et al 11 study in Sri Lanka stated that AN is highly predominant in urban areas with benefit of predicting the metabolic disorders.

V. CONCLUSION

There is significant association of alopecia areata with thyroid dysfunction, as evidenced by increased prevalence of thyroid dysfunction in individuals with alopecia areata compared to the healthy controls. Though thyroid dysfunction was more in individuals with mild to moderate form of alopecia areata.

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