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Growth Differentiation Factor-15 in psoriatic patients: a narrative review

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ABSTRACT

Background: Protein biomarkers in the bloodstream have the potential to aid in diagnosis, evaluate prognosis, and direct treatment. Multiple CV events have been linked to Growth Differentiation Factor 15, a cytokine released in response to cellular stress and inflammation. Psoriasis has been linked to cardiovascular disease, however the significance of this association is unclear. **Objectives:** Growth Differentiation Factor-15 (GDF-15) is being studied for its potential function in psoriasis. **Data Sources:** By searching and reviewing Medline databases (Pub Med and Medscape) and the role of GDF-15 in psoriasis available till 2022. **Study Selection:** The quality of each study was evaluated separately before inclusion. If they met any of the following criteria, we considered them for inclusion: 1. It is written and published in English. (2) Featured in reputable, academic publications. Third, explain why GDF-15 is so important for psoriasis sufferers..**Data Extraction:** There was a process of excluding studies that did not meet the inclusion criteria. Ethical permission, eligibility criteria, controls, information, and well-defined evaluation measures were all factors in determining the study's quality. Information relevant to our interested research outcomes was independently retrieved from each qualifying study utilising a data collecting form.**Conclusions:** We may infer that GDF-15's inflammatory actions may contribute to the aetiology and severity of psoriasis.

Key words: Psoriasis, growth differentiation factor-15, and the risk of cardiovascular disease.

1. Introduction

Psoriasis is a chronic, inflammatory skin disease that affects those who have a hereditary susceptibility to developing the condition. About 2% of the population is impacted by this, and half of all cases are diagnosed among people under the age of 30. [1]**.**

Psoriasis may present on the skin in a broad variety of ways, from small, pinpoint lesions to massive, plaque-like ones, and even systemic erythroderma. Plaque psoriasis is the most prevalent and well-known morphological manifestation of the disease.[***2***]**.**

Psoriasis is characterised by systemic inflammation and the presence of many concomitant diseases. Cardiovascular disorders (CVD), including diabetes, hypertension, and dyslipidemia, are strongly linked to psoriasis. [3]**.**

One member of the TGF- cytokine superfamily that responds to stress is called growth differentiation factor-15 (GDF-15). The placenta is the only normal human tissue where GDF-15 is strongly expressed. GDF-15 is generated by various cell types, including cardiovascular and non-cardiovascular, under pathological situations. [4]**.**

2. Materials and methods

Data Sources: By searching and reviewing Medline databases (Pub Med and Medscape) and the role of GDF-15 in psoriasis and its possible correlation with cardiovascular risk available till 2022.

Study Selection: The quality of each study was evaluated separately before inclusion. If they met any of the following criteria, we considered them for inclusion: 1. It is written and published in English. (2) Featured in reputable, academic publications. Third, explain why GDF-15 is important, and how it could affect cardiovascular risk in psoriasis patients.

Data Extraction: There was a process of excluding studies that did not meet the inclusion criteria. Ethical permission, eligibility criteria, controls, information, and well-defined evaluation measures were all factors in determining the study's quality. Information relevant to our interested research outcomes was independently retrieved from each qualifying study utilising a data collecting form.

3. Review of literature

Psoriasis and metabolic syndrome

Psoriasis is characterised by an autoimmune pathogenicity and a significant hereditary propensity. It has been linked to many disorders and manifests mostly as skin symptoms (but it may also affect the joints). Psoriatic inflammation has been proven to spread to other organs in addition to the skin. As a result, the idea has been advanced that psoriasis is not limited to the skin and is instead a systemic illness. [5]**.**

Psoriasis has been linked to metabolic syndrome, which includes being overweight in the middle, either having diabetes or being resistant to its effects, having high blood pressure, and having poor cholesterol levels.

Patients with psoriasis and those with metabolic syndrome both experience systemic inflammation, which is thought to be the cause of the correlation between the two conditions. [6].

[9] compared 30 people with persistent plaque psoriasis to 30 people without the condition. The average ages, sexes, BMIs, smoking rates, and fasting blood sugar levels were all similar.

[11] a link between PASI and hypertension was reported. Additionally, a studyby [12] conducted in the Middle East, the frequency of hypertension varied depending on the severity of psoriasis, with 32 percent of people with mild and medium psoriasis (PASI 10) experiencing hypertension, 40.3% of people with severe psoriasis (PASI > 10) experiencing hypertension, and 11.55 percent of people in the control group experiencing hypertension.

[13] hypertension was found to be substantially more common in the psoriatic patients than in the control group. The correlation between psoriasis and hypertension persists after controlling for demographic factors such age, gender, and smoking history.

[14] both unadjusted and adjusted analyses that accounted for age, sex, body mass index, smoking and alcohol use status, presence of comorbid conditions, and current use of antihypertensive medications and nonsteroidal anti-inflammatory drugs found a significant positive relationship between uncontrolled hypertension and psoriasis severity as objectively determined by the affected body surface area.

[15] suggested a link between psoriasis and a higher rate of hypertension, and suggested that this association existed for both moderate and severe cases of the skin condition. [16] hypertension is three times more common in those with psoriasis than in those with other skin diseases, according to a recent analysis. Meanwhile, [17] suggested that this trend was not obvious.

There were a lot of unknowns about the correlation between psoriasis and high blood pressure. To begin, psoriasis is associated with an increased risk of developing stress, anxiety, depression, increased propensity toward smoking, drinking, inactivity, and hypertension. Psoriasis medications like cyclosporine may also have unintended effects on hypertension, diabetes, and metabolic syndrome. [18].

[19] found that blood sugar levels in 685 psoriasis patients were significantly higher than those of the controls. Psoriatic patients and controls did not vary from one another in terms of blood lipid levels.

Different studies have shown conflicting results about the link between dyslipidaemia and psoriasis. There was no significant difference in HDL levels between psoriasis patients and controls, however triglyceride levels were considerably higher in several of the investigations.[20] **,** [21].

[22] hypertriglyceridemia and metabolic syndrome were more common in psoriasis patients than in controls; low HDL levels, diabetes, and hypertension were not significantly different between the two groups. [23] failed to demonstrate any difference between psoriasis patients and controls with regard to FBS, TG, cholesterol, HDL, LDL and VLDL.

GDF-15

High amounts of the stress response cytokine GDF-15 are produced in response to normal and pathological conditions, including apoptotic pathways in damaged body tissues, by cardiomyocytes, adipocytes, endothelial cells, macrophages, and vascular smooth muscle cells. It also has metabolic effects connected to weight. It also shows some resilience in the face of microbial and viral assaults. [7].

Several inflammatory and malignant disorders, including colon and thyroid malignancies, as well as cardiovascular events, may benefit from monitoring blood levels of GDF-15. Due to its inhibitory role in leukocytes activity, GDF-15 may also be exploited as a therapeutic target to regulate inflammatory processes. [8].

[10] tried to evaluate the relationship between GDF-15 serum levels as well as gene expression with psoriasis and its severity. There was a significant increase in the psoriatic patients according to positive family history of psoriasis.

[10] found that the mean serum levels of GDF-15 in the patients, and healthy controls were 1.98 and 0.93 pg/ml, respectively; and the mean of the gene expression level of GDF-15 in the patients and healthy controls were 9.7 and 7.6, respectively.

[24] GDF-15 levels were substantially varied across all patients in a study that looked for a connection between psoriasis and GDF-15 levels (mild, moderate and severe).

[25] type 2 diabetes (T2D) patients had higher mean blood GDF-15 levels compared to healthy controls when researchers looked for a connection between GDF-15 levels and cardiovascular risk. GDF-15 levels were observed to positively correlate with age, the HOMA-IR, HbA1c, and FBS.

[10] GDF-15 levels were observed to be 1.06 pg/ml in those with psoriasis for less than

a year and 3.25 pg/ml in those with psoriasis for more than a year. The average level of GDF-15 gene expression was 7.58 pg/mL in those with psoriasis for less than a year and 12.63 pg/mL in those with psoriasis for more than a year. There was also a strong correlation between GDF-15 gene expression and the length and severity of sickness. Similarly, a link with statistical significance was found by**[**24] between disease duration and GDF-15.

Moreover, **[**10] revealed that GDF-15 gene expression and serum levels were both increased in more severe psoriasis. Serum GDF-15 and gene expression levels were shown to be linearly correlated at 0.803 and PASI score at 0.848, respectively.. **[**24] observed a significant correlation between PASI score and disease duration.

[26] confirmed that metabolic syndrome was consistently associated with higher GDF-15 levels.

[24] The GDF-15 value that may be utilised to predict the severity of the PASI score was determined by splitting the ROC curve analysis into two separate models. In model 1, a GDF-15 value of >1120.5 pg/mL predicted a moderate PASI score with 84.6% sensitivity and 70.8% specificity [area under the curve (AUC): 0.821, 95% confidence interval (CI): 0.686-0.915, p0.001]; in model 2, same value was 77.8% sensitive and 73.2 % specific.

Multiple linear regression models done by **[**10] shown that a rise in serum GDF-15 levels, as well as its gene expression, is positively connected to the severity of psoriasis, even after controlling for other factors such as sex, age, and favourable family history. The influence of illness severity on blood levels of GDF-15 and its gene expression may be effectively explained using this regression model, as shown by adjusted R square analysis.

4.Conclusion

The results of the current investigation led us to hypothesise that growth differentiation factor 15 (GDF15) contributes to the development and severity of psoriasis and raises the risk of cardiovascular illnesses.

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