Evalution of liver function tests in patients with psoriasis

Evaluación de pruebas de función hepática en pacientes con psoriasis

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Abstract

Abnormal liver function tests are often seen in patients with Psoriasis (PS). This study was undertaken to examine the alanine aminotransferase (ALT; aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyltransferase (GGT), albumin) bilirubin in patients with Psoriasis.

Blood samples were collected from all patients with PS and healthy between 8 and 11 AM, after fasting overnight. ALT, ALP, GGT, albumin, bilirubin levels in each of the cases have been measured by spectrophotometric kit. There was a significant increase in serum ALT, ALP, GGT, while significant decreas in albumin, bilirubin levels in PS group when compared with healthy controls

Conclusion: Liver abnormalities are common among PS patients and are associated with oxidative stress, more severe disease and certain therapies.

Keywords: liver function tests, Transaminasese, pyridoxal-5'-phosphate-dependent enzymes

Resumen

Las pruebas de función hepática anormales a menudo se observan en pacientes con psoriasis (PS). Este estudio se realizó para examinar la alanina aminotransferasa (ALT; aspartato aminotransferasa (AST), fosfatasa alcalina (ALP), γ-glutamiltransferasa (GGT), albúmina) bilirrubina en pacientes con Psoriasis.

Se recogieron muestras de sangre de todos los pacientes con PS y sanos entre las 8 y las 11 de la mañana, después de ayunar durante la noche. Los niveles de ALT, ALP, GGT, albúmina, bilirrubina en cada uno de los casos se han medido mediante kit espectrofotométrico. Hubo un aumento significativo en los niveles séricos de ALT, ALP, GGT, mientras que hubo una disminución significativa en los niveles de albúmina y bilirrubina en el grupo de PS en comparación con los controles sanos.

Conclusión: Las anomalías hepáticas son comunes entre los pacientes con SP y están asociadas con el estrés oxidativo, la enfermedad más grave y ciertas terapias.

Palabras clave: pruebas de función hepática, transaminasas, enzimas dependientes de piridoxal-5'-fosfato

Introduction

Liver is one of the largest organs, located in the right upper quadrant of the body and below the diaphragm. Due to its unique position in the human body, the liver is exposed to a vast array of agents including alcohol and drugs, as well as pathogens that may able to impair its function[1-4].

Serum measurements of liver-derived enzymes, non enzymatic proteins, and metabolites of liver metabolism (colloquially known as liver function tests (LFTs)) which is a misnomer as many of the tests do not comment on the function of the liver and are perceived to be inexpensive, are checked ever more frequently in both primary and secondary care in an attempt to exclude liver disease, for the monitoring of potential adverse effects of drugs on the liver, and for the investigation of the generally unwell patient. These tests often produce an abnormal result, the clinical significance of which is unclear. The standardized batch of LFTs usually comprises alanine aminotransferase (ALT; and sometimes, aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyltransferase (GGT), and other nonenzymatic proteins (eg, albumin) and metabolites of heme metabolites, such as bilirubin[5-7].

Transaminasese are ubiquitous pyridoxal-5′-phosphate-dependent enzymes that catalyze reversible transfer of amino group from amino acids to α-keto acids. The transaminase reaction and identified 2 aminotransferases as most metabolically active - AST; EC 2.6.1.1; and ALT; EC 2.6.1.2[8,9].

Both ALT and AST catalyze the transfer of an amino group from an amino acid to αketoglutarate. The amino acids are L-alanine and L-aspartate and the reaction products are L-glutamate and either pyruvate or oxaloacetate, respectively.The overall effect is exchange of an amino group and a keto group. Pyridoxal 5′-phosphate serves as a coenzyme in both reactions[10].

In a normal person as well as most patients with liver disease, ALT is higher than AST. There are two reasons for the higher ALT levels: first, ALT is present in the cytoplasm and is released by minor injuries; second, ALT has a longer half-life than AST and life than AST and hence remains in the blood for a longer time. It is common practice to look at the ALT/ AST ratio though it has a limited role in the diagnosis and management of liver diseases. Normal ALT levels are higher than AST levels[11-13].

Gamma-glutamyl transferase (GGT) is an enzyme present in serum and on the outer surface of cells from different organs such as the the kidney, liver, spleen, pancreas, small intestine, seminal vesicles, biliary tract, and so on. Its content is the highest in the kidney, followed by the liver.GGT in the liver is mainly located in the capillary side of the liver cells and the membrane of the bile duct epithelial cells[14,15]. Oxidative stress upregulates intracellular GGT level, and thus intracellular GGT level can be considered a biomarker for oxidative stress associated with GSH metabolism[16].

A possible mechanism for the association between GGT level and lver damage is the role of GGT in intracellular antioxidant defense systems in relation to the main functionof modulating intracellular glutathione level[17].

These increased levels of GGT enhance free radicals and mitochondrial damage, increase transport of glutathione into cells which can cause severe proinflammation and oxidative stress. It was pointed out that GGT was regarded as an oxidative stress marker[18].

Alkaline phosphatase (ALP) is a membrane-bound metalloenzyme with phosphorylation properties and exists as many isozymes. Each isoenzyme is a glycoprotein encoded by different gene loci. At least four loci have been identified: tissue nonspecific, intestinal, placental, and germ cell ALP[19]. ALP catalyzes the hydrolysis of phosphomonoesters with releasing 8of inorganic phosphate (Pi) as well as hydrolyzing inorganic pyrophosphate (PPi) as pyrophosphatases. Pyrophosphate, a potent inhibitor of medial vascular calcification, is controlled by hydrolysis via a tissue-nonspecific ALP[20]. It is produced by various tissues including the in mucosal epithelia of small intestine, proximal convoluted tubule of kidney, bone, liver and placenta. The serum ALP activity is mainly from the liver with 50% contributed by bone[21].

Creatine kinase (CK) is the enzyme responsible for catalyzing the transfer of high-energy phosphate from creatine phosphate to adenosine triphosphate.

CK is involved in mitochondria and cytosol in muscle cells. The dimeric enzyme, consisting of two subunits, M and B, has three isoenzymes: CK-BB (CK1), CK-MB (CK2), and CK-MM (CK3). CK-MM is the dominant form found in all tissue. CK-BB is present in the brain, kidney, and gastrointestinal tract. CK-MB can be found in the heart, skeletal muscle, small intestine, diaphragm, uterus, tongue, and prostate. The CK-MB isoenzyme, which is normally undetectable or very low in the blood, increases in both heart and skeletal diseases by showing highest concentration in cardiac muscle (~22% of the total CK content of myocardium compared to ~1–3% in the skeletal muscle).

CK-MB isoenzyme activity is useful as it is an index for the initial diagnosis of any type of myocardial injury. Leakage of CK-MB into the circulation may occur when cell membranes become more permeable or rupture due to injury or oxidative stress. The amounts of this cellular enzyme in the serum reflect the alterations in myocardial plasma membrane integrity and/or permeability[22,23].

Albumin is a single protein species and the most abundant plasma protein representing approximately 3/5 in quantity is an anionic, flexible, heart-shaped molecule with a mo-

lecular weight of 66.5 kDa. Structurally, albumin contains three homologous alpha helical domains I, II and III. Each domain is comprised of two subdomains A and B, which comprise four and six alpha-helices, respectively[24-26].

Albumin is exclusively synthesized by hepatocytes at a rate of roughly 150 mg/kg/day with approximately 10–15 g of albumin produced and released in the vascular space daily, has a half-life of approximately 3 weeks. The rate of synthesis is dependent on the body's needs and on alterations in colloid osmotic pressure, as well as osmolality of the hepatic extravascular space[27]. Albumin is a negative acute phase protein known to be a carrier of a wide variety of both endogenous and exogenous compounds owing to its hydrophobic binding pockets facilitates the colloidal solubilization and transport of hydrophobic molecules such as fatty acids and steroids as well as different drugs. Furthermore, the surface of albumin is negatively charged making it highly water-soluble[28-30].

Materials and methods

This is a cross sectional, hospital based study. The protocol of this study was approved by the scientific committee of Tikrit University College of medicine, the agreement of attendance to, Kirkuk general hospital that approved by Kirkuk health directorate, to collect the samples from the patients. and Baghdad governorate in Medical City Hospital This study was carried out from 1st January 2022 to 30th June.

Blood samples were obtained from the patients and control. Blood samples of 5 ml were taken from antecubital vein puncture. The blood sample obtained from each subject was transferred into gel tube for separation of serum. Then blood in the gel tubes were then allowed to clot at room temperature (25˚C) for 30 minutes. After that centrifugation was done at (4000) rpm for 10 minutes to separate the serum. The serum of each patient and control was divided and stored in to 3 small tubes and immediately 3 test was done then the rest stored at -80˚C until the time of analysis to avoid thawing and refreezing. Thawing of the samples was allowed to take place at 25˚C before conducting the assay.

Study patients

This study included 90 adult participants divided into two groups:

Case group: Includes 62 patients diagnosed with psoriasis by a Consultant Dermatologist. 30 males (60%) and 20 females (40%) with a mean of age of 39.46±14.612 years,

Control group: The control group consists of 40 volunteers, 20 males (50%) and 13 females (50%), with a mean of age of 37.50 ±11.33 years

A detailed medical, general and family history was taken along with a detailed consent form from the study subjects.

Psoriasis patients were further graded according to the Psoriasis Area and Severity Index (PASI)that is usually implemented to measure the condition of skin changes[32].

The serum concentrations of T-bil, TP, albumin, GLB, ALT, AST, ALP, CK, were detected by an automatic biochemical analyzer (ERBA XL 600®) according to the manufacturer's instructions for the corresponding commercial kits.

Statistical analysis

Welch's t-test was used, which has higher statistical power than Student's t-test when the two samples have unequal variances and unequal sample sizes (Ruxton, 2006). Cohen's standard was used to evaluate the strength of the relationships, where coefficients between .10 and .29 represent a small effect size, coefficients between .30 and .49 represent a moderate effect size, and coefficients above .50 indicate a large effect size (Cohen, 1988).

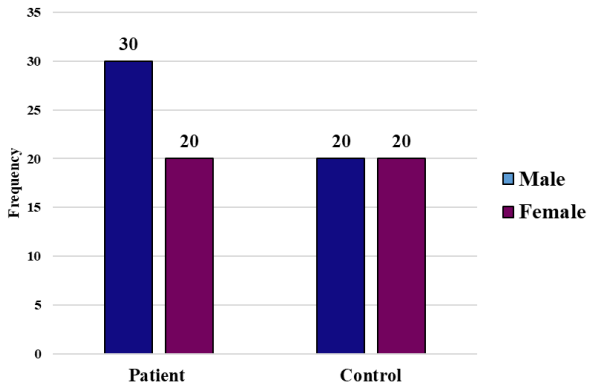
Results

A total of 50 diagnosed cases of (the disease name) aged between to years, and 40 age and sex matched controls were included in the study to assess the role of liver enzymes with lipid profilre in in patients with Psoriasis and healthy individuals

Table 3-1 Sex frequency and percentages by groups.

	Gender		
group	Female	Male	total
Control	20 (50.0%)	20 (50.0%)	40 (44.4%)
Patient	20 (40.0%)	30 (60.0%)	50 (55.6%)
total	40(44.4%)	50(55.6%)	90
Chi-squared	0.890		
DF	1		
Significance level	P = 0.3455		

Figure 3-1 Sex distribution according to Psoriasis and healthy individuals



There was not a statistically significant difference between the groups in terms of the genders that were already matched X^2 (1) 0.890 P = 0.3455. out of 50 patients, males made up 60% of cases, while females made up 40%. Among the healthy individuals, males and females each made up 50 percent of the sample size. Table 3-1 and (Figure 3-1) include both a frequency and a percentage breakdown of the data.

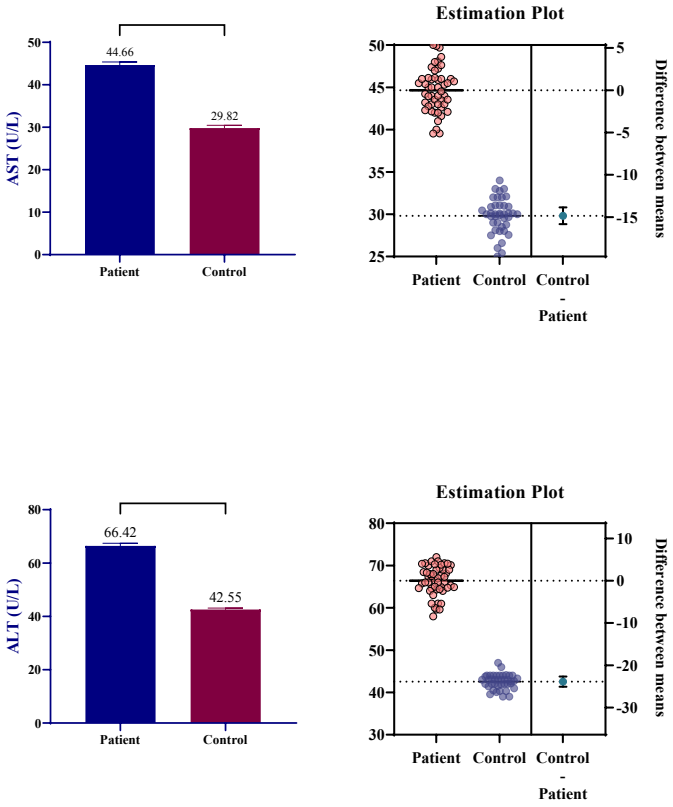
Table 3-2 Summary Statistics Table for liver functions biochemical markers as compared by groups using Two-Tailed Independent Samples t-Test

	Patient	Control	t	p	d
Variable	*M± SD*	*M± SD*			
AST	44.66± 2.55	29.82± 2.06	29.87	< .001	6.41
ALT	66.42± 3.46	42.55± 1.72	42.56	< .001	8.72
ALP	87.66± 4.08	73.47± 4.02	16.50	< .001	3.50
Albumin	3.66± 0.21	4.21± 0.37	-8.48	< .001	1.85
Globulin	3.43± 0.35	2.51± 0.24	14.85	< .001	3.08
LDH	226.06± 12.58	178.44± 6.10	23.53	< .001	4.82
GGT	40.26± 3.59	21.22± 1.45	34.20	< .001	6.96
T. bilirubin	11.26± 1.10	12.03± 1.00	-3.41	< .001	0.73

A comparison of the AST levels of psoriasis subjects with those of a control group was carried out (Table 3-2). When compared with the control group (29.82±2.06), the mean levels of serum AST in subjects with psoriasis were found to be significantly higher (44.66±2.55), with a t(75.02) value of 42.56, which indicated a significance level of p< .001. This finding suggests that the mean levels of AST in the Psoriasis group and the Control group were significantly different from one another. Table 3-2 present the results. Figure 3-2 illustrates a bar plot of the means of the variables.

The comparison of ALT of Psoriasis subjects with control group was carried out (Table 3-2). The mean levels of serum ALT were found to be significantly higher in Psoriasis subjects (66.42±3.46) when compared with control group (42.55±1.72), t(75.02)=42.56, p < .001. This finding suggests the mean of ALT was significantly different between the Psoriasis and Control groups. The results are presented in Table 3-2. A bar plot of the means is presented in Figure 3-2.

Figure 3-2 Bar plot of mean values with 95% CI error bars accompanied by Estimation plot with 95% Confidence intervals of mean differences between the groups for AST (Top) and ALT (bottom). **** Highly Significant at (p<0.0001).



The comparison of ALP of Psoriasis subjects with control group was carried out (Table 3-2). The mean levels of serum ALP were found to be significantly higher in Psoriasis subjects (87.66 ± 4.08) when compared with control group (73.47 ± 4.02), t(88) = 16.50, p < .001, This finding suggests the mean of ALP was significantly different between the Psoriasis and Control groups. The results are presented in Table 3-2. A bar plot of the means is presented in Figure 3-3.

The GGT had an average of (40.26± 3.59) for the Patient variable. The GGT had an average of (21.22 ±1.45) for the Control group, with t(67.56) = 34.20 and a significance level of p <.001. Based on these findings, it appears that the mean of GGT differed significantly between the Patient category and the Control category of groups. Table 3-2 contains the results. Figure 3-3 is a bar plot that illustrates the means and the means' estimation difference plot of the data.

Patients who suffered from psoriasis had a serum level of albumin that averaged 3.66 ±0.21, which was lower than the level of 4.21± 0.37 seen in the control group. The statistical comparison showed that there was a significant difference in the mean level of albumin between the Patient group and the Control group, with t(59.27) = -8.48 and a p < 0.001. The findings are presented in Table 3-2. The means of the variables are depicted in a bar plot,

which can be seen in Figure 3-4.

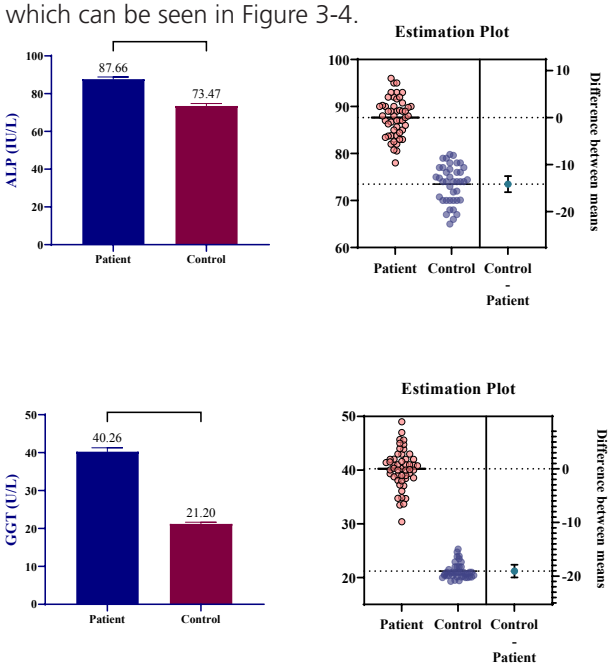
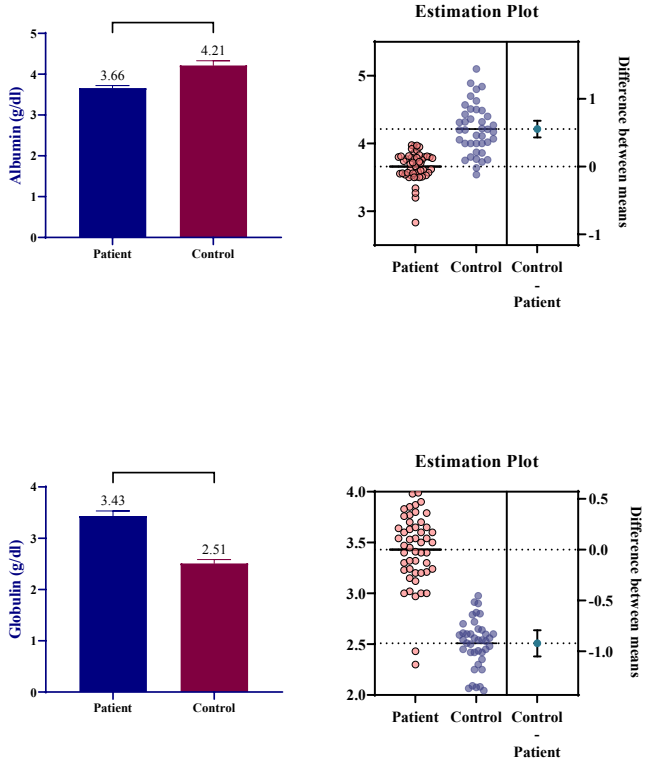


Figure 3-3 Bar plot of mean values with 95% CI error bars accompanied by Estimation plot with 95% Confidence intervals of mean differences between the groups for ALP (Top) and GGT (bottom). **** Highly Significant at (p<0.0001).

Patients with psoriasis had a serum level of LDH that averaged .43 ± 0.35 which was higher than that for Control 2.51 ± 0.24. The statistical comparison revealed that the mean level of LDH was significantly different between the Patient and Control groups, t(85.62) = 14.85, p < .001. The findings are detailed in Table 3-2. Figure 3-4 illustrates a bar plot of the means of the variables which can be found below



Patients with psoriasis had a total bilirubin level in their serum that averaged 11.26 with a standard deviation of 1.10. which came in below that of the Control 12.03 ±1.00. The statistical comparison revealed that the mean level of total bilirubin was significantly different between the Patient and Control groups, with t(88) = -3.41 and a p< .001. The findings are detailed in Table 3-2 above. Figure 3-5 illustrates a bar plot of the means of the variables which can be found below

Patients with psoriasis had a serum level of LDH that averaged 226.06 ± 12.58 which was higher than that for Control 178.44 ± 6.10. The statistical comparison revealed that the mean level of LDH was significantly different between the Patient and Control groups, t(74.01) = 23.53, p < .001. The findings are detailed in Table 3-2. Figure 3-5 illustrates a bar plot of the means of the variables which can be found below

Figure 3-4 Bar plot of mean values with 95% CI error bars accompanied by Estimation plot with 95% Confidence intervals of mean differences between the groups for Albumin (Top) and Globulin (bottom).. **** Highly Significant at p<0.0001

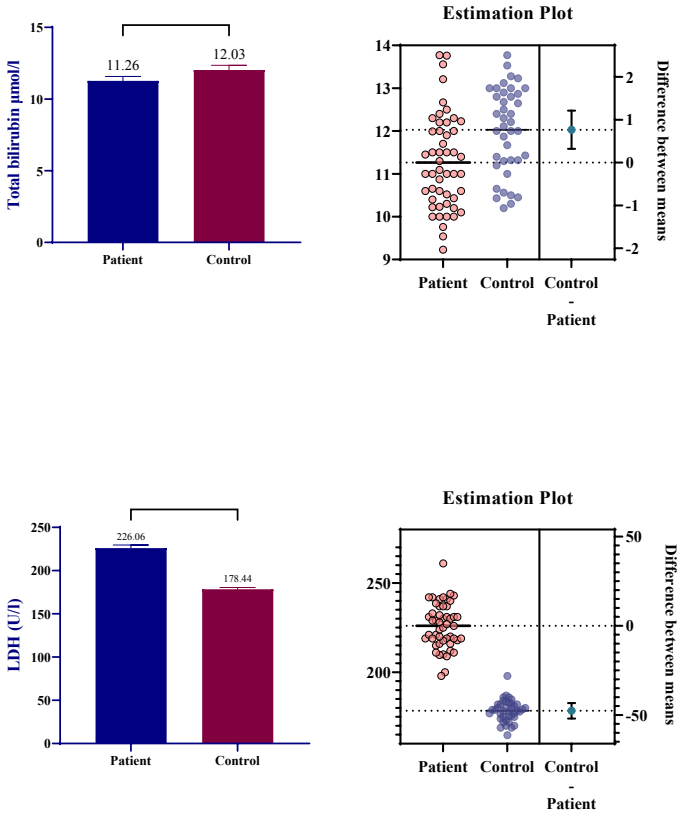


Figure 3-5 Bar plot of mean values with 95% CI error bars accompanied by Estimation plot with 95% Confidence intervals of mean differences between the groups for total bilirubin (Top) and LDH (bottom). ***Significant at the 0.001 level. ***** Highly Significant at 0.0001 (p<0.0001).

Discussion

Psoriasis is a multisystem disease that affects not only skin but also many other organs and interacts with metabolic syndrome, cardiovascular disease, diabetes, psychological disorders or inflammatory bowel disease. Psoriatic patients have a higher risk of liver abnormalities such as NAFLD, druginduced hepatitis, alcoholic hepatitis and neutrophilic cholangitis, than the general population[33]. In this study, we found liver dysfunction of psoriatic inpatients was common, particularly significantly high serum ALT, AST, GGT concentration in patients with psorasis versus healthy controls caused by due to intense systemic inflammation, mainly due to the leakage of these enzymes from the liver cytosol into the blood stream.

Alkaline Phosphatase ALP enzyme present in cell surface in most human tissues. associated with membrane lipid in canalicular ducts. The highest concentrations are found in the intestine, liver, bone, spleen and kidney. Impaired secretion of hepatic ALP may be accompanied by acute cell necrosis, so an increase in serum ALP activity indicates a biliary flow disturbance. Thus, extra and intrahepatic interference with the bile flow elevates ALP serum levels. Serum concentration of bilirubin is specific for possible serious liver damage or biliary obstruction and indicates loss of liver function[34,35]. Zinc and copper are an integral part of as many as 40 metalloenzymes, including alkaline phosphatase, and changes in their serum levels may reflect in changes in the activity of these enzymes. Researchers have noted that psoriatic lesions retain a high content of zinc compared with uninvolved skin suggesting an imbalance in zinc distribution between serum and psoriatic lesions. Exfoliation of large quantities of skin can thus decrease the serum levels of zinc[36].

Increased activation of ALP may play a role in a change of sebaceous lipid that mainly leads to comedogenesis. ALP is distributed in human sebaceous glands. Oxidative stress causes a distinct increase in ALP activity with cell toxicity in enterocyte which suggests that ALP activity may reflects the burden of oxidative stress. Thus, elevated level of ALP may reflect the increased burden of cutaneous or systemic oxidative stress which is known to the representative as a starter gun in However, whether level of serum ALP may have intercorrelation with the pilosebaceous ALP activity or burden of cutaneous or systemic oxidative stress should be validated though further studies[37]. [Jue MS, 2020].

Our study demonstrated that total protein and serum albumin levels were significantly decreased among psoriasis patients compared to controls, which is agreed with our findings[32,38-39]. Albumin is an important blood component, and its serum level reflects synthetic liver capacity. Moreover, albumin is a carrier for many biological substances, e.g., essential fatty acid transport from adipose tissue to muscles. Consequently, decreased albumin levels suggest significant liver dysfunction[34]. Albumin, which is synthesized by the liver, is a negative acute-phase protein and that shows decreased levels in acute inflammation, changes in total protein, reduced albumin levels in psoriasis patients have been attributed to to scales losing in the extensive lesion and increased turnover rates of keratinocytes lowered rates of albumin synthesis. Hypoalbuminemia in psoriasis patients may also be the result of increased endogenous catabolism of albumin by the liver and splenic dysfunction without significant loss through urine, stools, or skin. Increased uptake of albumin by liver and splenic macrophages has also been discussed as one of the potential mechanisms. The further biological study is needed to verify the mechanism of serum albumin changes in psoriasis[39,40].

Bilirubin is an orange-yellow pigment of bile that results from the degradation of various heme-containing proteins, especially from hemoglobin catabolism. Heme is broken down into biliverdin, which is converted into unconjugated or indirect bilirubin (UCB). UCB is water-insoluble and enters circulation bound to albumin. In the liver, glucuronic acid is added to UCB (conjugation) to render it water-soluble (direct bilirubin); finally, it is either excreted into bile or recirculated back to the bloodstream, where it is filtrated by the kidneys and excreted through urine[41,42.] Our study showed that serum totalbilirubin levels was significantly lower in psoriatic patients compared to controls. This result was in line with some researchers like; Zhou et al(2016)[43.]. assessed, in a comparative study (214 psoriasis patients versus 165 healthy counterparts), total bilirubin and CRP values and discovered that, in psoriasis, there is a significant reduction in total bilirubin ($p < 0.001$) and an elevation in CRP ($p < 0.001$). Total bilirubin is associated with oxidative stress and chronic inflammation and predisposes individuals with psoriasis to atherosclerosis, regardless of the PASI (Psoriasis Area Severity Index). Balta et al(2014)[44.]. also observed lower levels of total bilirubin ($p < 0.05$), direct bilirubin ($p < 0.001$) and higher levels of indirect bilirubin ($p < 0.05$) and CRP ($p <0.001$) in this dermatosis, emphasizing once again the association between total bilirubin, atherosclerosis and cardiovascular diseases (as systemic complications of psoriasis), as these subjects display an elevated carotid intima-media thickness[45,46.].

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