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META-ANALYSIS OF PSORIASIS AND CARDIOVASCULAR RISK FACTORS

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ABSTRACT

Background & Purpose: More recently, research have shown that psoriasis is a systemic inflammatory disease which may be related to numerous comorbidities. particularly, psoriasis is associated with an accelerated threat of developing intense vascular events such as myocardial infarction and stroke. in addition, the prevalence rates of cardiovascular risk factors are accelerated, including high blood pressure, diabetes mellitus, dyslipidemia, obesity, and metabolic syndrome. The Aim of this work is to provide cumulative data about the effect of cardiovascular risk factors on psoriasis patients. ***Methods:*** A systematic search was performed of PubMed, Cochrane library Ovid, Scopus & Google scholar to identify Dermatology RCTs, clinical trials, and comparative studies, which studied the outcome of Psoriasis group versus Control group of patients. A meta-analysis was done using fixed and random-effect methods. The primary

outcome was the rate of Ischemic Heart Disease (IHD). Secondary outcomes were atherosclerosis and hypertension (HTN). ***Results:*** A total of 5 studies were identified involving 1255118 patients, with 32171 patients in Psoriasis group, and 1222947 patients in Control group. Regarding primary outcome measures, the fixed-effects model of the meta-analysis study showed highly significant increase in IHD in Psoriasis group compared to Control group ($p< 0.01$). Regarding secondary outcome measures, the random-effects model of the meta-analysis study showed highly significant increase in atherosclerosis in Psoriasis group compared to Control group ($p < 0.01$). The random-effects model of the meta-analysis study showed highly significant increase in HTN in Psoriasis group compared to Control group ($p = 0.001$). ***Conclusion:*** To conclude, there is strong association between the prevalence of cardiovascular risk factors and major cardiovascular events and psoriatic patients.

KEYWORDS: Psoriasis, Ischemic Heart Disease, atherosclerosis, hypertension.

INTRODUCTION

Psoriasis is an immune-mediated, chronic inflammatory skin disease that affects about 2% to 3% of the population within the USA. Psoriasis, possibly as a result of enhanced systemic inflammation and resulting atherosclerosis, has been related to cardiovascular disorder.[1]

More recently, research have shown that psoriasis is a systemic inflammatory disease which may be related to numerous comorbidities. particularly, psoriasis is associated with an accelerated threat of developing intense vascular events such as myocardial infarction and stroke. in addition, the prevalence rates of cardiovascular risk factors are accelerated, including high blood pressure, diabetes mellitus, dyslipidemia, obesity, and metabolic syndrome.[2]

Psoriasis is thought to be a chronic mediated inflammatory disorder manifesting itself inside the skin and affecting 2% of the population. severe psoriasis has been related to an extended cardiovascular mortality.[3]

Patients with rheumatoid arthritis (RA), psoriasis (PsO), and psoriatic arthritis (PsA) have elevated rates of cardiovascular (CV) disorder and adverse CV outcomes including myocardial infarction, stroke, and CV death. A part of this danger appears to be mediated with the aid of the systemic inflammatory burden related to chronic inflammatory arthritis in RA and PsA as well as the inflammatory process in PsO, which is a key driver of increased

CV risk in these patients. The heightened inflammatory state of these conditions is connected to accelerated atherosclerosis, with systemic inflammation exacerbating adverse changes in both traditional and novel CV risk factors. traditional CV hazard factors including high blood pressure, diabetes mellitus, hyperlipidemia, and weight problems additionally play an vital role in development of CV consequences.[4]

Patients with psoriasis and psoriatic arthritis (PsA) have an accelerated cardiovascular (CV) risk. based on current meta-analyses, patients with psoriasis and PsA have a 29% and 55% better risk of developing incident myocardial infarction, respectively. at the same time as the increased CV risk in psoriatic patients is attributed in part to the chronic systemic inflammation associated with skin and joint disorder, the excessive prevalence of traditional CV risk factors (CVRF) in psoriatic patients significantly contributes to their excessive CV risk. certainly, the presence of traditional CVRF, including hypertension (HTN), smoking, dyslipidemia, and diabetes mellitus (DM), is related to a higher burden of atherosclerosis and accelerated risk of developing CV diseases (CVD) in patients with psoriatic disorder.[5]

Aim of the study: The Aim of this work is to provide cumulative data about the effect of cardiovascular risk factors on psoriasis patients.

METHODS

This review was carried out using the standard methods mentioned within the Cochrane handbook and in accordance with the (PRISMA) statement guidelines.[6]

Identification of studies

- An initial search carried out throughout the PubMed, Cochrane library Ovid, Scopus & Google scholar using the following keywords: Psoriasis, Ischemic Heart Disease, atherosclerosis, hypertension.
- We will consider published, full text studies in English only. Moreover, no attempts were made to locate any unpublished studies nor non-English studies.

Criteria of accepted studies

- **Types of studies**

The review will be restricted to RCTs, clinical trials, and comparative studies, either prospective or retrospective, which studied the outcome of Psoriasis group versus Control group.

- **Types of participants:** Psoriasis patients.
- **Types of outcome measures**

1. Rate of IHD (1ry outcome)
2. Rate of atherosclerosis (2ry outcome)
3. Rate of HTN (2ry outcome)

Inclusion criteria

✓ English literature.
✓ Journal articles.
✓ Between 2009 until 2019.
✓ Describing Psoriasis group or Control group.
✓ Human studies.

Exclusion criteria

✓ Articles describing other types of skin lesions.
✓ Irrelevance to our study.

Methods of the review

■ **Locating studies**

Abstracts of articles identified using the above search strategy will be viewed, and articles that appear of fulfill our inclusion criteria will be retrieved in full, when there is a doubt, a second reviewer will assess the article and consensus will be reached.

■ **Data extraction**

Using the following keywords: Psoriasis, Ischemic Heart Disease, atherosclerosis, hypertension, data will be independently extracted by two reviewers and cross-checked.

Statistical analysis

Statistical analysis done using MedCalc ver. 18.11.3 (MedCalc, Ostend, Belgium). Data were pooled and odds ratios (ORs) as well as standard mean differences (SMD), were calculated with their 95 per cent confidence intervals (CI). A meta-analysis was performed to calculate direct estimates of each treatment, technique or outcome. According to heterogeneity across trials using the I^2-statistics; a fixed- effect model ($P \geq 0.1$) or random-effects model ($P < 0.1$) was used.

Study selection

We found 134 records; 110 were excluded based on title and abstract review; 24 articles are searched for eligibility by full text review; 9 articles cannot be accessed or obtain full text; 5 studies were reviews and case reports; 5 were not describing functional outcome; leaving 5 studies that met all inclusion criteria (Fig. 1).

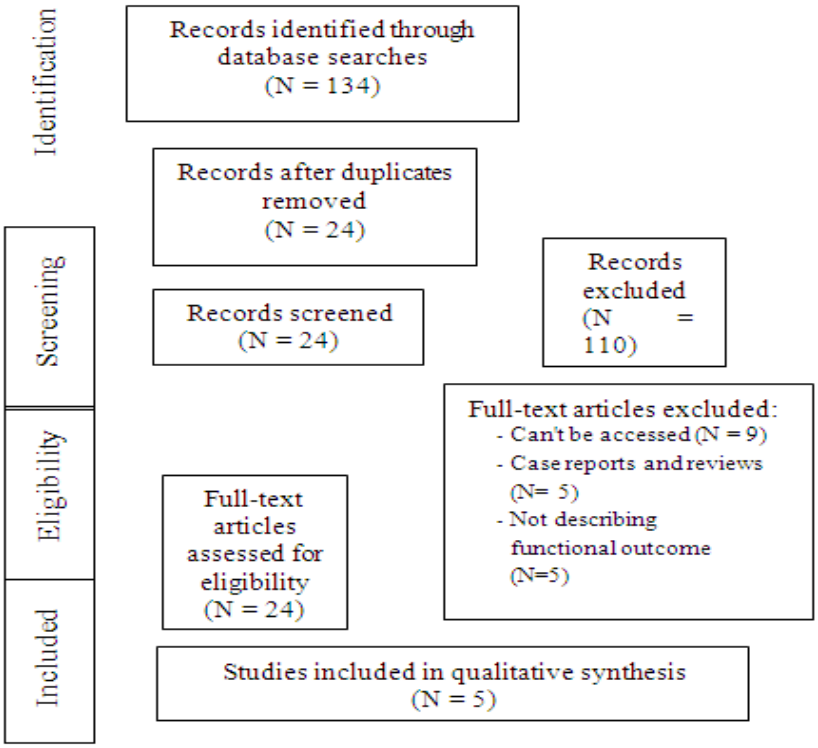

Figure 1: Flow chart for study selection.

RESULTS

Descriptive analysis of all studies included (Tables 1, 2)

Table 1: Patients and study characteristics.

N	Author	Number of patients			Age (average years)	Male	Female
		Total group	Psoriasis	Control group			
1	***Prodanovich et al., 2009***	5736	3236	2500	66.5	5295	441
2	***Ahdout et al., 2012***	117	65	52	51	62	55
3	***Shapiro et al., 2012***	2158	1079	1079	68.65	1202	956
4	***Cooksey et al., 2018***	1212336	24630	1187706	50	597086	615250
5	***Kibari et al., 2019***	34771	3161	31610	58	16214	18557

#Studies were arranged according to publication year.

Table 2: Summary of outcome measures in all studies.

N	Author	Primary outcome		Secondary outcomes			
		IHD		Atherosclerosis		HTN	
		Psoriasis group	Control group	Psoriasis group	Control group	Psoriasis group	Control group
1	***Prodanovich et al., 2009***	---	---	1023	240	1945	532
2	***Ahdout et al., 2012***	5	6	15	11	21	10
3	***Shapiro et al., 2012***	516	438	598	564	556	461
4	***Cooksey et al., 2018***	2371	79811	2796	86258	7368	256665
5	***Kibari et al., 2019***	---	---	2022	16904	1442	11313

The included studies published between 2009 and 2019.

The total number of patients in all the included studies was 1255118 patients, with 32171 patients in Psoriasis group, and 1222947 patients in Control group.

Regarding patients' characteristics, the average age of all patients was (58.8 years), with 619859 (49.4%) male patients and 635259 (50.6%) female patients.

Meta-analysis of outcome measures

Data were divided into two groups:

1) Psoriasis group
2) Control group

Meta-analysis study was done on 5 studies which described and compared the 2 different groups of patients; with overall number of patients (N=1255118).

Patients who achieved outcome measures were pooled:

Each outcome was measured by

✓ **Odds Ratio (OR)**

- Rate of IHD (1ry outcome)
- Rate of atherosclerosis (2ry outcome)
- Rate of HTN (2ry outcome)

Regarding primary outcome measure, We found 3 studies reported rate of IHD with total number of patients (N= 1214611).

I^2 (inconsistency) was 30% with non-significant Q test for heterogeneity ($p > 0.05$), so fixed-effects model was carried out; with overall OR= 1.46 (95% CI 1.4 to 1.53).

The fixed-effects model of the meta-analysis study showed highly significant increase in IHD in Psoriasis group compared to Control group ($p < 0.01$).

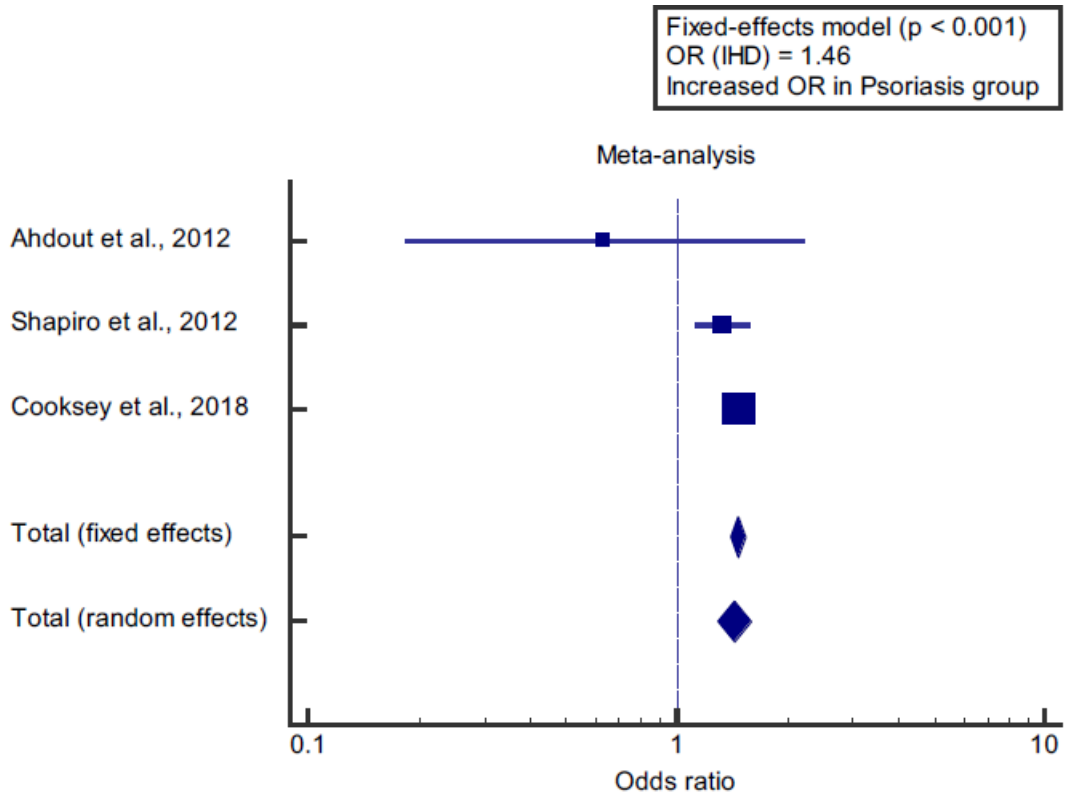

Figure 2: Forest plot of (IHD) on Psoriasis group vs Control group – Odds ratio.

Regarding secondary outcome measures, We found 5 studies reported rate of atherosclerosis with total number of patients (N=1255118).

I^2 (inconsistency) was 97% with highly significant Q test for heterogeneity ($p < 0.01$), so random- effects model was carried out; with overall OR= 1.79 (95% CI 1.29 to 2.47).

The random-effects model of the meta-analysis study showed highly significant increase in atherosclerosis in Psoriasis group compared to Control group ($p < 0.01$).

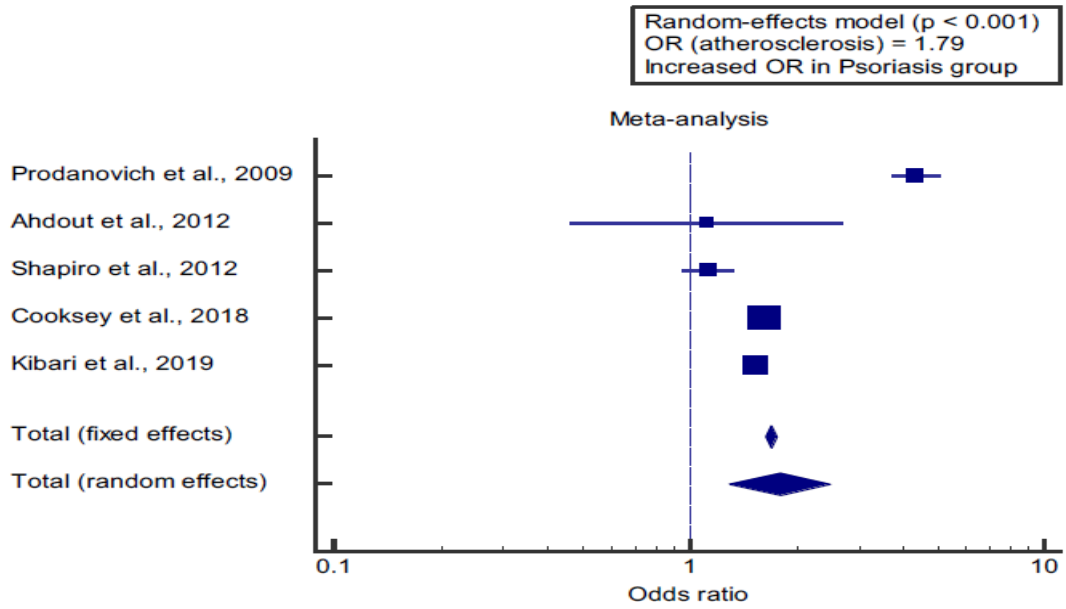

Figure 3: Forest plot of (atherosclerosis) on Psoriasis group vs Control group – Odds ratio.

We found 5 studies reported rate of HTN with total number of patients (N=1255118).

I^2 (inconsistency) was 99% with highly significant Q test for heterogeneity ($p < 0.01$), so random- effects model was carried out; with overall OR= 2.06 (95% CI 1.33 to 3.19).

The random-effects model of the meta-analysis study showed highly significant increase in HTN in Psoriasis group compared to Control group (p = 0.001).

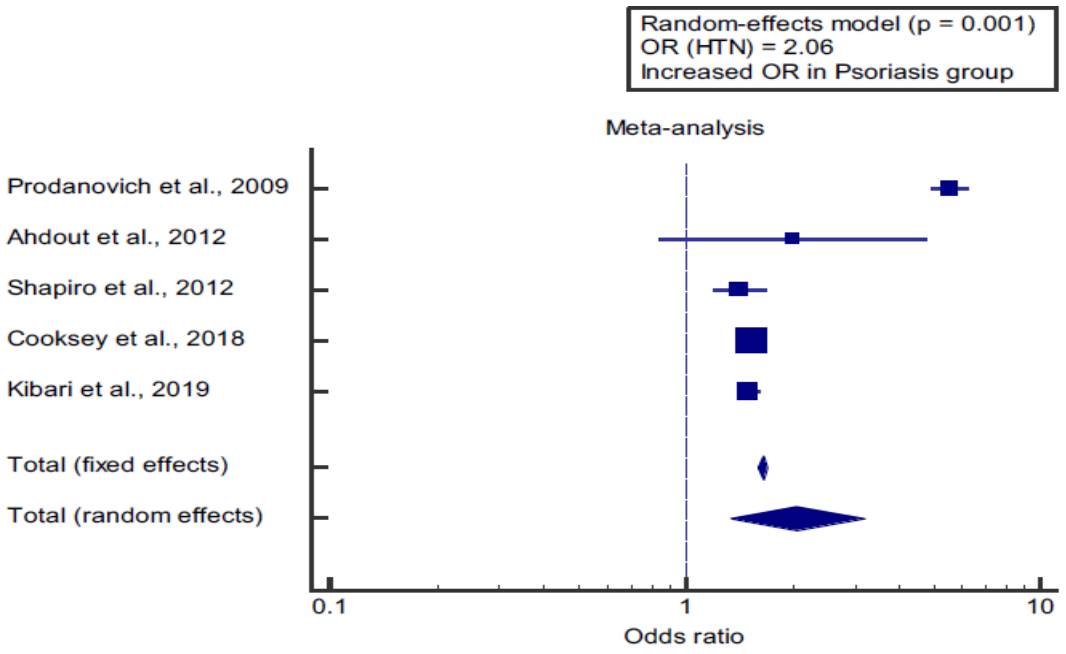

Figure 4: Forest plot of (HTN) on Psoriasis group vs Control group – Odds ratio.

DISCUSSION

The Aim of this work is to provide cumulative data about the effect of cardiovascular risk factors on psoriasis patients.

The included studies published between 2009 and 2019.

The total number of patients in all the included studies was 1255118 patients, with 32171 patients in Psoriasis group, and 1222947 patients in Control group.

Regarding patients' characteristics, the average age of all patients was (58.8 years), with 619859 (49.4%) male patients and 635259 (50.6%) female patients.

Regarding Meta-analysis of outcome measures; Data were divided into two groups (Psoriasis group and Control group).

Regarding primary outcome measure; We found 3 studies reported rate of IHD with total number of patients (N= 1214611).

The fixed-effects model of the meta-analysis study showed highly significant increase in IHD in Psoriasis group compared to Control group ($p < 0.01$) which came in agreement with ***Lai and Yew 2016***[1] and with ***Fernández-Armenteros et al. 2019.***[7]

Lai and Yew 2016[1] reported that Psoriatic patients were at significantly higher risks of developing MI (odds ratio [OR] 2.24; 95%; P = .005) and ischemic heart disease (OR 1.90; 95%; P = .008), but not stroke (OR 1.01; 95%; P = .744), after adjustment was made for major cardiovascular risk factors.

Fernández-Armenteros et al. 2019[7] reported that Our statistics corroborate the increased risk of struggling a major cardiovascular event in patients with psoriasis, both ischemic heart disease (OR 1.87, 95%, p<0.001) and cerebrovascular disease (OR 1.55, 95%, p <0.001). The incidence of principal cardiovascular events was studied in patients with psoriasis and non-psoriatic population. The history of ischemic heart disease turned into evidenced in 229 patients with psoriasis (3.3%) (OR 1.87, 95%, p<0.001).

Regarding secondary outcome measures; We found 5 studies reported rate of atherosclerosis with total number of patients (N=1255118).

The random-effects model of the meta-analysis study showed highly significant increase in atherosclerosis in Psoriasis group compared to Control group ($p < 0.01$) which came in agreement with ***Ibáñez- Bosch et al. 2017***[8] and with ***Hu and Lan 2017.***[2]

Ibáñez-Bosch et al. 2017[8] reported that according to carotid ultrasound, the 30.2% of patients with Psoriatic arthritis (PsA) had atherosclerosis (presence of carotid plaques and/or carotid intima-media thickness (IMT) more than 0.9 mm) in comparison to 9.4% of controls $p = 0.007$.

Hu and Lan 2017[2] reported that Atherosclerosis is the principal pathological change preceding the development of myocardial infarction and stroke. patients with psoriasis have been observed to have elevated arterial stiffness in comparison to healthy controls, and there's a positive correlation among arterial stiffness and psoriasis disorder duration.

We found 5 studies reported rate of HTN with total number of patients (N=1255118).

The random-effects model of the meta-analysis study showed highly significant increase in HTN in Psoriasis group compared to Control group ($p = 0.001$) which came in agreement with ***Imbalzano et al. 2015***[9] and with ***Arnold et al. 2019***[10]

Imbalzano et al. 2015[9] reported that In 2009, in an observational study of 3236 patients with psoriasis reported an increase in prevalence of traditional CV risk factors (diabetes mellitus, hypertension, dyslipidemia, and smoking) compared with controls.

Arnold et al. 2019[10] reported that there is significant difference in hypertension between African American patients with psoriasis and without psoriasis (p value< 0.001).

CONCLUSION

To conclude, there is strong association between the prevalence of cardiovascular risk factors and major cardiovascular events and psoriatic patients.

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Conflict of interest

None.

Authorship

All the listed authors contributed significantly to conception and design of study, acquisition, analysis and interpretation of data and drafting of manuscript, to justify authorship.

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