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ORIGINAL ARTICLE

Comparison between the Claudin-3 and the Ratio of Monocyte to High-Density Lipoprotein Cholesterol as Markers for Psoriasis in a Sample of Iraqi Patients

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ABSTRACT

The index score of psoriasis severity (PASI) cannot always be of value as a marker in non- plaque psoriasis. Alternative biomarkers have been used for the diagnosis and prognosis of the disease. Among these markers are the transmembrane protein Claudin-3 and the Monocyte to High- density lipoprotein cholesterol Ratio (MHR).

Objective: The present work was carried on to evaluate the prognostic and diagnostic ability of the two biomarkers for psoriasis, Claudin-3 and MHR, relate them to the PASI score in psoriatic patients, and find the correlation between the two markers.

Subjects and methods: forty patients with psoriasis (25 males and 15 females) of 7.3 ±3.7 years disease duration, and 30 healthy control subjects of 19 males and 11 females were enrolled in the study from March to July 2021.

The following tests were done for each patient and control subjects: Complete blood count (CBC) by VCS Technology Hemoglobinometry, Claudin-3 by ELISA technique, and serum lipids by enzymatic spectrophotometric methods.

Results: Both markers (Claudin-3 and MHR) showed significantly higher values in the patient's group than their controls in a manner proportional to the severity of the disease. As diagnostic markers, the receiver operating characteristic curve (ROC) analysis for both of them gave acceptable sensitivity and specificity.

Conclusion: Claudin-3 and MHR can be used alternatively as adjuvant diagnostic and prognostic markers to PASI score for psoriasis.

Keywords: Psoriasis, PASI score, Claudin-3, Monocyte-HDLc ratio.

INTRODUCTION

The skin inflammatory disease, psoriasis, is a chronic, autoimmune, condition mostly affecting the skin of 1- 3% of the world population [1,2], in young and old ages (16-22 and 57-60 years respectively) of both sexes[3]. It was found to associate many comorbidities as arthritis , obesity, metabolic syndrome, cardiovascular and cerebrovascular disorders.[4] Environmental and genetic factors have been considered the main causes of Psoriatic Pathogenesis[5] . The mechanism suggested, by some authors, involves the activation of keratinocytes (KCs) to generate some cytokines ,which were thought to activate resident skin macrophages and dendritic cells (DCs)[6].

Measuring the severity and magnitude of psoriasis is done clinically by the Psoriasis Area Severity Index (PASI)[7]. It is based on many factors including visual examination of the skin lesions, the disease severity and the percentage of the affected area[7]. Then a cumulative composite score from 0 to 72, was invented for this purpose.[8]

Evaluation and marketing of new anti-psoriatic drugs depends largely on the ability to reduce PASI score[9].

Measurement of systemic inflammation is done by using biochemical and hematological markers which were sensitive and specific enough to be used in the diagnosis and prognosis of the disease[10], in addition to the PASI which has been considered of limited value in non- plaque psoriasis.[11] Of these markers are the ratios of neutrophil to lymphocyte (NLR), platelet to lymphocyte (PLR) , lymphocyte to monocyte (LMR) , and Monocyte to High-density lipoprotein cholesterol (MHR) , in addition to C- reactive protein, CRP13 [11,12].

Tight junctional proteins maintain the barrier function, and regulate cell polarity, proliferation and differentiation.[13] Of these proteins are Junctional Adhesion Molecules (JAMS), Occludins, Ocln, Claudins, Cldn, and members of the Tight-Junctional Associated Marvel Protein, TAMP.[14]

Claudins were first identified in 1998[15]. They are transmembrane proteins thought to be responsible for the regulation of paracellular transport and maintaining proper physiological conditions through the formation of tight junctional components.[16] There are 24 types of claudins that are classified either according to structural features (classical and non-classical) or according to their functions.[17]. The belief that gut-skin-axis is important in the pathogenesis of psoriasis came from the relationship which exists between the gut microbiome, the intestinal barrier and the immune system.[18]

Monocytes and macrophages may have an important role in the development of atherosclerosis. The circulating monocytes might migrate to the subendothelial space of the arterial wall, where they develop into macrophages. The oxidized Low-density lipoprotein, and other lipids go inside these macrophages in the early stage. This is followed by differentiation into foam cells, and the release of proinflammatory cytokines at the site of inflammation. The end result is the activation of T-lymphocytes, platelets, and monocytes.[12]

The high-density lipoprotein cholesterol "HDL-c" was, also, found to decrease monocyte development and results in a lower macrophage number, with a consequent reduction in the release of cytokines[12] this has led to the use of both , monocytes and HDLc as an index for psoriatic prognosis[19].

The aim of the present study was to evaluate the association of each of the two markers for psoriasis, Claudin-3 and the MHR, with the PASI score, and the correlation of these markers with each other.

MATERIAL AND METHODS

The patient's and control groups were described in our previous report, including 40 patients (25 males and 15 females with mean age of 46.3 ±15.5 years) and 30 healthy control subjects (19 males and 11 females with mean age of 45.6 ± 12.1 years).[1]

Medical assessment: The PASI score was estimated by a consultant dermatologist. The mean of the disease duration in the present patients was 7.3 ±3.7 years. Patients with PASI score of less than 7.5 were excluded from the study.

Laboratory methods: involved CBC by VCS Technology, Hemoglobinometry, serum claudin by enzyme-linked immunosorbent assay, and serum lipids by enzymatic spectrophotometric methods.

Statistical analysis: As in the previous paper, the statistical package for social sciences (SPSS) version 25.0 were used to analyze the data., mean, and standard Error. The groups were compared using the independent sample t-test (unpaired t-test between two groups). the cut off value, sensitivity, and specificity

were determined by using the Receiver operative characteristics (ROC) [1].

RESULTS

Changes in serum Claudin-3 with the severity of the disease were presented in our previous report, showing highly significant positive correlation with the PASI score[1]

Changes in the MHR with disease severity are shown in table 1 where the MHR in the psoriatic patients was 19 ± 5.34 (mean ± SD), with a range of 10-30, and was significantly higher than that of the healthy controls who had 11.2± 2.6 (mean ± SD) and a range of 9-16, (P < 0.001) with a significant difference between the group of patients with severe – moderate cases and those with mild cases (p≤0.05).

There was a highly significant positive correlation between MHR and PASI (fig .1).

Table 1: Mean (±SD) value of Psoriasis diagnostic marker MHR in the two subgroups of patients (mild and severe - moderate) and their controls.

Parameters Groups	MHR	P Value
All Patients (n= 40)	19 ±5.34(10-30)	P<0.01
Severe & Moderate (n= 19)	23.6±3.84 (20-30) A	
Mild (n=21)	15.1±2.8 (10-19) B	
Control (n= 30)	11.2± 2.6 (9-16) C	

The different litters refer to significant differences, (p≤0.05),

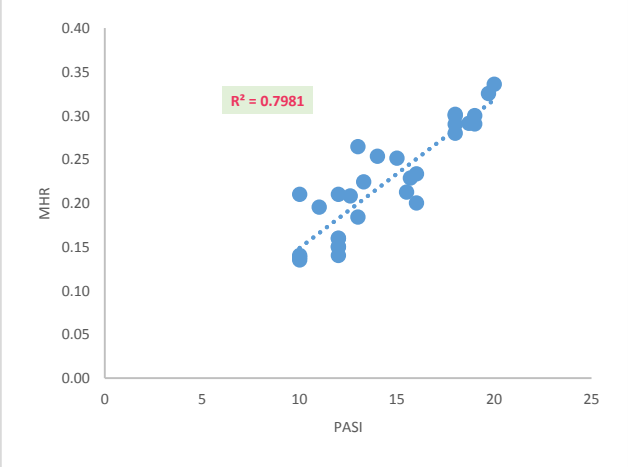

Fig 1: Correlation of the ratio of Monocyte to the High-density lipoprotein cholesterol with the Psoriasis Area Severity Index, PASI score (R^2 =0.798; P < 0.001).

The diagnostic Value of MHR for psoriasis: To evaluate the diagnostic value of MHR between patients and controls, the receiver operating characteristic curve (ROC) was used. Figure 2 shows ROC for MHR to discriminate between patients and controls.

The area under the curve (AUC) was 0.848, p<0.001. The sensitivity and specificity of the test at cut off value of MHR >12 were 81.82 % and 83.33 % respectively (against 73.33% and 94.74 % sensitivity and specificity, respectively, for Claudin-3).

The correlation between serum Claudin-3 and MHR in psoriatic patients: The relationship between Claudin-3 and MHR was found through their relationships with PASI score. Both tests were closely correlated with the severity of the disease. By arranging the examination results in descending order for both tests and plotting one against the other, results showed a positive relationship between the two markers, (R^2= 0.6842, p ≤ 0.01) as shown by fig 3.

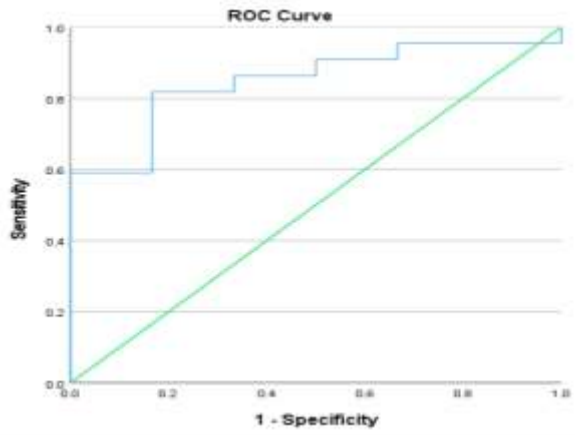

Fig 2: The ROC for MHR as a diagnostic marker for psoriasis.

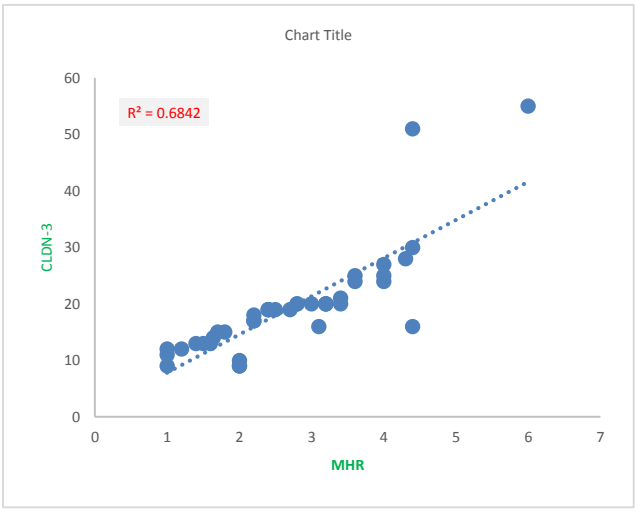

Fig 3: The correlation between the Claudin-3 and MHR in psoriatic patients (p ≤0.01)

DISCUSSION

The results of Claudin-3 of the present work were presented in a previous report[1] and were showing, clearly, a significant elevation in psoriatic patients when compared to the controls. This is in accord with Sikora et al 2019, who had, also, reported a positive correlation of this marker with PASI and neutrophil-to-lymphocyte ratio[18]. Increased Claudin-3 in psoriasis is thought to be due to the mucosal barrier dysfunction which is caused by altered gut microbiota.[20, 21] These changes have subjected the psoriatic patients to the risk of cardiovascular and cerebrovascular disorders, or other comorbidities as arthritis, obesity, and metabolic syndrome[4].

The disease process is characterized by impaired differentiation and hyperproliferation of epidermal keratinocytes, and infiltration of T and dendritic cells, followed by the activation of neutrophils and monocytes by pro-inflammatory cytokines[22], this information led to the suggestion of using the MHR as another marker for psoriasis.[23]

The marked increase in the MHR marker in the present psoriatic patients coincides with recent findings [23, 24]. We also found a highly significant correlation of the MHR with the PASI score, similar to that of Claudin-3 (P < 0.001. for both).

As diagnostic markers the ROC analysis revealed acceptable sensitivity and specificity for Claudin-3[1], and the MHR, however the MHR of the present data show a higher sensitivity than the Claudin-3 reported by our previous report.[1]

Recent report showed that Claudin-3 sensitivity and specificity to discriminate between patients and controls were 81.1 % and 84.3 % respectively[25], which differ from our previous figures (73.33 % and 94.74%, sensitivity and specificity, respectively) [1]. This difference could arise from using different diagnostic kits for Cloudin-3 with different sensitivities.

Nothing could be found in the literature about the sensitivity and specificity of the MHR marker in psoriasis.

In the trial to correlate Claudin-3 with MHR, the results of the present study revealed a good association between the two markers (R^2=0.6842, p 0.01).

From the present data we can conclude that both parameters (Claudin-3 and MHR) could be used alternatively in the diagnosis and prognosis of psoriasis along with the PASI score.

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