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## Risk Factors of Coronary Artery Disease in Affected Patients With and Without Psoriasis: The First Case-control Study in the Literature

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Since metabolic abnormalities are common in psoriasis, some investigators have suggested that the risk of Coronary Artery Disease (CAD) may be increased in psoriatic patients. The underlying causes of this connection, however, have not been examined. This study sought to investigate common risk factors of CAD in patients with psoriasis. In a retrospective, case-control setting, profiles of 89 patients with angiographically proven CAD were reviewed. These patients were 47 cases with psoriasis and 42 controls without psoriasis. Demographic data, overweight/obesity, family history of CAD, hypertension, diabetes mellitus, smoking, increased level of serum low-density lipoprotein (LDL) and triglyceride and decreased serum level of high-density lipoprotein (HDL) were outcome variables which were compared between the two groups. The case group was consisted of 33 males and 14 females with a mean age of  $51.04 \pm 8.79$  years. The controls were 29 males and 13 females with a mean age of  $57.00 \pm 9.37$  years. Patients in the case group were significantly younger ( $p = 0.003$ ). Increased serum LDL (59.6 vs. 38.1%,  $p = 0.04$ ) and increased serum triglyceride (66 vs. 31%,  $p = 0.001$ ) were significantly higher in psoriatic patients than in controls. These differences, as well as for age, remained significant after logistic regression analysis. The two groups were comparable in terms of sex ( $p = 0.91$ ), overweight/obesity ( $p = 0.54$ ), family history of CAD ( $p = 0.86$ ), hypertension ( $p = 0.42$ ), diabetes mellitus ( $p = 0.97$ ), smoking ( $p = 0.28$ ) and decreased serum level of HDL ( $p = 0.65$ ). In conclusion, this study showed that patients with both CAD and psoriasis are younger than those with CAD only. Abnormal lipid profile is probably an underlying cause of the increased risk of CAD in psoriasis.

**Key words:** Psoriasis, coronary artery disease, lipid profile, age

## INTRODUCTION

In dermatology, psoriasis is regarded as a common chronic inflammatory disease of the skin with an estimated prevalence of 1-3% in the community (Langley *et al.*, 2005; Amirnia *et al.*, 2012; El-Gayyar *et al.*, 2012). However, due to its probable underlying etiology which is believed to be a systemic inflammatory process, the consequences of psoriasis are not limited to the skin (Ghoreschi *et al.*, 2007; Dhama *et al.*, 2013; Sabeti *et al.*, 2013). For example, many researchers have shown that metabolic abnormalities such as overweight and obesity, insulin resistance and glucose intolerance, abnormal serum lipid profile and increased blood pressure are more common among psoriatic patients than in normal population (Moller and Kaufman, 2005; Mahajan *et al.*, 2010; Navali *et al.*, 2011; Mori *et al.*, 2013).

Since the association of such metabolic abnormalities with Coronary Artery Disease (CAD) is confirmed, some investigators suggest a direct connection between psoriasis and CAD (Armstrong *et al.*, 2012).

Those authors who proposed a significant association between CAD and psoriasis explain it by the chronic inflammation that is usually evident in psoriatic patients, because many metabolic problems in psoriasis such as insulin resistance and abnormal lipid profile are supposed to be mediated through inflammatory cytokines namely IL-1, IL-6 and tumor necrosis factor- $\alpha$  (Azfar and Gelfand, 2008) and at the same time, the role of inflammation in development of atherosclerotic plaques in CAD has been also advocated by others (Frostegard *et al.*, 1999; Shapiro *et al.*, 2012).

Despite these hypotheses, to the best of the authors' knowledge, there is no study in the literature that is focused on contributors of CAD in patients with psoriasis, directly. So, this study aimed to investigate possible role of major known risk factors of CAD in a well-designed, case-control study comprising of CAD patients with and without psoriasis.

## MATERIALS AND METHODS

After being approved by the ethics committee of a local university, profiles of 89 patients with angiography-confirmed CAD were reviewed in this retrospective, case-control study from May 2007 through to March 2014 in a referral heart center. The patients were categorized in two groups: With previous psoriasis (cases, n = 47) and without previous psoriasis (controls, n = 42). Majority of cases (89%) had plaque-psoriasis.

An increased serum level of Low-Density Lipoprotein (LDL) was defined when it was over 160 mg dL<sup>-1</sup>, a decreased serum level of high-density lipoprotein was defined when it was below 40 mg dL<sup>-1</sup> and an increased serum level of triglyceride was defined when it was over 150 mg dL<sup>-1</sup> (Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001). Overweigh/obesity was defined as having a body mass index (BMI) greater than or equal to 25 (Damevska *et al.*, 2013).

Study variables including demographic data (age and sex), overweight/obesity, family history of CAD in first degree relatives, history of hypertension, history of diabetes mellitus, history of smoking and the status of lipid profile (increased serum LDL and triglyceride, decreased serum level of HDL) were documented and compared between the case and control groups.

**Statistical analysis:** The SPSS software version 19.0 (IBM Corporation, New York, USA) was used for statistical analysis. Normal distribution of numerical data was ensured using Kolmogorov-Smirnov test and QQ plots. Independent samples t test or chi-square test were used for comparisons, where appropriate. Logistic regression analysis was used for determining independency of variables (Fattahi *et al.*, 2011). A significance level of  $p \leq 0.05$  was used.

## RESULTS

A total of 89 patients with CAD were studied in two groups: Cases included those with psoriasis who were 33 males (70.2%) and 14 females (29.8%) with a mean age of 51.04 $\pm$ 8.79 years (range: 35-70) and controls without psoriasis who were 29 males (69%) and 13 females (31%) with a mean age of 57.00 $\pm$ 9.39 years (range: 37-79).

Frequency of patient age in the two study groups is shown in Fig. 1. Study variables are compared between the two groups in Table 1.

Based on this data, the two groups were comparable for sex ( $p = 0.91$ ), overweight/obesity ( $p = 0.56$ ), family history of CAD ( $p = 0.86$ ), hypertension ( $p = 0.42$ ), diabetes mellitus ( $p = 0.97$ ), smoking ( $p = 0.28$ ) and decreased serum HDL ( $p = 0.65$ ).

The mean age of patients in the control group, however, was significantly higher than that of the cases (57.00 $\pm$ 9.39 years vs. 51.04 $\pm$ 8.79 years,  $p = 0.003$ ). In addition, raised serum LDL and hypertriglyceridemia were significantly more frequent in cases than in controls (59.6 vs. 38.1%,  $p = 0.04$  and 66 vs. 31%,  $p = 0.001$ , respectively).

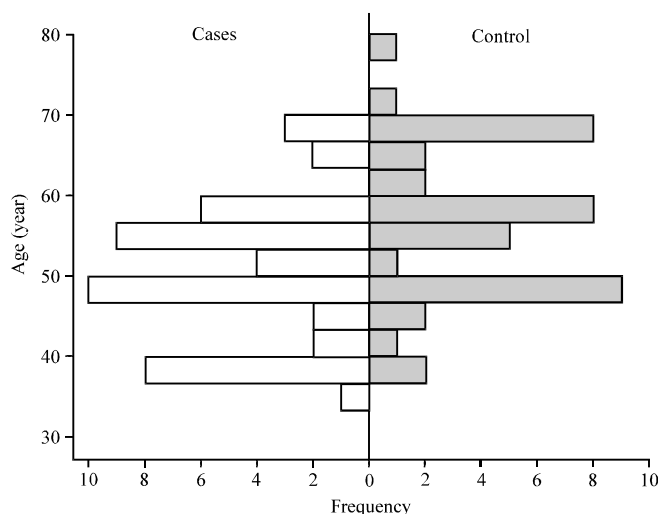


Fig. 1: Frequency of patient age with coronary artery disease with (case) and without (control) psoriasis

Table 1: Study variables in patients with coronary artery disease with (case) and without (control) psoriasis

Variable	Case (n = 47)		Control (n = 42)		p-value	OR	95%CI
	No.	Percentage	No.	Percentage			
Age (y)	51.04±8.79		57.00±9.37		0.003*	-	-
Sex (male)	33	70.2	29	69.0	0.91	1.06	0.43-2.61
Overweight/obesity	15	31.9	16	38.1	0.54	1.31	0.55-3.15
Positive family history	21	44.7	18	42.9	0.86	0.93	0.40-2.15
Hypertension	12	25.5	14	33.3	0.42	1.46	0.58-3.65
Diabetes mellitus	10	21.3	9	21.4	0.97	1.00	0.37-2.79
Smoking	16	34.0	19	45.2	0.28	1.60	0.68-3.77
Increased serum LDL	28	59.6	16	38.1	0.04*	2.38	1.02-5.56
Decreased serum HDL	19	40.4	19	45.2	0.65	1.22	0.53-2.83
Increased serum triglyceride	31	66.0	13	31.0	0.001*	4.35	1.79-100

CI: Confidence interval, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, OR: Odds ratio, Data is shown as Mean±SD (for age) or number (%), \*p<0.05 is significant

According to the result of logistic regression analysis, age (p = 0.01), increased serum LDL (p = 0.01) and increased serum triglyceride (p = 0.002) were all independently different between the two groups.

### DISCUSSION

Association between CAD and psoriasis is a hot topic among researchers. Some investigators have suggested that psoriasis is a risk factor for developing coronary artery disease, because they have shown that psoriatic patients, in comparison with normal population, are more obese, tended to have dyslipidemia more frequently and usually are more prone to hypertension (Coimbra *et al.*, 2009; Armstrong *et al.*, 2011; Love *et al.*, 2011).

For example, in a study by Kimball *et al.* (2010) on 1591 patients with psoriasis, they found that in comparison with normal subjects, psoriatic patients had 28% greater risk of CAD within 10 years. This association between psoriasis and CAD has been supported by others, too (Mallbris *et al.*, 2004; Cohen *et al.*, 2008).

Although the connection between psoriasis and CAD has been supported previously and as mentioned before, some etiologies have been proposed, to the best of the authors' knowledge, no study have reported a scientific documentation in this regard.

In the present study, for the first time in the literature, it was shown that firstly, CAD develops at younger ages in psoriatic patients compared with uninvolved individuals (mean age of 51 years vs. 57 years) and secondly, psoriatic patients are more prone to CAD possibly through increased levels of serum LDL and triglyceride which are independent risk factors, as well.

Although the exact physiopathology of a direct relation between psoriasis and CAD is yet to be defined, some hypotheses exist. For example, it has been shown that the atherosclerotic lesions in CAD contains large numbers of T lymphocytes and macrophages and so, a cellular immune response has been implicated in this regard (Frostegard *et al.*, 1999; Shakeri *et al.*, 2011 a, b;

Shapiro *et al.*, 2012; Tarzamni *et al.*, 2012). The same cellular aggregation has been documented in psoriasis and as a result, a common physiopathology has been suggested through immune responses (Ghoreschi *et al.*, 2007; Dhama *et al.*, 2013; Sabeti *et al.*, 2013). Beside this direct role of inflammatory agents in the development of atherosclerotic plaques, a secondary role of inflammation in inducing lipid profile abnormalities has been also proposed in psoriasis (Pietrzak *et al.*, 2010).

Lipid profiles abnormality is the main suggested mechanism justifying a connection between psoriasis and CAD. In line with our results in this regard, Akhyani *et al.* (2007) also showed that dyslipidemia (including hypertriglyceridemia) is more frequent in psoriatic patients than in normal controls. Abnormality in triglyceride level in the serum of psoriatic patients has been also confirmed by other investigators (Seishima *et al.*, 1994; Bajaj *et al.*, 2009; Ali *et al.*, 2014).

Similar reports are also available in terms of serum cholesterol and LDL (Fortinskaia *et al.*, 1996; Pietrzak *et al.*, 2000; Mallbris *et al.*, 2004; Sarvtin *et al.*, 2014). But it should be noted that in the present study, as mentioned before, it is for the first time that the atherogenic role of abnormally raised LDL and triglyceride was documented in cases with psoriasis and at the same time with CAD.

Interestingly, the level of HDL did not differ significantly between the two groups in the present study. Although similar finding has been reported previously in psoriatic patients (Akhyani *et al.*, 2007; Farshchian *et al.*, 2007; Bajaj *et al.*, 2009), having no role by HDL abnormality in the development of CAD is a novel and clinically significant finding.

It has been shown that the concentration of cholesterol in psoriatic crusts is higher than that in crusts normal skin shed. As a result, due to high loss of cholesterol during active phase of the disease a compensatory increase in cholesterol synthesis occurs and the level of serum cholesterol elevates (Lea *et al.*, 1958). Apart from the role of inflammation, this mechanism may also underlie the pathogenesis of hypercholesterolemia in psoriasis.

In addition to lipid profile abnormalities, age, like in other dermatological conditions (Babaeinejad *et al.*, 2011; Khodaeiani *et al.*, 2012, 2013; Babaeinejad and Fouladi, 2013), was another significant factor in relation between CAD and psoriasis. Further studies, particularly prospective ones, are recommended in this regard.

## CONCLUSION

The mean age of patients with coronary artery disease and psoriasis is significantly lower than the mean age of patients with psoriasis. Increased level of serum LDL and triglyceride is possibly a major etiology of increased risk of coronary artery disease in psoriatic patients.

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