Atherogenic Index and Protein Fractions in Psoriasis

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ABSTRACT

Context: Psoriasis is a common non-contagious chronic inflammatory skin disorder characterized by patchy inflammatory lesion covered with silvery white scales. Its etiology is still unknown while genetic, metabolic and immunological mechanisms have been recommended as its cause. An increased ratio of triglycerides to HDL-cholesterol (TG/HDL-c) is considered a risk for the development of coronary heart disease is reported by several studies. Excessive shedding of scales from the skin in the course of disease causes loss of proteins. Objective: To estimate and compare atherogenic index in psoriatic patients and controls and to analyze the electrophoretic pattern of serum protein fractions in psoriatic patients and controls. Materials and methods: 50 patients with psoriasis of various degrees of severity and 50 age and gender matched non psoriatic subjects were included in the study. Serum lipid profile and serum total proteins and protein fractions was determined. Statistical analysis was done using SPSS software. Results: Atherogenic index showed statistically significant increase in psoriatic patients compared to normal individuals (p < 0.05). The mean serum total proteins showed statistically significant decrease due to decrease in albumin. However, the protein fractions showed statistically significant increase due to increase in α, β and γ globulins in psoriatic patients compared to normal individuals (p < 0.05). Conclusions: Meticulous follow up of dyslipidemia and protein levels with adequate protein supplementation throughout the course of the disease can go a long way in improving patient’s nutritional status and also can prevent the complications associated with hyperlipidemia and hypoproteinemia.

Key words: psoriasis, atherogenic index, protein fractionation.

INTRODUCTION

Psoriasis is a common non-contagious chronic inflammatory skin disorder characterized by patchy inflammatory lesion covered with silvery white scales. Its etiology is still unknown while genetic metabolic and immunological mechanisms have been recommended as its cause.

The biochemical basis for the pathogenesis of Psoriasis, which is an equal varied as the genetic basis can be attributed to both overexpression and underexpression of certain proteins in psoriatic lesions. The anomalies in protein expression can be divided into 3 areas: 1) Abnormal keratinocyte differentiation, 2) Hyperproliferation of keratinocytes and 3) Infiltration of the inflammatory Element.

The accelerated proliferation of basal keratinocytes, and an abnormal differentiation of spinous and granular keratinocytes results in incomplete differentiation. Hence in psoriasis, the stratum corneum is not formed correctly resulting in a defective barrier and the shedding of stratum corneum fragments in large sheets of scales / flakes. Studies of Weinstein and Frost revealed that the turn over time of cells in Psoriasis was reduced to 37 hours compared to 457 hours of normal epidermis.

Excessive shedding of scales from the skin in the course of disease causes loss of proteins thereby decreasing the total proteins, mainly leading to hypoalbuminemia. Since the course of the disease is chronic, the globulin fraction of the total proteins tends to increase. In severe cases there maybe reversal of Albumin: Globulin ratio. Electrophoretic separation of serum proteins in psoriasis presents a variable pattern of, α, α, β and γ globulin fractions.

Abnormalities in lipid metabolism have also been considered to play an important role in the pathogenesis of psoriasis and patients with psoriasis may have increased risk of arterial and venous occlusive diseases. Although changes in plasma lipid composition in psoriatic patients have been suggested
as being the cause of the increased risk of atherosclerosis in these patients, many of the results remain controversial. Atherogenic Index (AI) defined as log (TG/HDL-c in mmol/l) has recently been proposed as a marker of atherogenicity, was found to be increased in psoriatic patients. The atherogenic index has proven to be a highly significant risk factor of myocardial infarction, even stronger than TC/HDL-c and LDL-c/HDL-c. The Copenhagen Male Study showed triglycerides on their own to be another strong risk factor, but it found that stratifying triglyceride levels by HDL-c levels led to more accurate detection of increased risk of coronary disease.

The link between Psoriasis and cardiovascular disease has been reported in several studies. Recent evidence strongly suggest that chronic inflammation, a characteristic feature of Psoriasis per se may play an important role in initiation and progression of Dyslipidemia and Atherosclerosis.

MATERIALS AND METHODS

The study was carried out in the Department of Biochemistry in association with Department of Dermatology and Medicine, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda District, AP, India, after the approval of the institutional ethical committee, from October 2007 to September 2009.

PATIENTS INCLUSION CRITERIA:

50 patients with psoriasis of various degrees of severity. Patients not on systemic regime for psoriasis or any other disease. The percentage of the body surface with psoriasis was lower than 25% in all the patients. The percentage was determined by using the rule of nine. Wallace rule of nine is used to assess the percentage of body surface area involved in disease. Rule of nine divides the body surface area into multiples of nine and is used as a rule of thumb to allow a quick calculation of the total body surface area involved in disease process. It is a good method for measuring medium to large involved area but it does tend to overestimate the diseased area.

Patient exclusion criteria: Patients suffering from psoriatic erythroderma. Patients with diseases that can cause secondary hyperlipidemia such as hypothyroidism, diabetes mellitus, nephrotic syndrome, chronic renal insufficiency, obstructive liver disease and connective tissue disorder and patients on medications such corticosteroids, retinoids, cyclosporin and lipid lowering agents were excluded. Patients with diseases that can cause secondary hypolipidemia and hypoproteinemia such as malnutrition, liver failure, malabsorption syndromes and hyperthyroidism were excluded. Patients with diseases that can cause secondary hyperproteinemia were also excluded.

Control inclusion criteria: 50 age and gender matched non psoriatic subjects who were not suffering from any medical or surgical illnesses were included in the study.

Control exclusion criteria: Healthy controls with a family history of psoriasis were excluded from the study.

After a 8-10hr fasting period, 5ml venous blood was taken in the morning from all the subjects.

The statistical analysis was performed using SPSS software 11.0 version. The descriptive results are expressed as mean and standard deviation, significance of difference between the patients and control groups observed is assessed by using the unpaired student’s t test. The p value is expressed along with mean values and standard deviation. The p value less than 0.05 were considered statistically significant.

Serum Total Proteins were analysed by Biuret method. Serum Albumin was analysed by Bromocresol green method, Serum Total Cholesterol, Triglycerides and HDL Cholesterol were analysed by enzymatic colorimetric method using Semiautoanalyzer.

Serum LDL Cholesterol values were calculated according to Friedwalds formula. Serum VLDL was calculated by dividing serum Triglycerides by 5. (TGL/5).

Serum protein electrophoresis was done using Agarose gel. Quantitation of electrophoresis slides was done using Platinum Helena (1) Software.

RESULTS

Table 1: In our study shows that the age and sex distribution among psoriatic patients is more in age group of 41-60 years. In the age group of 0-20 and 81-100 there were no female patients.

Table 2: In our study shows that there is no significant difference of age between patient and control group, (p > 0.05)

Table 3: The study shows that psoriasis is more common in males than females.

Table 4: In our study, Mean and SD of serum total proteins showed statistically significant decrease in psoriatic patients compared to normal individuals (p < 0.05), and protein fractions showed statistically significant increase(except Serum α1 globulin, p > 0.05) in psoriatic patients compared to normal
Table 1: Age and Sex Distribution among Cases and Controls. N = 100

<table>
<thead>
<tr>
<th>RANGE: AGE (years)</th>
<th>CASES</th>
<th>CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MALES n=50</td>
<td>FEMALE n=9</td>
</tr>
<tr>
<td>0 – 20</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>21 – 40</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>41 – 60</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>61 – 80</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>81 – 100</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Mean and SD of age among cases and controls. N=100

<table>
<thead>
<tr>
<th>Age in years</th>
<th>CASES n = 50</th>
<th>CONTROL n = 50</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>19-85</td>
<td>21-85</td>
<td>0</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>48.12 ± 14.52</td>
<td>55.9 ± 14.80</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

Table 3: Sex distribution among cases and controls. N=100

<table>
<thead>
<tr>
<th>GENDER</th>
<th>CASES n = 50</th>
<th>CONTROL n = 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALES</td>
<td>41</td>
<td>41</td>
</tr>
<tr>
<td>FEMALES</td>
<td>9</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 4: Mean and SD of serum total proteins and protein fraction among cases and controls. N=100

<table>
<thead>
<tr>
<th>PARAMETERS (With normal values)</th>
<th>CASES n = 50 (Mean ± SD)</th>
<th>CONTROL n = 50 (Mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total proteins (6-8 gm/dl)</td>
<td>7.07 ± 0.56</td>
<td>7.30 ± 0.47</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Albumin (3.5-5 gm/dl)</td>
<td>4.05 ± 0.49</td>
<td>4.52 ± 0.40</td>
<td>&lt; 0.010</td>
</tr>
<tr>
<td>Total globulin(2.5-3.5 gm/dl)</td>
<td>3.01 ± 0.27</td>
<td>2.78 ± 0.37</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>α1 globulin(0.3-0.5 gm/dl)</td>
<td>0.53 ± 0.12</td>
<td>0.53 ± 0.12</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>α2 globulin(0.4-0.8 gm/dl)</td>
<td>0.89 ± 0.11</td>
<td>0.79 ± 0.16</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>β globulin(0.6-1.1 gm/dl)</td>
<td>0.68 ± 0.12</td>
<td>0.63 ± 0.12</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>γ globulin(0.8-1.8 gm/dl)</td>
<td>0.91 ± 0.16</td>
<td>0.83 ± 0.11</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Albumin:Globulin ratio</td>
<td>1.32 ± 0.21</td>
<td>1.64 ± 0.32</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
individuals (p < 0.05). The A:G ratio was also statistically decreased in cases compared to controls (p < 0.001).

Table 5: In our study, Mean and SD of serum total cholesterol, serum LDL, serum VLDL, serum Triglycerides, risk ratio and Atherogenic index showed statistically significant increase in psoriatic patients compared to normal individuals (p < 0.05), whereas Serum HDL showed no statistically significant decrease in psoriatic patients compared to controls (p > 0.05).

Figure 3: In our study, Mean and SD of serum total cholesterol, serum LDL, serum VLDL, serum Triglycerides, risk ratio and Atherogenic index showed statistically
significant increase in psoriatic patients compared to normal individuals \((p < 0.05)\), whereas Serum HDL showed no statistically significant decrease in psoriatic patients compared to controls \((p > 0.05)\).

**DISCUSSION:**

Psoriasis is a common non-contagious chronic inflammatory skin disorder characterized by patchy inflammation lesion covered with silvery white scales.\(^1\) Its etiology is still unknown while genetic metabolic and immunological mechanisms have been recommended as its cause.\(^2\)

High protein loss through scaling in psoriasis possibly due to high cell turnover which is further exacerbated due to inflammation has been reported. Studies done by Kanthraj et al.\(^5\) showed that serum total protein level is inversely proportional to the amount of protein loss through scaling, severity and duration of the disease.

Our study showed statistically significant decrease in Serum total protein levels in psoriatic patients \((7.07 \pm 0.56)\) compared to normal individuals \((7.30 \pm 0.47)\) \((p < 0.05)\). The levels of Serum albumin were also significantly decreased in psoriatic patients \((4.05 \pm 0.49)\) compared to normal individuals \((4.52 \pm 0.40)\) \((p < 0.001)\). The statistically significant increase in total globulin levels in psoriatic patients \((3.01 \pm 0.27)\) compared to normal individuals \((2.78 \pm 0.37)\) \((p < 0.05)\), found in our study was in consistent with the study done by Bhatnagar et al.\(^6\) (Table no.6).

Electrophoretic separation of serum proteins in psoriasis presented a variable pattern of serum \(\alpha_1\), \(\alpha_2\), \(\beta\) and \(\gamma\) globulin fractions. A little higher \(\alpha_2\) globulin but significantly higher \(\beta\) and \(\gamma\) globulin as compared to controls was a significant observation in the study done by Bhatnagar.\(^6\) Our study showed similar results with statistically significant increase in alpha\(_4\) globulin, beta globulin and gamma globulin levels \((p < 0.05)\) in psoriatic patients compared to normal healthy controls, however there was no statistically significant change in alpha\(_1\) fraction \((p > 0.05)\). The total globulin fraction was statistically significantly increased in psoriatic patients compared to controls \((p < 0.05)\). The Albumin: Globulin ratio was statistically significantly decreased in cases \((1.32 \pm 0.21)\) compared to controls \((1.64 \pm 0.32)\) in our study (Table no. 6).

**PREVIOUS STUDIES ON LIPIDS IN PSORIASIS**

Many previous studies have shown an aberrant lipid profile associated with Psoriasis. Table no.7 depicts comparison of serum lipid profile in present study with that of similar other studies.

Mallbris et al. in a study on 200 psoriatic cases proved that there was higher serum total cholesterol, HDL-c, LDL-c,
triglycerides and VLDL levels corresponding to normal control group.\textsuperscript{1} Piskin in his study on 100 psoriasis cases showed serum total cholesterol and LDL cholesterol levels to be significantly higher than that of control group, but HDL-c and triglycerides showed no statistical difference between patients and controls.\textsuperscript{1}\textsuperscript{11}

Rocha-preira reported increase in serum cholesterol, serum triglyceride, VLDL, LDL, apolipoprotein B, lipoprotein A values and decrease in serum HDL values in psoriatic patients compared to normal controls.\textsuperscript{7} Vahlquist et al. reported significant increase in Serum total cholesterol, LDL-c, VLDL, triglycerides in psoriatic patients but the HDL-c shown to be significantly decrease in patients when compared to normal controls.\textsuperscript{12}

Collectively in various studies, serum cholesterol level of psoriatic patient was high,\textsuperscript{7, low}\textsuperscript{15} and has even been reported normal\textsuperscript{16} but it was significantly higher in cases (191.32 ± 40.03) than control group (159.37 ± 37.39) in our study (p < 0.001). Serum triglyceride level have been reported to be high\textsuperscript{7}, low\textsuperscript{15} and normal\textsuperscript{16} in different studies. Serum triglyceride level of patient were significantly higher in cases (135.46 ± 22.44) than normal group (116.08 ± 41.60) in our study (p < 0.05). This dissimilarity was also observed for HDL and VLDL. HDL level of cases (39.56 ± 3.05) found in our study was not significantly different compared to controls (40.24 ± 8.15) (p > 0.05). LDL-c was normal\textsuperscript{7} or high\textsuperscript{11} in different assays and we found higher results in cases (124.71 ± 35.69) compared to controls (96.10 ± 34.79) (p < 0.001).

Hypertriglyceridemia secondary to VLDL elevation is associated with both procoagulant and prothrombotic factors in the blood. VLDL mediated platelet adhesion may play an important role in atherosclerosis. Furthermore, VLDL remnants are susceptible to retention within the arterial intima, thereby promoting atherosclerotic plaques growth.

Atherogenic Index (AI) defined as log (TG/HDL-c in mmol/l) has been proposed as a marker of atherogenicity and has proven to be a highly significant risk factor of myocardial infarction, even stronger than TC/HDL-c and LDL-c/HDL-c. It was found to be increased in psoriatic patients in the present study. The mean and SD of Atherogenic index (log TG/HDL mmol/l) was 0.17 ± 0.07 in cases and 0.08 ± 0.20 in controls. There was a statistically significant increase Atherogenic index (log TG/HDL mmol/l) in cases compared to controls. (p < 0.001).

A predisposition to occlusive vascular disease has been reported in patients with psoriasis and it has been suggested that some patients with psoriasis have some disorders of lipid metabolism. This predisposition seems to be related to the severity of psoriasis.\textsuperscript{7} However the severity of psoriasis in our patients was not classified.

The variety of data on lipid profile presented in different studies may be due to the fact that the patients included in statistical analyses suffer from different forms of psoriasis such as localised plaque psoriasis, pustular psoriasis or erythroderma and they may be undergoing various forms of treatments, but our patients had no erythroderma or generalized pustulosis. Furthermore they were not on any medical treatment.

The link between psoriasis and cardiovascular disease has been reported by several studies. Although the pathogenesis of increased cardiovascular events in patients with psoriasis remains to be established, there are several possible biological factors which may explain such a link. Firstly, psoriasis appears to be associated with traditional risk factors for cardiovascular disease, including increased BMI, hypertension, hyperlipidemia, Type II diabetes and cigarette smoking.\textsuperscript{17} Secondly, recent evidence strongly suggests that chronic inflammation, a characteristic feature of psoriasis, per se may play a role in the initiation and progression of dyslipidemia\textsuperscript{18} and atherosclerosis.\textsuperscript{19} Finally, there is evidence that established treatments for psoriasis such as cycloporin and retinoid\textsuperscript{12} may induce hyperlipidemia which can promote future Cardio vascular disease.

The cause for changes in lipid metabolism in psoriatic patients is not clearly explained in the literature, Functional and structural abnormalities in almost all parts of gastrointestinal system have been observed in psoriatic patients.\textsuperscript{11} However, the abnormalities of the digestive system may be attributed to dermatogenic enteropathy.\textsuperscript{20}

**CONCLUSION**

The protein loss occurring through scaling and through gastrointestinal tract when severe, can result in negative nitrogen balance resulting in hypoaalbuminemia, edema and loss of muscle mass. Careful follow up of protein levels and adequate protein supplementation throughout the course of the disease can go a long way in improving patient's nutrition status and also can prevent the complications associated with hypoproteinemia.

Atherogenic Index (TG/HDL-c in mmol/l) which has recently been proposed as a marker of atherogenicity was found to be increased in psoriatic patients. Hence Triglycerides and HDL-c should be regularly assayed and monitored in psoriatic patients at presentation and during follow-up.
Management of dyslipidemia should be considered as a part of cardiovascular risk management in psoriatic patients. It can be possible that tight disease control lowers the cardiovascular risk in patients with psoriasis and may also have some beneficial effects on lipid profile. In addition cardiovascular risk factor screening and appropriate treatment is necessary for evaluating and controlling the risk to atherosclerosis and vascular obstructive disorders in patients with psoriasis.

ACKNOWLEDGEMENT

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