Markers of inflammation and thrombophilia in psoriasis
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Abstract

Background: Psoriasis is a common chronic and recurrent inflammatory skin disease associated with increased risk of cardiovascular disease and cardiovascular risk factors such as obesity, diabetes mellitus, hypertension and hyperhomocysteinemia. Psoriasis also associated with increased risk of atherothrombosis.

Objective: Evaluation of serum levels of inflammation and thrombophilia markers in psoriatic patients.

Patients & Methods: Thirty patients with psoriasis and twenty gender and age-matched controls were included in this study. All of them were subjected to: history taking, clinical assessment, body mass index (BMI) calculation, blood pressure (BP) measurement and calculation of PASI score. Laboratory investigations to determine the following: High sensitivity C-reactive protein (hs-CRP), Homocysteine (Hcy), folic acid and vitamin B12, Antithrombin III (AT-III), Prothrombin time (PT) and Activated partial thromboplastin time (APPT).

Results: The marker of inflammation (hs-CRP) was significantly increased in the patients group compared with the control group and it positively correlated with PASI score. In the patients' group there was significant increase in serum Hcy level with significant positive correlation between Hcy level and PASI score. There was significant decrease in serum level of antithrombin III, PT, folic acid and VB12 levels in patients group when compared to control group.

Conclusion: Increased concentration of inflammatory markers and homocysteine may play a role in the atherothrombotic state which may increase cardiovascular risk in psoriatic patients.

Key words: Homocysteine - Inflammatory markers- PASI score - Psoriasis.

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INTRODUCTION

Psoriasis is a common chronic immune mediated skin disorder affecting about 2-3% of world population. Several clinical types of psoriasis have been described; however, 90% of cases presented with plaque psoriasis. The clinical features of psoriasis include erythematous plaques with thick, silvery scales, and sharply defined margins involving the scalp and extensor surfaces of the elbows, knees, and back. (1) It is widely believed that psoriasis is not just a skin disease but a systemic inflammatory process and this inflammation drives the process of atherosclerosis in psoriasis patients. (2)

There is a considerable evidence that psoriasis patients have a significantly increased risk of cardiovascular disease as obesity, diabetes mellitus, hypertension, hyperlipidemia and smoking compared to the general population. (3) Hyperhomocystenemia which considered a risk factor for atherosclerosis and thrombosis has also been reported in psoriatic patients. (4) An increased risk of atherothrombosis has been reported in psoriasis patients, (5) but the relationship between inflammatory markers, haemostatic variables and coagulation markers in patients with psoriasis have not been adequately studied. (6) In this study, inflammatory markers, haemostatic and coagulation parameters were evaluated in psoriatic patients and healthy controls.

PATIENTS AND METHODS

Thirty psoriatic patients attending the dermatology outpatient clinic, Benha University Hospital were included in the study (age 36±8.035 years). Twenty apparently healthy individuals were selected as a control group (age 32±7.925 years). Severity of psoriasis was calculated using Psoriasis Area and Severity Index (PASI). (7) Patients with obesity (body mass index >30 kg/m2), diabetes mellitus, dyslipidaemia, hypertension, severe cardiovascular disease, history of previous venous thromboembolic disease, chronic hepatic or renal diseases, autoimmune disorders, neoplasms, recent trauma, patients on medications known to cause hyperhomocysteinaemia, such as phenytoin, carbamazepine, theophylline, azathioprine, and thiazide diuretics, and patients on anti-psoriatic agents, anticoagulants and immunosuppressive agents in the last 6 months were excluded. Seven milliliters venous blood were collected from each patient and control and subjected to the following: [I] Five milliliters of blood were centrifuged to separate serum for determination of the following: (a) High sensitivity C-reactive protein was measured using Accu-bind ELISA kits provided by Monbind Inc. lake fores, CA92630 USA. (b) Homocysteine was measured using high pressure liquid chromatography (HPLC) method using the apparatus Hwelet Packard ,1050 (USA). (c) Folic acid and vitamin B12 were measured using IMMULITE 1000 analyzer (competitive chemiluminescent enzyme immunoassay), and the kits were provided by Symtron Bioresearch Inc.2774 Loker Avenue West. Carlasbad. USA. (d) AT-III level using the Assay Max AT-III ELISA kit which detect human AT-III in plasma and serum provided by Assaypro; address :41 Triad South Drive,St Charles,Mo 63304,United States. (II) Two milliliters of the blood sample from each patient and control were citrated and plasma were separated for determination of prothrombin time and activated partial thromboplastin time.

STATISTICAL ANALYSIS :

The collected data were tabulated and analyzed using SPSS (Statistical program for social science) version 17 soft ware. Categorical data were presented as number and percentages while quantitative data were expressed as mean and standard deviation and error. Chi square test ( X2), student “t” test and Spearman’s correlation coefficient (r) were used as tests of significance, the accepted level of significance in this work was stated at 0.05 (P <0.05 was considered significant and P<0.01 highly significant).

RESULTS

The inflammatory markers-CRP, was significantly higher in the patients’ group than in control group (p=0.001). As for the haemostatic parameters, AT-III levels were significantly lower and tHcy levels were significantly higher in the patients’ group than control group (p<0.001). Also,folic acid and VB12 levels were significantly lower in the patients’ group than control group (p<0.001). As for coagulation parameters, there was highly significant decrease in PT in the patients’ group when compared with the control group, where P value <0.001. PTT did not differ significantly between the two studied groups.

Table (I): Baseline clinical characteristics for patients and control groups (mean ± SD)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study group (n=20)</th>
<th>Control group (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.300±8.035</td>
<td>32.200±7.925</td>
<td>0.082</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>24.083±1.884</td>
<td>24.900±2.779</td>
<td>0.220</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>119.500±8.939</td>
<td>119.750±7.539</td>
<td>0.838</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>76.500±9.926</td>
<td>74.750±9.662</td>
<td>0.540</td>
</tr>
<tr>
<td>Duration of psoriasis (years)</td>
<td>8.100±4.063</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI score</td>
<td>16.300±11.880</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

BMI: body mass index; PASI: Psoriasis Area and Severity Index; SD: standard deviation.
Table II. Prothrombotic state and inflammatory profile of the patients’ and control groups (mean ± SD)

<table>
<thead>
<tr>
<th>Parameters (normal range)</th>
<th>Study group (n=20)</th>
<th>Control group (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP 7.043±1.205</td>
<td>4.075±0.595</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Hcy 19.653±8.087</td>
<td>10.980±1.692</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Folic acid 5.173±1.132</td>
<td>11.460±1.171</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>VB12 199.413±15.950</td>
<td>268.305±17.141</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>PT 10.957±1.430</td>
<td>13.140±0.698</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>aPTT 33.460±3.827</td>
<td>34.030±4.589</td>
<td>0.636</td>
<td></td>
</tr>
<tr>
<td>AT-III 20.530±3.314</td>
<td>31.710±7.190</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

CRP: C-reactive protein; Hcy: homocysteine; VB12: vitamin B12; PT: prothrombin time; aPTT: activated partial thromboplastin time; AT-III: antithrombin-III; SD: standard deviation.

A significant positive correlation was observed between psoriasis severity (PASI score) and CRP, Hcy, but a significant negative correlation was observed between PASI score and folic acid, VB12, PT, aPTT and AT-III.

Table III. Correlation of PASI with inflammatory, haemostatic and coagulation parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Rsq</th>
<th>P_value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>0.791</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hcy</td>
<td>0.608</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PT</td>
<td>0.767</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>aPTT</td>
<td>0.651</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AT-III</td>
<td>0.810</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Rsq: R square.

A significant positive correlation was observed between serum Hcy level and the age of the studied psoriasis patients where p<0.001 and r=0.763. A significant positive correlation was also observed between serum Hcy level and the duration of psoriasis in the studied psoriasis patients where p<0.001 and r=0.888.

There was a significant negative correlation between serum level of Hcy and folic acid where p<0.001 and r=0.737. Also, the correlation between serum level of Hcy and VB12 was negative where p<0.001 and r=0.758.

DISCUSSION

Psoriasis is considered a disease of dysregulated inflammation which is driven and maintained by interaction among multiple component of immune system in genetically predisposed individuals that leads to production of cytokines, chemokines and growth factor which act on epidermal cells, dermal blood vessels and other inflammatory cells, and this in turn leads to development of the skin lesion of psoriasis. (8)

In the present study, it was observed that CRP levels were significantly increased in the patients’ group more than in control group supporting the idea that psoriasis is a systemic inflammatory disease and correlates with previous findings of Rocha-Pereira et al., (9) Ohtsuka (10) and Sergeant et al. (11) who found that CRP levels were significantly increased in psoriasis patients than in control group. Psoriasis inflammation may act independently in promoting an accelerated atherosclerosis by eliciting endothelial dysfunction and oxidative stress similarly to other chronic inflammatory systemic diseases such as rheumatoid arthritis, systemic lupus erythematos and Crohn’s disease. (12)

As regard the correlation between CRP level and the degree of psoriasis severity (PASI score), it was found that CRP level was Positively correlated with PASI score and this was consistent with the findings of Chodorowska et al. (13) and Karabudak et al. (6) CRP elevation may be attributed to psoriasis inflammation as CRP levels fall when psoriasis was successfully treated. (5)

The results of the present study showed that psoriasis patients had higher mean level of serum Hcy than control group, and this was consistent with the results of McDonald et al. (14), Malebra et al. (15) and Karabudak et al. (6) Higher Hcy level was found also by Tobin et al. (16) in 20 psoriatic patients when compared with control group. They concluded that higher Hcy level in psoriatic patients might be due to Hcy export from rapidly proliferative germinative cell layer and low folate levels in psoriasis patients.

In addition, Kural et al. (17) studied plasma Hcy level and its relationship with atherothrombotic markers in psoriatic patients and reported elevated Hcy levels in psoriasis patients more than in control group and concluded that the increased homocysteine concentration and altered endothelial cell-mediated proteins associated with increased lipids and LDL oxidation may play an important role for the development of atherothrombotic complications with psoriasis.
In the present study a significant positive correlation was found between Hcy level and the age of the patients, and this was in agreement with Schneede et al., (13) who linked this to the diseases and conditions which increase with aging such as deterioration of renal function, malabsorption disorder, malignancy and rheumatic disease, all contribute to impaired folate status, VB6 and VB12 that are important in Hcy metabolism.

Also, it was found in the present study, a significant positive correlation between serum Hcy level and duration of psoriasis, but Cakmak et al. (19) found no correlation between serum Hcy level and duration of psoriasis.

As regard the correlation between Hcy level and psoriasis severity (PASI score), it was observed in the current study, a significant positive correlation between serum Hcy level and PASI score and these results were consistent with that of Malebra et al. (15) and Cakmak et al. (19) who found higher Hcy levels in those with more severe psoriasis. Moreover, Mallbris et al. (20) suggested that psoriasis severity is a risk factor for CVD complications in psoriatic patients. On the other hand, these results were inconsistent with the results of Tobin et al., (16) who found no significant correlation between serum Hcy level and PASI score.

In the present study, as regard the correlation between AT III levels and psoriasis severity (PASI score), it was found in the current study, a significant positive correlation between serum AT III levels and PASI score and this was another support to the development of a hypercoagulable state in psoriasis patients. These findings were consistent with the results of Karbudak et al., (15) and Karabudak et al. (6) who found higher Hcy levels associated with lower folate levels in psoriasis patients. This may be attributed to the fact that folic acid is an important cofactor in Hcy metabolism and its deficiency can cause hyperhomocysteinemia. (21)

In the present study, a significant negative correlation was observed between the levels of serum Hcy and serum folic acid in the studied psoriasis patients, and this was consistent with the results of McDonald et al. (14), Malebra et al. (15) and Karabudak et al. (6) who found that higher Hcy levels associated with lower folate levels in psoriasis patients. This may be linked to the fact that folic acid is an important cofactor in Hcy metabolism and its deficiency can lead to hyperhomocysteinemia. (21)

Also, it was found in the current study that serum levels of vitamin B12 were significantly lower in the studied psoriasis patients than in control group, and this was in agreement with the results of McDonald et al. (14), Malebra et al. (15) and Karabudak et al. (6) who found that low folate levels in psoriasis patients might be due to increased vitamin utilization in the skin as well as reduced folate absorption from the gut.

In the present study, a significant negative correlation was observed between the levels of serum Hcy and serum folic acid in the studied psoriasis patients, and this was consistent with the results of McDonald et al. (14), Malebra et al. (15), Karabudak et al. (6) who found that higher Hcy levels associated with lower folate levels in psoriasis patients. This may be attributed to the fact that folic acid is an important cofactor in Hcy metabolism and its deficiency can cause hyperhomocysteinemia. (21)

In contrary to the results of the current study, Cakmak et al. (19) found no significant difference in serum Hcy, folic acid and vitamin B12 levels between 70 psoriasis patients and 70 healthy controls. The current study revealed a hypercoagulable state supported by a significant decrease in PT levels of the studied psoriasis patients when compared with control group, but this disagree with Kural et al. (16) who found no significant difference between PT of psoriasis patients and control group.

In the present study, there was no significant difference between the PTT of the studied psoriasis patients and control group. This agrees with the results of Karbudak et al. (6) who found no significant difference between the PTT of the studied psoriasis patients and controls. In the current study, there was a significant negative correlation between both PT and PTT levels and PASI score.

It was found in the current study that AT-III levels were significantly decreased in the studied psoriasis patients than in control group and this was another support to the development of a hypercoagulable state in psoriasis patients. These findings were consistent with the results of Karbudak et al., (6) but inconsistent to that of Marongiu et al. (21) who reported that the levels of AT-III were not changed significantly in both psoriasis patients and control group.

In the present study, as regard the correlation between AT-III levels and PASI score, there was a significant negative correlation between AT-III levels and psoriasis severity (PASI score).

Finally, this study concluded that psoriasis patients have a hypercoagulable state which increases the risk to develop atherothrombosis, and this is likely related to psoriasis inflammation which cause endothelial dysfunction and oxidative stress, and is also related to Hcy which is considered an established risk factor for atherosclerosis and thrombosis, because it may cause direct endothelial injury followed by facilitated thrombosis, and causing oxidative damage to the endothelium.
REFERENCES


