

## THESIS ABSTRACT

### Psoriasis: Paraoxonase and Lipoprotein (a) Role

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**Background:** Psoriasis is a common chronic skin disorder with prevalence of 2.7% in Iraqi community. Psoriasis is a skin disease that its prevalence is affected by many factors which include genetic, environmental, infectious, immunological, biochemical, endocrinological and psychological. Psoriasis is a chronic inflammatory disease with unknown exact pathogenesis, which may be started as a skin condition that subsequently associated with systemic complications. The recurrent proliferative inflammatory processes in subjects with psoriasis may lead to abnormal lipid metabolism and associated with cardiovascular diseases.

**Aim:** This study aims at determining some biochemical parameters of psoriasis.

**Results:** Paraoxonase enzyme which acts as an antioxidant was significantly decreased in patients with psoriasis as compared to healthy controls. Thus the present study data suggest that PON 1 plays an important role in the pathogenesis of psoriasis. There was a high significant increase of lipoprotein (a) compared with controls. Lipoprotein (a) may be a risk factor contributing to an increased cardiovascular risk in patients with psoriasis. The frequency of positivity of CRP as inflammatory markers of psoriasis was significantly more in patients with psoriasis as compared to controls. Although, reported studies suggest that increased levels of CRP in psoriasis may be a good assessment of disease severity and prognosis, however, there are some discrepancies in this area. But PASI and CRP are good predictors of psoriasis severity. A non-significant difference in the serum mean of fasting blood level between patients with psoriasis relative to controls. All lipid profiles (cholesterol, triglyceride, HDL, LDL, VLDL, and NHDL) were significantly higher in psoriasis patients compared to controls. While HDL was significantly lower in patients with psoriasis than in controls. In addition, the differences between male psoriasis and male controls were significant. The same pattern was demonstrated for comparison of female psoriasis to female controls.

Lipid profile, lipoprotein (a) and paraoxonase indices were at least twice higher in patients with psoriasis than those in controls. In addition, the total sum of these 9 rates (indices) was 18.23 in controls, while it was 57.33 in psoriasis patients, indicating a 214% higher difference between the two groups. This finding suggests

that patients with psoriasis are prone for development of cardiovascular disease. Lipid profile, Lp(a) and PON1 ratios were significantly higher (> twice) in patients with psoriasis than in control. This illustrates the high discriminatory power for the risk in psoriasis for coronary heart disease presented by these ratios, as their predictive capacity. Thus this study findings confirmed that patients with psoriasis are prone to develop cardiovascular events.

Lp(a)/HDL, Lp(a)/PON, TC/HDL, and NHDL/HDL were with higher predictivity as risk factors in patients with psoriasis compared to other rates. However, this study finding shows that TC/PON, NHDL/PON and TG/HDL were significantly with good predictivity for determination of risk factors for development of cardiovascular disease in psoriasis. Although, on individual basis, Lp(a)/HDL is the biomarker excellent predictivity (10.25 in psoriasis versus 1.5 in controls), followed by TC/HDL, NHDL/HDL, and TC/PON. The using of overall atherogenic index that is determined by sum of all ratios is with more significant predictivity as reported before. Furthermore, the present study add another 6 indices that can be used as biomarkers of cardiovascular risk development in psoriasis. These indices include: Lp(a)/HDL, Lp(a)/MON, LDL/PON, NHDL/PON, TC/PON, TG/PON. These finding suggest that ratios were more predictive than using the serum concentration of individual net figures such as total cholesterol, NHDL, and LDL.

The increase of lipoprotein (a) is an atherogenic oxidative marker, while PON 1 is an anti-atherogenic antioxidant marker. The high frequency of CRP positivity that associated with reduced PON 1 in our psoriasis studied cases suggest relationship between PON1 activity and inflammation in psoriasis. TC/HDL was with highly significant relative risk indicating that the rate is better than total or LDL cholesterol in determining risk of CVD development in patients with psoriasis. But was with predictive value when the lipid profile is within desirable range. Total cholesterol and LDL cholesterol are closely correlated since about 2/3 of total cholesterol found in LDL and so LDL/HDL cholesterol ratio was similar to TC/HDL ratio as with predictivity in assessment of CVD. High TC/HDL and LDL/HDL is a reflection of the imbalance between protective and atherogenic lipoproteins and thus have a higher CVD risk. The present study added Lp(a)/HDL, Lp(a)/MON, LDL/PON, NHDL/PON, TC/PON, TG/PON indices and shift of their value toward left side is an indication of imbalance between oxidative and antioxidative status, reflecting oxidative damage. While the shift toward right side is an indication of antioxidative and anti-inflammatory responses.

The ratio of log TG/HDL reflect the balance between atherogenic and protective lipoprotein. This ratio was correlated positively with the HDL esterification rate and an inversely correlated with LDL size. This ratio as this study indicated, was with a value of 2 times in psoriasis patients than in controls. This ratio is a reflection of overall lipoprotein metabolism and predict atherogenicity. The ratio of log TG/PON was 2.8 times in psoriasis than in control and TG/PON was 4.33 in patients with psoriasis and 1.76 in controls. The reduction in this ratio is an indication of good antioxidant activity, while its increase is an indication of inflammatory process. NHDL/HDL ratio was with 2<sup>nd</sup> rank (6.13) in the conventional rates (TC/HDL, TG/HDL, LDL/HDL and NHDL/HDL) following TC/HDL (7.13). However, the present study shows the superiority of Lp(a)/HDL (10.25) and Lp(a)/PON (8.47) over TC/HDL (7.13) and NHDL/HDL (6.13).

NHDL is the surrogate marker for apoB and with apoB form a risk factor better predictors of cardiovascular events than LDL. But calculation of NHDL can be performed easily and cost effective and reflect the amount of apoB and LDL

atherogenicity in hypertriglycemic subjects. Inflammatory and dyslipidemia biomarkers used in this study confirmed that psoriasis are at risk factor for development of cardiovascular disease. Gender seems not influence the levels of paraoxonase, lipoprotein (a), CRP, fasting blood level, total cholesterol, triglyceride, HDL, LDL, VLDL, and NHDL in patients with psoriasis and controls. Paraoxonase serum levels in male compared to female were not with significant differences in patients with psoriasis and controls. A significant inverse correlation between paraoxonase and lipoprotein serum levels in patients with psoriasis was found. These inverse correlation indicated the imbalance between oxidative stress and antioxidant capacity in patients with psoriasis. The positive correlation between lipoprotein (a) and disease severity as this study indicated confirmed the association between oxidative stress and disease comorbidities.

The present study support the significance of lipoprotein (a) as a potential cardiovascular risk factor in psoriasis as it was significantly higher in cases compared to controls. In addition, inverse correlation between paraoxonase 1 and Lp(a) serum levels, Lp(a)/HDL, Lp(a)/PON, TC/HDL. and NHDL/HDL another risk factors that support their association with development of CVD in patients with psoriasis. Our study findings provide evidence that increased lipoprotein (a) and decreased paraoxonase 1 levels occur more frequently in psoriasis patients than in controls.

The present study indicated a positive correlation between lipoprotein (a) levels and disease severity which suggests that abnormal elevation levels of lipoprotein (a) may be linked to psoriasis pathogenicity. Thus this correlation suggests that there may be a physiologic link between lipoprotein (a) and psoriasis specific processes. Antipsoriatic therapy studies provide indirect evidence for the link between lipoprotein (a) and paraoxonase serum levels and psoriasis disease pathogenicity. Paraoxonase 1 reduced significantly in patients with psoriasis to that in healthy controls as this study indicated. Indices of Lp(a)/ PON, LDL/PON, NHDL/PON, TG/PON and TC/PON were significantly increased in psoriasis suggest presence of oxidative stress / antioxidant capacity imbalance which may contribute to pathogenicity of psoriasis.

**Conclusions:** Thus the present study findings indicated dyslipidemia in our studied psoriasis population and decreased antioxidant capacity and increased oxidative stress as demonstrated by decreased PON 1 and increased Lp(a) in psoriasis suggest role of oxidative stress and dyslipidemia in psoriasis comorbidities. Lipid profile rates, Lp(a)/HDL, LDL/PON, NHDL/PON, TG/PON, and TC/PON were highly significant risk factors in individuals with psoriasis. However, the highest relative risk was achieved by calculating the rates of Lp(a)/HDL in psoriasis. This may a risk biomarker for development of cardiovascular disease in patients with psoriasis, but it needs evaluation in a large scale study. Imbalance between oxidative stress and antioxidant capacity and its association with abnormal lipid metabolism play a role in psoriasis pathogenesis.

**Key words:** Psoriasis, paraoxonase, lipoprotein (a), CRP, Cholesterol, HDL, LDL, VLDL, NHDL and triglyceride.