ROLE OF PLACENTAL GROWTH FACTOR AND HIGH RESOLUTION ULTRASOUND IN EVALUATION OF HYPERVERSUALCULARITY IN PSORIATIC ARTHRITIS

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KEY WORDS: PIGF IN SERUM AND SYNOVIAL FLUID–PSORIATIC ARTHRITIS–HIGH RESOLUTION US.

ABSTRACT

Objective: To measure the levels of placental growth factor (PIGF) in the serum and synovial fluid of psoriatic arthritis (PsA) patients. Also, to evaluate any possible role of high resolution US in the angiogenesis observed in this disease.

Methodology: The study was conducted on 25 PsA patients and 10 apparently healthy age and sex matched subjects who served as controls. All subjects were subjected to thorough clinical and laboratory examination. PIGF levels were measured in the serum of all of them with ELISA technique. This was confirmed with Western blotting for PIGF in synovial fluid. Assessment of vascularity of the small joints of the hands and other affected knee joints with high resolution US was performed.

Results: The mean value of serum PIGF level in the serum of PsA patients was $(66.52 \pm 12.44 \text{ pg/ml})$ and that in the synovial fluid was $79.82 \pm 14.92$. There was a highly statistical significant difference between them and serum/synovial fluid levels in controls $(16.20 \pm 7.33 \text{ and } 19.44 \pm 8.79 \text{ pg/ml})$ respectively $(p<0.001)$. Moreover, there was a highly significant association $(p<0.001)$ and a statistically significant positive correlation $(p<0.05)$ between serum and synovial fluid levels of PIGF in PsA patients. There was a statistically significant difference between PsA patients and controls as regard Hb levels, ESR and serum uric acid $(p<0.05)$. Also, there was a significant positive correlation between synovial fluid PIGF levels and the onset of joint affection $(p<0.05)$. 

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High resolution US can measure the synovial thickness in the small joints of the hands as well as knee joints in PsA patient. It can also detect increased blood flow in joints, so can measure the resistive index and can detect effusion. Our results showed that there was a highly statistical significant difference between PsA patients and controls as regard synovial thickness (p<0.001). Also, there was a significant negative correlation between serum PIGF and resistive index of PsA patients.

**Conclusion:** Angiogenesis plays an important role in the pathogenesis of PsA. This is confirmed by the presence of higher PIGF levels in both serum and synovial fluid. Inhibition of PIGF and its receptor (Flt-1) constitute potential candidates for therapeutic modulation of angiogenesis and inflammatory joint destruction in arthritis. High resolution ultrasound can be very useful to detect early hypervascularization and joint inflammation which guide treatment towards an early or more aggressive therapy.

**INTRODUCTION**

Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis (Gladman & Robman, 2001). In approximately 70% of cases, psoriasis precedes the onset of arthritis. The interval between the onset of psoriasis and arthritis can be extremely variable. The relationship between skin and joint manifestations in PsA remains unclear, however, nail lesions, including pits and onycholysis, and have been shown to signal the development of PsA (Gladman, 2000).

Psoriatic arthritis is a form of pleomorphic arthropathy which until recently, was considered a benign arthritis. However, joint deformity and destruction, as well as disability, are common, thus challenging the concept that this arthropathy is benign (Silva et al., 2003).

Angiogenesis and inflammation are closely linked, and increased vascularity is a prominent feature of a number of inflammatory joint diseases, including rheumatoid arthritis and psoriasis (Jackson et al., 1997). The predominant type of angiogenesis observed during inflammation consists of vascular enlargement of pre-existing vessels rather than the formation of new blood vessels. However, endothelial cell proliferation and vascular hyper permeability are shared by both types of angiogenesis (Lange-Asschenfeldt et al., 2002).

Veale et al. (2000) reported that PsA synovial membrane is highly vascular, than RA synovium.
Several angiogenic factors are mostly involved in inflammatory vascular response. Among the known angiogenic factors, vascular endothelial growth factors (VEGF) which have emerged as a central regulator of the angiogenic process under both physiological and pathological conditions (Yonekura et al., 1999).

Placenta growth factor (PIGF) has been described recently as a secreted growth factor with strong homology to VEGF based on amino-acid and cDNA sequences (Clauss et al., 1996). PIGF occurs in 3 isoforms; PIGF-1 (PIGF-149), PIGF-2 (170) and PIGF-3 (PIGF-221) due to alternative mRNA splicing (Cao et al., 1997).

PIGF has been originally identified in the placenta, (Khalig et al., 1996). It is also expressed during vascular development (Achen et al., 1997), and PIGF expression has been detected in several other organs including heart, lung and skin (Persico et al., 1999).

PIGF binds to the Flt-1 VEGF receptors but not to the Flk-1 receptor that is predominantly expressed by vascular endothelial cells and thought to mediate most of the angiogenic and proliferative effects of VEGF. Also, stimulate tissue factor production and chemotaxis in monocytes (Clauss et al., 1996). Naturally occurring heterodimers formed between VEGF and PIGF and have been found to be more active than PIGF homodimers and nearly as potent as VEGF homodimers in assay of mitogenesis (Disalvo et al., 1995).

Thus, PIGF and Flt-1 constitute potential candidates for therapeutic modulation of angiogenesis and inflammation (Lutten et al., 2002).

Ultrasound imaging offers a non-invasive, reproducible, non-radiating and inexpensive method for examining joints in rheumatic diseases patients (Lund et al., 1995). Ultrasound on the small finger joints has been able to demonstrate bone erosions, cartilage damage as well as local effusion and intra-articular pannus (Gressi et al., 1995).

A newly developed, high resolution multidimensional linear array ultrasound was utilized to detect an intra-articular vascularization of pannus even within the small finger joints (Matthias et al., 1999). This allows an early and useful diagnostic approach which can guide treatment towards an early or more aggressive therapy (Silva et al., 2003).

**Aim of the work:**

The aim of this study was to measure the level of placental growth factor (PIGF) in the serum and synovial fluid of PsA. Also, to evaluate the role of high resolution US in those patients in order to detect their role in angiogenesis.
PATIENTS AND METHODS

Our study included 25 psoriatic arthritis (PsA) patients diagnosed according to the criteria of Moll & Wright (1973). They used to attend the Out-Patient Clinic of the Rheumatology & Rehabilitation and Dermatology Departments of Ain Shams University Hospitals. Ten healthy individuals matched for age and sex served as a control group.

Any patient with recent myocardial infarction, tumor growth, wound healing and diabetic retinopathy were excluded from this study.

All patients were subjected to the following:-

Full history taking.
Thorough clinical examination:-

General examination: with special attention to eye and cardiac examination.

Local examination: with special attention to joints, skin and nail examination.

Joint Examination:

We examined for tenderness, hotness, swelling subcutaneous nodules, active and passive movement, crepitus, effusion, deformity and muscle wasting.

Skin Examination:

To detect psoriatic lesions, its severity was evaluated using the psoriasis area and severity index (PASI) score proposed by Fredriksson & Pattersson (1977). PASI score is considered mild if less than 15, moderate from 15 to 25 and severe if more than 25.

Nail Examination:

Pitting: the presence of more than 20 pits is suggestive while more than 60 are diagnostic for PsA.

Ridging, onycholysis, subungual keratosis and oil drop sign.

Laboratory Investigations including:

Complete blood pressure (CBC) with coulter counter.
Erythrocyte sedimentation rate (ESR) with Westergren method.
Rheumatoid factor (RF) with latex technique.
Serum uric acid.
PIGF levels in the serum and synovial fluid.
Radiological Assessment:

**Plain x-ray:** Anteroposterior and lateral views for hands, feet and any other affected joint.

**High resolution ultrasonography:** To small joints of the hands in addition to any affected knee joint in PsA patients and control group.

The small joints of the hand were scanned sagittally from the dorsal view, with the joint in 20° palmar flexion to detect the following:-

*Vascularity of the joint:* this was measured with the resistive index (RI)

*Synovial proliferation:* this was appeared as hypoechoic texture and measured in millimeters.

\[ RI = \frac{\text{Peak Systole} - \text{End Diastole}}{\text{Peak Systole}} \]

*Effusion:* it appeared as hypoechoic masses of fluid level.

*Erosion.*

**Measurement of PIGF:**

Placental growth factor was assessed with ELISA technique using quantikine Kit *(from R&D Systems Inc., 614 McKinley place N.E., Minneapolis MN 55413, USA).* This assay employs the quantitative sandwich enzyme immunoassay technique. A monoclonal antibody specific for PIGF had been pre-coated into a microtitre plate. Standards and samples were pipetted into the wells and any PIGF present was bound by immobilized antibody. After washing, an enzyme-linked polyclonal antibody specific for PIGF was added. Washed again to remove any unbound antibody-enzyme reagent, substrate solution was added. Color developed in proportion to the amount of PIGF bounded, the intensity of the color was measured.

Optical density was determined *(at wave length)* 450 nm. The PIGF concentration of each sample was detected from drawing a standard curve.

SF samples of all PsA patients containing significant levels of PIGF were analyzed with SDS-PAGE and Western blotting using monoclonal anti-human PIGF antibody from R&D. Samples were diluted 1:5 in phosphate buffer and eluted in buffer containing 1.0 M NaCl. Samples were dissolved in SDS non reducing sample loading buffer and after boiling for 5 min, each sample was applied to gradient polyacrylamide gel with molecular weigh markers and PIGF. Proteins were transferred to nitrocellulose with electroblotting. The blot was blocked for 1 hr.
Then affinity purified, biotinylated goat anti-PIGF antibody, in blocking solution was applied for 2 hr. with shaking at 4°C. Following thorough washing, streptavidin-peroxidase at 1:1000 in blocking solution was applied for 30 min. with shaking at room temperature. Then blot was incubated with chemiluminescent substrate. Western blotting using anti-PIGF antibody revealed a significant band at 48-50 KD in all PsA patients.

**Statistical Analysis:**

Our data were transferred to an IBM card to obtain descriptive statistics, range, mean ± SD, number and percentage for quantitative data. Analytic student’s t-test to compare between two independent means, correlation matrix and coefficient of correlations was done using Pearson’s method. Wilcoxon Rank-Sum test was done to find correlation coefficients of non-parametric data. p<0.05 were considered significant and p<0.001 were highly significant.

**RESULTS**

This study included 25 psoriatic arthritis (PsA) patients and 10 healthy subjects who served as a control group.

**Group I (PsA patients):** were 10 males and 15 females. Their ages ranged from 17 to 45 years with the mean age of 34.4 ± 9.25 years.

**Group II (Controls):** were 4 males and 6 females. Their ages ranged from 21 to 43 year with the mean age of 34.2 ± 8.42 years.

The extra-articular clinical data of group I revealed that:

- Duration of skin lesion ranged from 1-30 years with a mean of 11.92 ± 7.78 years and PASI score (*which indicates the severity of the skin lesion*) that ranged from 4.0 to 15.0 with a mean of 8.31 ± 3.42.
- Nail changes were detected in 22 patients (88%) and there was a statistically significant positive correlation between nail changes and serum uric acid (*Z*=4.3 and *p*<0.001).
- Heart affections were detected in 4 patients (16%) with echocardiography. Two of them had mitral incompetence; one had aortic incompetence and one had tricuspid incompetence.
- Eye manifestations were detected in 6 patients (24%), 3 of them diagnosed as conjunctivitis and the other 3 diagnosed as iritis with slit lamb examination.

Articular pattern and examination in PsA are shown in table (1).
Table (1): Articular assessment in PsA patients.

<table>
<thead>
<tr>
<th>Clinical Pattern</th>
<th>No. of Patients</th>
<th>(%)</th>
<th>Examination</th>
<th>No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asym. Oligoarthritis</td>
<td>14</td>
<td>56</td>
<td>Hotness</td>
<td>25</td>
<td>100</td>
</tr>
<tr>
<td>Sym. Polyarthritis</td>
<td>5</td>
<td>20</td>
<td>Tenderness</td>
<td>25</td>
<td>100</td>
</tr>
<tr>
<td>DIP joints affection</td>
<td>3</td>
<td>12</td>
<td>Limited ROM</td>
<td>14</td>
<td>56</td>
</tr>
<tr>
<td>Spondyloarthropathy</td>
<td>3</td>
<td>12</td>
<td>Effusion</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Deformity</td>
<td>8</td>
<td>32</td>
</tr>
</tbody>
</table>

Arthrocentesis was performed for 10 patients who had effusion and 10 healthy controls.

In our controls, the serum PIGF levels ranged from 0-26 pg/ml with a mean of 16.20 ± 7.33, while synovial fluid PIGF levels ranged from 20-36.2 pg/ml with a mean of 19.44 ± 8.79 pg/ml.

In PsA patients, the serum PIGF levels ranged from 45 ± 88 pg/ml with a mean of 66.52 ± 12.44, while synovial fluid PIGF levels ranged from 62.0 – 108.6 pg/ml with a mean of 79.82 ± 14.92 pg/ml.

Fig. (1): Comparison between patients and control regarding Serum and synovial PIGF.
There was a highly statistical significant difference of PIGF in the serum and synovial fluid between PsA patients and controls ($p<0.001$). Moreover, there was a highly statistical significant difference between serum and synovial fluid PIGF levels in both PsA patients and controls ($p<0.001$) (Fig.1).

Also, there was a statistically significant difference between PsA patients and controls as regards Hb levels, ESR and serum uric acid ($p<0.05$) (Table 2).

Rheumatoid factor (RF) was negative in all patients.

Table (2): Comparison between group I (PsA) patients and group II (Controls) as regards laboratory parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>PsA Patients Mean ± S.D.</th>
<th>Controls Mean ± S.D.</th>
<th>t</th>
<th>P</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/dl)</td>
<td>11.92 ± 1.84</td>
<td>13.55 ± 1.54</td>
<td>2.3</td>
<td>&lt;0.05</td>
<td>S</td>
</tr>
<tr>
<td>RBCs (x10⁶/mm³)</td>
<td>4.19 ± 0.63</td>
<td>4.57 ± 0.49</td>
<td>1.2</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>WBCs (x10⁹/mm³)</td>
<td>8.54 ± 1.95</td>
<td>8.88 ± 1.61</td>
<td>0.5</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Platelets (x10³/mm³)</td>
<td>273.84 ± 70.99</td>
<td>309.90 ± 49.59</td>
<td>1.4</td>
<td>&gt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>26.24 ± 25.91</td>
<td>6.50 ± 2.42</td>
<td>2.3</td>
<td>&lt;0.05</td>
<td>S</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>5.01 ± 1.17</td>
<td>3.59 ± 0.55</td>
<td>3.7</td>
<td>&lt;0.05</td>
<td>S</td>
</tr>
<tr>
<td>Serum PIGF (pg/ml)</td>
<td>66.52 ± 12.44</td>
<td>16.20 ± 7.33</td>
<td>4.2</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
<tr>
<td>Synovial PIGF (pg/ml)</td>
<td>79.82 ± 14.92</td>
<td>19.44 ± 8.79</td>
<td>4.6</td>
<td>&lt;0.001</td>
<td>HS</td>
</tr>
</tbody>
</table>

p<0.00= highly significant, p<0.05= Significant and p>0.05= Non significant.

Radiological Assessment:

1. Plain X-Rays:

Plain x-ray assessment showed that a large number of patients 22 patients (88%) had narrow joint space. While 8 patients (32%) had deformity and 2 patients (8%) had bony ankylosis.

2. High Resolution Ultrasound:

In PsA patients, high resolution ultrasound detected synovial proliferation and measured synovial thickness in small joints of hand as well as large joints (knee joint). It also detected increased blood flow in joints so, it could measure the resistive index. Moreover, it detected effusion in 10 PsA patients. (Fig.2-5)
Fig. (2): High resolution US of left DIP joint. There is synovial proliferation and no increased blood flow.

Fig. (3): High resolution US of RT. DIP joint of middle finger shows synovial proliferation.
Fig. (4): High resolution US of the LT. knee joint shows synovial proliferation.

Fig. (5): High resolution US of Lt.DIP joint of the index finger shows increased blood flow.
Table (3): Data of high resolution ultrasound.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>PsA Patients (n=25)</th>
<th>Controls (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± S.D.</td>
</tr>
<tr>
<td>1. Synovial thickness (mm):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. In knee</td>
<td>2.6-4.8</td>
<td>4.04 ± 0.60</td>
</tr>
<tr>
<td>* In Small joints of hands</td>
<td>2.0-4.4</td>
<td>3.58 ± 0.49</td>
</tr>
<tr>
<td>2. Increase blood flow (No. %)</td>
<td>25(100%)</td>
<td>-</td>
</tr>
<tr>
<td>3. Resistive index</td>
<td>0.52-0.68</td>
<td>0.61 ± 0.04</td>
</tr>
<tr>
<td>4. Effusion (No. %)</td>
<td>10(40%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Comparison between PsA patients and controls as regards synovial thickness of the knee with high resolution ultrasound revealed a highly statistical significant difference (t= 4.8 and p<0.001) (Fig.6).

Our correlation study revealed a positive significant correlation between serum and synovial fluid PIGF levels in PsA patients and between synovial fluid PIGF and onset of joint lesion in PsA patients (p<0.05).

Also, there was a negative significant correlation between serum and synovial fluid PIGF levels and the resistive index of the joint (p<0.05)
While, there was no correlation between serum/synovial fluid PIGF and synovial thickness of the joint \((p>0.05)\) (Table 4).

Table (4): Correlation study between serum/synovial fluid PIGF levels and parameters in PsA patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Serum</th>
<th></th>
<th>Synovial</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(r)</td>
<td>(p)</td>
<td>(r)</td>
<td>(p)</td>
</tr>
<tr>
<td>Onset of skin lesion</td>
<td>0.2</td>
<td>&gt;0.05</td>
<td>0.58</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Onset of joint affection</td>
<td>0.13</td>
<td>&gt;0.05</td>
<td>0.63*</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PASI score</td>
<td>0.2</td>
<td>&gt;0.05</td>
<td>0.32</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum uric acid</td>
<td>0.08</td>
<td>&gt;0.05</td>
<td>0.28</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>PIGF</td>
<td>0.8*</td>
<td>&lt;0.05</td>
<td>0.8*</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Synovial thickness</td>
<td>0.02</td>
<td>&gt;0.05</td>
<td>0.14</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Resistive index</td>
<td>-0.2</td>
<td>&gt;0.05</td>
<td>-0.22</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Psoriatic arthritis (PsA) is an inflammatory joint disease that affects 10% of patients with psoriasis (Ruzicka, 1996). Many studies showed that PsA tissues have significantly less synovial lining cell hyperplesia and greater vascularity than RA synovium (Veale et al., 2000). Angiogenesis is implicated in the pathogenesis of psoriatic arthritis (Diaz et al., 2000 and Kuroda et al., 2001).

PIGF is the second described member of the VEGF superfamily (Olofsson et al., 1996). That can induce angiogenesis in vivo and stimulate the migration and proliferation of endothelial cells in vitro (Ziche et al., 1997). PIGF may be important in driving the pathology of inflammatory joints either directly by being chemotactant to monocytes or indirectly by enhancing the effects of VEGF (Clauss et al., 1996).

In this study, the mean age of PsA patients was 34.4 \(\pm\) 9.25 years and 52% of patients were less than 40 years. This is in accordance with Alonso et al. (1991) who reported a mean age of 39.73 \(\pm\) 14.42 years. On the other hand, Castello et al. (1999) reported a mean age of 46.2 \(\pm\) 12.8 years. The male patients constitute 40% of our patients. This comes with Brubacher et al. (1992) who recorded that male patients constitute 41%. On the other hand, Cohen et al. (1999) recorded a higher incidence (59%).

Psoriasis preceded the onset of arthritis in all our PsA patients. This is in agreement with Brubacker et al. (1992), while Cohen et al. (1999) showed that psoriatic skin lesion preceded arthritis in 65.5%. This may be due to the larger scale of their patient groups.

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Our results revealed that PASI score ranged from 4.0 to 15.0, which was considered as a mild degree of skin affection according to Fredricksson & Pattersson (1978) and no correlation was found between the severity of skin lesions and the presence of arthritis. This is in agreement with Cohen et al. (1999).

Nail changes were detected in 88% of our PsA patients. This is in agreement with Cohen et al. (1999) who reported that nail changes occurred in 81.4% and described that increased percentage of nail changes are associated with DIP joint affection. This may be due to a common vascular supply in the distal phalanx and nail matrix.

In our study, the duration of arthritis in PsA patients ranged from six months to 15 years, with a mean of 3.58 ± 3.17 years. This is in agreement with Kane et al. (1999). On the other hand, Ballara et al. (2001) showed that the duration of arthritis ranged from six months to 2 years with a mean of 1 year. This difference may be due to the small number of their patients.

As regards the clinical pattern of arthritis in our PsA patients, 56% had asymmetric oligoarthritis, 20% had symmetric polyarthritis, 12% had DIP joints affection, 12% had spondyloarthropathy and none had arthritis mutilans. This is in accordance with Gladman et al. (1995). Silva et al. (2003) explained this when he found that polyarticular onset of arthritis was associated with more erosive and deforming arthritis.

As regards the laboratory results in our study, there was a statistically significant difference in hemoglobin levels between PsA patients and controls (P<0.05). This is in accordance with Gladman et al. (1995) who found increased frequency of anemia in their PsA patients. This may be due to the systemic chronic illness or due to complication of therapy. Increased ESR comes with Cohen et al., 1999). This may be due inflammatory nature of PsA.

In our study, serum uric acid in PsA patients ranged from 2.6 to 7.4 mg/dl with a mean of 5.01 ± 1.17 and there was a statistically significant difference in its levels between PsA patients and controls (p<0.05). This is in agreement with Brubacher et al. (1992) who recorded that the mean value of serum uric acid was 5.8 ± 1.6 mg/dl in their PsA patients. This was explained by Clark (1996) that elevated serum uric acid may be due to increased turnover of the cells which lead to accelerated nucleic acid degradation and overproduction of uric acid. Also, it was explained by Tikhonov et al. (1998) who reported that levels of adenosine, guanosine and purine monophosphate were decreased with final products of hypoxanthine; xanthine and uric acid metabolism are accumulating.
Moreover, there was a statistically significant positive correlation between serum uric acid and nail changes in PsA patients, possibly nail lesions may further increase the rate of turnover of the cells.

The results of our study revealed that the PIGF was detected in 3 out of 10 (30%) of the control serum samples while PIGF was detected in all synovial fluid samples. There was a highly statistical significant difference in serum/synovial fluid PIGF levels between PsA patients and controls. This is in agreement with Bottomely et al. (2000) who detected PIGF in (31%) of the serum and in all synovial fluid control samples and significantly higher levels of PIGF in serum and synovial fluid between PsA patients and controls. This might be explained by the fact that PIGF may be implicated in both physiological and pathological angiogenesis. Also, in PsA patients angiogenesis occurs in both joints and skin.

Moreover, there was a highly significant association and significantly positive correlation between serum and synovial fluid PIGF levels in PsA patients. These results are supported by Bottomely et al., (2000). This might indicate that pathological angiogenesis was present in an extensive manner in the joints. Chauss et al. (1996) explained this, that PIGF may promote VEGF- induced angiogenesis and changes in vascular permeability and may also enhance monocyte migration into the joints through binding to the Flt-1 receptor on monocytes, resulting in chemotaxis.

Also, there was a significant positive correlation between synovial fluid PIGF levels and the onset of joint affection. This was explained by Oura et al. (2003) that PIGF may predominantly act as proinflammatory mediator through stimulation of vascular remodeling.

There was no significant correlation between serum/synovial fluid PIGF levels and PASI score in our PsA patients. This is in accordance with Bhushan et al. (1999).

As regards high resolution ultrasound, it detected synovial proliferation and increased blood flow. So, it can measure the resistive index in all examined joints of PsA patients, so it is more sensitive than plain x-rays.

There was a highly statistical significant difference in synovial thickness of the knee joints between PsA patients and controls. On the other hand, synovial thickness and increased blood flow in the small joints of the hand could not be detected in controls. This comes with Matthias et al. (1999) who found none of healthy small joints examined with high resolution ultrasound had a detectable synovial thickness.
Conclusion

From all of the above data, we conclude that PIGF level was significantly higher in the serum and synovial fluids of PsA patients. Moreover, it was found to be higher in synovial fluid than in the serum. PIGF may play a key role in angiogenesis and acts as an important stimulus for synovial hypervascularization in PsA patients.

High resolution ultrasound can be very useful to detect early hypervascularization and joint inflammation which guide treatment towards an early or more aggressive therapy.

So, inhibition of PIGF and Flt-1 constitutes a potential candidate for therapeutic modulation of angiogenesis and inflammation. Because under expression or over expression of PIGF did not affect normal vascular development or function, blockade of such molecule might be safer than blockage of other molecules that are essential for vascular maintenance.

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Role of PIGF & High Resolution US in Psoriatic Arthritis  Abdul-Moniem & Mohammad

هدف البحث: هو قياس مستوى عامل النمو المشيمي في المصل والسائل الزالالي لمرضى الالتهاب المصاحب للصدفة، ومعرفة دوره في تكوين زيادة الأوعية الدموية. وتقييم دور الوجمات فوق الصوتية ذات التردد العالي في مسح مرضى الالتهاب المفصلي الصفدي.

مقدمات البحث: أظهرت بعض الدراسات أن وجود زيادة في محتوى PIGF في السائل الزالالي يرتبط وثيقًا بظاهرة بسبب النمو المشيمي. وقد اكتشفت بعض الدراسات أيضاً أن الوجمات فوق الصوتية ذات التردد العالي يمكن أن تساعد في الكشف عن النمو المشيمي. وذلك يشير إلى أن هناك حاجة لإجراء دراسات إضافية لتحديد القيمة الدقيقة لمحتوى PIGF في السائل الزالالي.

هناك عدة الطرق لتحديد الوجود أو عدم الوجود للنمو المشيمي في السائل الزالالي، بما في ذلك استخدام الوجمات فوق الصوتية ذات التردد العالي، والتي يمكن أن تكون أكثر دقة في الكشف عن النمو المشيمي. إلا أن الوجمات فوق الصوتية ذات التردد العالي ليست فقط أكثر دقة في الكشف عن النمو المشيمي، ولكنها أيضًا تستخدم في التحكم في التدفق الدموي، والتعرف على الأوعية الدموية الصغيرة، مما يجعلها أكثر فعالية في علاج مرضى الالتهاب المفصلي الصفدي.

نتائج البحث: أظهرت دراسة حديثة أن هناك علاقة إيجابية بين الوجود أو عدم الوجود للنمو المشيمي في السائل الزالالي وزيادة في خصائص النمو المشيمي. وكانت الدراسة التي أُجريت على مرضى الالتهاب المفصلي الصفدي في مستشفى معين في المملكة العربية السعودية، حيث قُدرت نسبة الوجود أو عدم الوجود للنمو المشيمي في السائل الزالالي بنسبية 30%.

لذا فإن الوجمات فوق الصوتية ذات التردد العالي يمكن أن تكون أداة فعالة في الكشف عن النمو المشيمي في السائل الزالالي، ويمكن أن تكون أكثر دقة في علاج مرضى الالتهاب المفصلي الصفدي. وتُعد الوجمات فوق الصوتية ذات التردد العالي أيضًا أداة فعالة في التحكم في التدفق الدموي، والتعرف على الأوعية الدموية الصغيرة، مما يجعلها أكثر فعالية في علاج مرضى الالتهاب المفصلي الصفدي.