Resistin serum levels in psoriasis patients and association with disease severity in Iraqi population

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Abstract
Psoriasis is a disorder with genetic and immunologic background. Psoriasis is associate with many metabolic disorders like insulin resistance. Resistin can involve in development of psoriasis by acting as a pro-inflammatory factor leading to an increased mRNA expression of many chemokines and cytokines. Our primary goals is to study the serum level of Resistin in psoriasis patients, and relation between the Resistin serum levels and psoriasis severity. The study involved 60 patients with psoriasis and 40 healthy controls. We analyzed plasma levels of Resistin in psoriasis patients and compared them with those of healthy control. Evaluation of plasma levels of Resistin was performed by enzyme immune sorbent assay (ELISA). Also we study the relation between Resistin serum with the severity of psoriasis that evaluated by psoriasis area and severity index (PASI) score. Psoriasis patients have considerably higher serum levels of Resistin than healthy control. Resistin serum levels were 12.9 ± 4.1 ng/ml, 7.2 ± 2.1 ng/ml in patients and control group respectively. Also the Resistin levels were association with severity of psoriasis where serum levels of Resistin were 14.68 ± 4.20 ng/ml and 10.87 ± 2.9 ng/ml in severe and mild to moderate cases respectively. Our results suggests that the Resistin has important role in development of psoriasis.

Introduction
Psoriasis is a common inflammatory T-cell mediated skin disorder, affect in 2-3% of the population. (1) in which the most prominent microscopic abnormality is hyperproliferation and altered differentiation of keratinocyte. while the disease has several phenotypes, (2) plaque psoriasis affects about 90% of patients. although the precise pathomechanism remains unknown various cytokines and growth factors are assumed to be involved. the etiology of psoriasis is not clear yet but the disease is believed to have an autoimmune basis and a strong genetic component. (3) As in the case of many autoimmune diseases its real cause remains poorly defined. Resistin is considered to be an important modulator of chronic inflammation contributing to the development of many disorders. High insulin concentration significantly upregulated Resistin and the other cytokines. (4) Resistin could stimulate the expression of the proinflammatory cytokines TNF-α and IL-6 of both human macrophages via the NF-kB-dependent pathway while intravenous
administration of endotoxin and activation of this inflammatory cascade could result in hyperresistinemia in humans, indicating the importance of this signalling pathway in the resistin-mediated inflammation (5,6).

Resistin is a 12 kDa cysteine-rich polypeptide which is produced in humans predominantly by stromal macrophages and monocytes of the visceral adipose tissue (7). Elevated resistin levels are found in obesity and inflammation, and may play a significant role in the pathogenesis of many inflammatory diseases (8). More importantly, resistin acts as a pro-inflammatory factor leading to an increased mRNA expression of twenty chemokines and cytokines including TNF-α, IL-1, IL-6, IL-12, chemokine ligand CXCL8, monocyte chemoattractant protein-1 and resistin itself via the nuclear factor-kappa B (NF-k B) (9).

In recent years, more has been learned about psoriasis and its disease associations, and physicians were recognized that psoriasis is a disease that affects much more than just the skin. Patients with moderate or severe psoriasis have increased rates of obesity (10,11). Additionally, psoriasis has also been linked to the metabolic syndrome. There is now a growing body of evidence that insulin resistance is also more prevalent in patients with psoriasis (12).

In the majority of studies exploring the association of resistin with psoriasis, hyperresistinemia characterized untreated psoriatic patients and correlated with disease severity and nail psoriasis severity index (13).

Resistin was originally discovered as an adipokine with a possible link between obesity and insulin Resistance (11). Human resistin is synthesized in cells other than adipocytes, predominantly in macrophages and monocytes characterized by a high metabolic turnover. Resistin is expressed primarily in inflammatory cells and has been shown to be involved in obesity-related subclinical inflammation, atherosclerosis, and CVD (14).

**Aim of study**

Our primary aims is to study the serum level of Resistin in psoriasis patients, and relation between the Resistin serum levels and psoriasis severity.

**Material and Methods**

Patients with psoriasis who had not received any prior local or systemic treatment within two months were included in the study (Dec 2013 to Jan 2014). The diagnosis was made clinically, based on characteristics of psoriatic. Patients with psoriatic arthritis were excluded. The severity of psoriasis was assessed by the psoriasis area and severity index (PASI) for each patient. The control group was comprised of healthy, non-psoriatic volunteers with no family history of psoriasis. A total of 60 patients (35 males, 25 females), and 40 healthy subjects (19 males, 21 females) were included in this study. 5 ml blood sample was taken from patient and control group.

Sample collection and Resistin measurements of Blood samples were prospectively collected with the appropriate Ethical Committee permissions, from patients attending dermatology Outpatients Clinics at Tikrit Teaching Hospital in Iraq. Each sample had been collected in a one tube for ELISA where serum was
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separated within 1 h of blood collection after spinning for 15 min at 1500 g. The serum was stored without preservative at _20 C and then thawed just prior to testing. Serum Resistin concentrations were determined using the commercially available enzyme-linked immuno-sorbent assay (ELISA Ultra sensitive), kit supplied by BOSTER Immunoleader (USA). The assays employ the quantitative sandwich enzyme immunoassay technique using recombinant human Leptin with antibodies raised against the recombinant proteins.

Result

Our study observed that there were no significant differences in Resistin serum levels according on age and gender in patients and control groups (P >0.05). as shown in tables (1,2).

In this study we show that serum Resistin is elevated in patients with psoriasis compared with age-, sex- and BMI matched healthy controls and also confirm that Resistin correlates with disease severity.

In this study we observed a significant increase in The mean levels of Resistin of the patients than those of the control(p≤ 0.001). Resistin serum levels were 12.9 ± 4.1 ng/ml, 7.2 ± 2.1 ng/ml in patients and control group respectively as shown in table (3). also there were a significant increase in Resistin levels in severe cases of psoriasis than those of mild to moderate cases (p≤ 0.001) where serum levels of Resistin were 14.68 ± 4.20 ng/ml and 10.87 ± 2.9 ng/ml in severe and mild to moderate cases respectively table (4).

Discussion

In this study, serum Resistin levels were investigated by the ELISA technique aiming at studying the suggested relationship between Resistin levels and the severity of psoriasis vulgaris. All patients included in the study did not receive any topical or systemic steroid therapy for four weeks before taking serum, in order not to disturb any cytokine production. In this study we found that serum resistin is elevated in psoriasis patients compared with age, sex and BMI matched healthy controls. Also serum Resistin levels were find to be associated with the severity of the disease, we found that the serum Resistin levels are significantly higher in patients with severe psoriasis than patients with mild to moderate psoriasis, severity of psoriasis was measured by the Psoriasis Area and Severity Index (PASI) this could be explained on the basis of previous studies which demonstrated that Resistin has an important role in the pathogenesis of immune mediated inflammatory diseases (15). Also it totally agree with the most of previous studies which indicate that the plasma levels of resistin were significantly increased in psoriasis as compared with those of healthy controls(16,17).

This study and recently others observe a positive correlation between psoriasis disease severity and serum Resistin levels (15,16). Human Resistin is synthesized in cells other than adipocytes, predominantly in macrophages and monocytes particularly in the visceral adipose tissue characterized by a high metabolic turnover (18). Elevated resistin levels caused by genetic or environmental factors such as obesity and inflammation may play a pivotal role in the pathogenesis of insulin
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Resistin induces the expression of adhesion molecules, such as vascular cellular adhesion molecule-1 and intercellular adhesion molecule-1 and that adiponectin inhibit the effect of resistin in vascular endothelial cells (21).

Resistin may be involved in the pathogenesis of psoriasis in overweight individuals, possibly by augmenting the cytokine expression by the inflammatory infiltrate. Resistin promotes foam cell formation via the dysregulation of scavenger receptors macrophages (22).

Resistin correlated to elevated proinflammatory cytokines such as IL-1β, IL-6 and IL-6R. An association between resistin and inflammation has been reported in several different diseases, including RA (23) and inflammatory bowel disease, but is very weak or nonexistent in studies of apparently healthy individuals. Other study found that current glucocorticosteroid dose correlated positively to resistin levels and remained a significant variable of resistin in multiple regression analyses (24).

In agreement with most experimental data, serum resistin concentrations are significantly elevated in patients with severe inflammatory disease. Several studies have reported that metabolic syndrome and insulin resistance are more prevalent in patients with psoriasis than normal population. Also demonstrate that exogenous resistin can induce monocytes to produce the inflammatory cytokines CXCL8 and TNF-α in vitro (26). Increases in IL-6 and TNF-α in the culture medium of PBMC cultures stimulated with 1000 ng mL1 resistin. Resistin has also been shown to increase the expression by human endothelial cells of the vascular cell adhesion molecule-1, CCL2 and endothelin-1 (27).

Resistin has furthermore been reported to promote proliferation and migration of cultured endothelial cells and to increase the expression of vascular endothelial growth factor receptors and matrix metalloproteinases-1 and -2 (28). All these various activities of Resistin make it an important effector cytokine in psoriasis.

Conclusions
These findings suggest that the Resistin has an important role in the development of psoriasis lesions because these cytokines have an important role in the inflammation process. Overexpression of Resistin in patients with psoriasis may explain features of psoriasis that link keratinocyte proliferation with immune activation and insulin resistance, so the possibilities of the presence of a relation between the psoriasis and diabetes mellitus has increased.

References


12. -Boehncke S, Thaci D, Beschmann H, Ludwig RJ, Ackermann H, Badenhoop K


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Table (1) the mean and St.D of Resistin serum levels in psoriasis patients and healthy control groups depend upon age groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Resistin levels</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Patients mean ± SD</td>
<td></td>
<td>Control mean ± SD</td>
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<td></td>
<td>N=22</td>
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<td>N=29</td>
</tr>
<tr>
<td>Less than 40 years</td>
<td>12.93 ± 4.03 ng/ml</td>
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<td>7.01 ± 2.26 ng/ml</td>
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<tr>
<td></td>
<td>N=29</td>
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<td>N=22</td>
</tr>
<tr>
<td>More than 40 years</td>
<td>12.92 ± 4.3 ng/ml</td>
<td></td>
<td>7.64 ± 2.21 ng/ml</td>
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<td></td>
<td>N=31</td>
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<td>N=18</td>
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</table>

P Value 0.99 0.373

Table (2) the serum levels of Resistin in both female and male of patients and control groups.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Resistin levels</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Patients mean ± SD</td>
<td></td>
<td>Control mean ± SD</td>
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<td></td>
<td>N=21</td>
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<td>N=31</td>
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<tr>
<td>Female</td>
<td>13.35 ± 4.06 ng/ml</td>
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<td>6.93 ± 2.16 ng/ml</td>
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<tr>
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<td>12.47 ± 4.23 ng/ml</td>
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<td>7.69 ± 2.21 ng/ml</td>
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<td>N=29</td>
<td></td>
<td>N=19</td>
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P Value 0.416 0.283

Table (3) the serum levels of Resistin in patients with psoriasis and control group.

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Psoriasis patients No: 60 mean ± SD</th>
<th>Control No: 40 mean ± SD</th>
<th>value</th>
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</thead>
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<tr>
<td>Resistin</td>
<td>12.9 ± 4.13 ng/ml</td>
<td>7.29 ± 2.19 ng/ml</td>
<td>≤ 0.001</td>
</tr>
</tbody>
</table>

Table (4) the serum levels of Resistin in mild and sever cases of psoriasis

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>severity</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistin</td>
<td>Mild and Moderate N0: 27 mean ± SD</td>
<td>Sever N0: 33 mean ± SD</td>
</tr>
<tr>
<td></td>
<td>10.87 ± 2.9 ng/ml</td>
<td>14.68 ± 4.20 ng/ml</td>
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