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REVIEW ARTICLE

Association of total oxidant status, total antioxidant status, and malondialdehyde and catalase levels with psoriasis: a systematic review and meta-analysis

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Abstract

Although oxidative stress plays a major role in psoriasis, the association between oxidative stress biomarker levels and psoriasis in humans remains controversial. Relevant articles were retrieved by searching the following databases: PubMed, Web of Science, and EMBASE, without any time limit (updated March 10th, 2019). The pooled weighted mean difference (WMD) and 95% confidence interval (CI) for the total oxidant status (TOS), total antioxidant status (TAS), malondialdehyde (MDA), and catalase (CAT) were calculated for each study. Heterogeneity test, publication bias analysis, and sensitivity analysis were performed. A total of 28 case-control studies, containing a combined total of 2724 subjects (1485 psoriasis patients and 1239 healthy controls), were enrolled in this meta-analysis. The combined results showed a significant difference in the TAS levels (WMD = − 0.213 mmol/L, $p < 0.001$, 95% CI = − 0.216 to − 0.165), TOS levels (WMD = 2.196 μmol/L, $p < 0.001$, 95% CI = 1.667 to 2.726), MDA levels (WMD = 1.854 nmol/L, $p < 0.001$, 95% CI = 1.494 to 2.215), and CAT levels (WMD = − 22.341 kU/L, $p = 0.008$, 95% CI = − 38.934 to − 5.748) between psoriasis patients and controls. Moreover, the combined results showed a significant difference in the TAS, MDA, and CAT levels in patients with mild vs. moderate psoriasis and moderate vs. severe psoriasis. TAS and CAT levels in psoriasis patients were significantly lower than in healthy controls, whereas the TOS and MDA levels were significantly higher. Furthermore, the TAS, MDA, and CAT levels are associated with the severity of disease. These results indicate that redox imbalances play a major role in the pathogenesis of psoriasis.

Keywords Catalase · Malondialdehyde · Meta-analysis · Oxidative stress · Psoriasis · Total antioxidant status · Total oxidant status

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Introduction

Psoriasis is one of the most common chronic inflammatory skin diseases, characterized by skin scaling and erythema, and can severely impair the health and quality of life, affecting 3% of the population worldwide [1]. In addition, the prevalence of psoriasis has been increasing among the population [2]. Recently, the treatment for psoriasis has gone from the use of non-selective drugs such as corticosteroids, methotrexate, and acitretin, to more selective compounds such as cyclosporine and highly selective biological therapies (interleukin-17 inhibitors, tumor necrosis factor-α inhibitors) [3]. Furthermore, other small molecules such as A3 adenosine receptor agonists, Janus kinase inhibitors, and phosphodiesterase inhibitors are under investigation for their potential use in treatments. Genetic, immunological, and metabolic mechanisms have been proposed to play a vital role in the onset/development of psoriasis, but the etiology of psoriasis is still

unknown [4]. However, recent studies have shown that oxidative stress is central to the pathogenesis of psoriasis [5].

Redox imbalances are increasingly implicated in the pathogenesis of psoriasis and manifest throughout the disease [5]. Many studies have shown a significant and abnormal rise in the levels of oxidative stress biomarkers in psoriasis patients [6]. However, the association between oxidative stress biomarkers and psoriasis in humans remains controversial. For example, Karababa et al. [7] reported that psoriasis patients had higher total oxidant status (TOS) levels and lower total antioxidant status (TAS) levels than control individuals. However, Gavan et al. [8] found that psoriasis patients had higher TAS levels than the control group. Similarly, Asha et al. [9] reported that the level of malondialdehyde (MDA) was significantly higher in patients with psoriasis than in normal subjects. No significant differences between the patients and controls were found in terms of MDA and TAS levels, as reported by Toker [10]. Moreover, several studies have found abnormal levels of TOS and catalase (CAT) in psoriasis patients compared with controls, although this difference is limited [11, 12].

Therefore, we carried out a systematic review and meta-analysis of all published case-control studies on this topic, to collate evidence and provide a precise estimate of the relationship between oxidative stress biomarkers and psoriasis patients.

Materials and methods

Search strategy

To search relevant psoriasis studies that measured TAS, TOS, MDA, and CAT levels, two independent reviewers (Youcan Zhang, Zhen Mu) systematically searched PubMed, Web of Science, and EMBASE database, without any time limit (updated March 10th, 2019). The search terms included "psoriasis" "total antioxidant capacity OR total antioxidant status OR total antioxidant response OR antioxidant potential" AND "total oxidant capacity OR total oxidant status" AND "malondialdehyde" AND "catalase." Varying combinations of the search terms were used for identifying the relevant literature, and the search strategies were customized to suit each database.

Study selection and data extraction

Study selection was carried out by two independent reviewers (Youcan Zhang, Zhen Mu) according to the following inclusion criteria: (1) case-control study, (2) random sampling or cluster sampling, (3) laboratory assessment of TAS, TOS, MDA, and CAT, (4) published in English, (5) full article access, (6) clear diagnostic criteria, (7) human subjects, and (8) characteristics of participants. Articles that did not meet the inclusion criteria were excluded. Full-text articles were evaluated for eligibility. For each study, the following data were collected independently by the two reviewers (Youcan Zhang, Zhen Mu): the first author's name, country, publication year, mean age, sample size, male vs. female sample size, TAS concentration, TOS concentration, MDA concentration, and CAT concentration. Any disagreement between the reviewers was settled by a discussion.

Quality assessment

The quality assessments for the study were based on the Newcastle–Ottawa Scale [13, 14]. The quality score for each study was reviewed independently by two investigators (Youcan Zhang, Zhen Mu), who evaluated the three categories (8 items), i.e., selection, comparability, and exposure, for case-control studies. The selection category contains four quality items (4 scores), comparability contains one item (2 scores), and exposure contains three items (3 scores). The quality score of a study directly reflects how adequate its quality is considered.

Statistical analysis

Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood Cliffs, NJ, USA; http://www.meta-analysis.com) was used for the meta-analysis. The weighted mean differences (WMDs) in TAS, TOS, MDA, and CAT levels between psoriasis and control groups, and 95% confidence intervals (CIs), were calculated for each study. The between-study heterogeneity was tested with the χ^2-based Q statistic and I^2 statistic. A funnel plot analysis and Egger's test were performed to assess publication bias. Sensitivity analysis was performed using the leave-one-out strategy. A p value < 0.05 (two-tailed) was considered indicative of a statistically significant difference between groups.

Results

Characteristics of the included studies

The flow diagram of the article search process is presented in Fig. 1. The initial search strategy identified 66 studies in PubMed, 87 in Web of Science, and 54 in EMBASE. Finally, 28 case-control studies [7–12, 15–36], containing a combined total of 2724 subjects (1485 patients with psoriasis and 1239 healthy controls), were used for the meta-analysis. The main characteristics of the included studies are provided

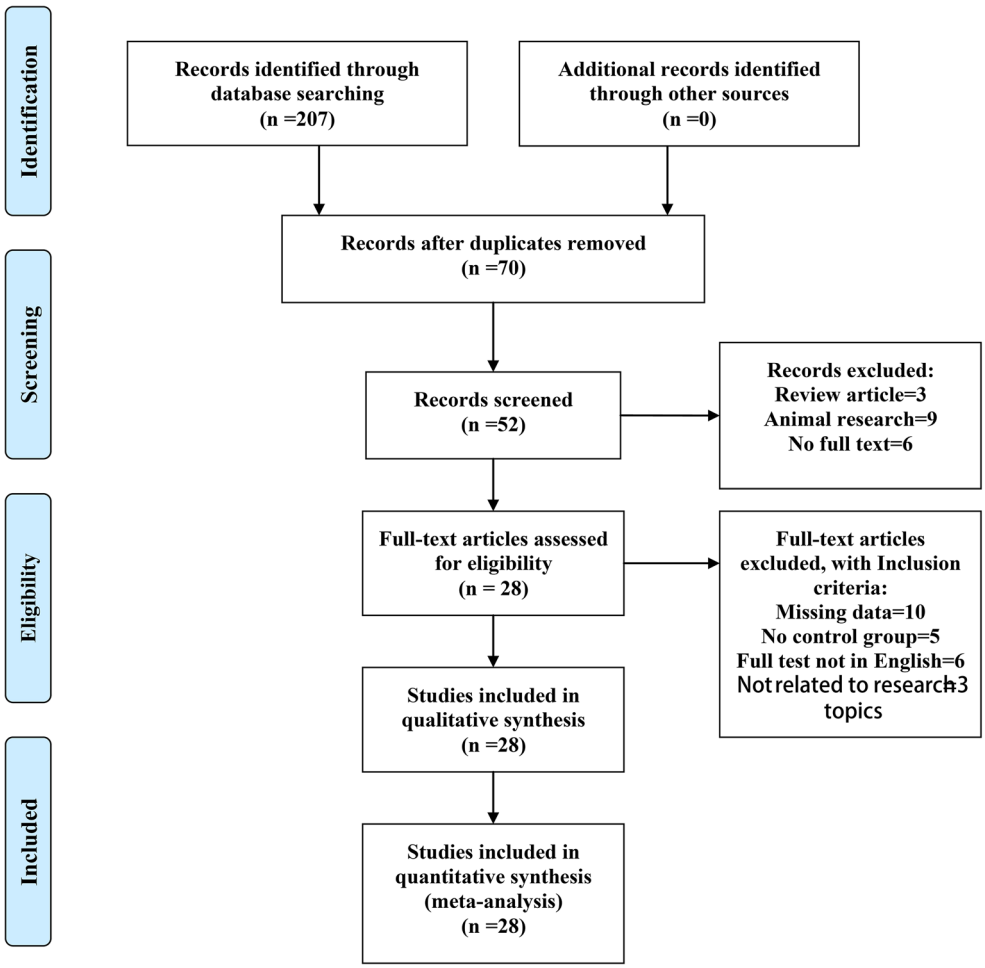


Fig. 1 The flow diagram of the article search process

in Table 1. The quality scores of these studies ranged from 5 to 9, with a mean of 8.32. The detailed scoring results are presented in Table 2.

According to the type of oxidative stress biomarkers, the 28 studies were categorized into four groups. As some studies discussed several types of oxidative stress biomarkers, they were eligible for inclusion into more than one group. Thus, according to the different types of oxidative stress biomarkers considered (TAS/TOS/MDA/CAT), the following categorizations were identified:

(1) A total of 15 articles [7, 8, 10–12, 15, 20, 21, 24, 25, 28, 32–35] reported the relationship between TAS levels and psoriasis (722 cases and 563 controls) (Table 3),
(2) A total of 4 articles [7, 11, 22, 35] reported the relationship between TOS levels and psoriasis (167 cases and 178 controls) (Table 3),
(3) A total of 14 articles [9, 10, 12, 16–19, 27–29, 31, 32, 36] reported the relationship between MDA levels and psoriasis (814 cases and 702 controls) (Table 3), and
(4) A total of 3 articles [12, 17, 32] reported the relationship between CAT levels and psoriasis (245 cases and 150 controls) (Table 3).

Meta-analysis of the association of total antioxidant status with psoriasis

The meta-analysis revealed a significant level of between-study heterogeneity for TAS among the available studies ($I^2 = 96.69\%$, $p < 0.001$). Random-effects modeling of the combined results revealed a significant difference in the TAS levels between psoriasis patients and controls (WMD = − 0.213 mmol/L, $p < 0.001$, 95% CI = − 0.216 to − 0.165, Fig. 2).

Meta-analysis of the association of total oxidant status with psoriasis

The meta-analysis revealed a significant level of between-study heterogeneity for TOS among the available studies

Table 1 Characteristics of the included studies

First author	Year	Country	Psoriasis group				Control group			
			Number	Male	Female	Age	Number	Male	Female	Age
M Hashemi	2010	Iran	40	24	16	30.6	46	29	17	34.3
Nemati Houshang	2014	Iran	100	55	45	35.7 ± 10	100	55	45	35.7 ± 13
Marta Wacewicz	2017	Poland	60	30	30	41.23 ± 12.46	58	17	41	40.12 ± 13.80
Petronila Rocha-Pereira	2001	Portugal	48	30	18	47 ± 12	40	22	18	47 ± 13
Kumari Asha	2017	India	150	95	55	39.56 ± 11.86	150	95	55	37.50 ± 12.55
Medha Rajappa	2016	India	60	50	10	41.97 ± 13.40	60	49	11	43.75 ± 11.14
Ufuk Sezer	2016	Turkey	120	64	56	42.68 ± 11.57	40	20	20	44.45 ± 10.85
Norina Gavan	1997	USA	7	7		48.7 ± 5.7	6	6		46.3 ± 3.2
Birgül Vanizor Kural	2003	Turkey	35	17	18	34.8	35	19	16	36.2
Fatih Karababa	2013	Turkey	39	17	22	28 ± 7	25	10	15	28 ± 7
Vijaykumar M. Pujari	2010	India	90				90			
Hacer Altın Sürücü	2015	Turkey	40	22	18	37.90 ± 10.75	47	23	24	36.60 ± 8.29
Susana Coimbra	2010	Portugal	34	16	18	43 ± 15	37	21	16	47 ± 15
Sami A. Gabr	2012	Egypt	55	35	20	29 ± 13.6	20	12	8	23 ± 1.5
Dipali P. Kadam	2010	India	90				30			
Aysun Toker	2009	Turkey	30	12	18	30.4 ± 10.6	23	11	12	29.5 ± 7.1
Sirje Kaur	2013	Estonia	60	42	18	43.2 ± 12.4	47	33	14	40.7 ± 10.2
K.H. Basavaraj	2013	India	30				10			
S. Emre	2012	Turkey	28	16	12	39.89 ± 11.07	46	26	20	35.11 ± 10.58
Serap Utas	2002	Turkey	20	12	8	35.15 ± 12.12	15	8	7	40.13 ± 12.38
I~brahim Ko¨kc¸am	1999	Turkey	34	20	14		34	20	14	
Vineet Relhan	2002	India	40	34	6		40	35	5	
A. S¸ ikar Aktu¨ rk	2012	Turkey	23	11	12	42.8 ± 16.5	23	11	12	42.2 ± 15.9
Kiymet Baz	2003	Turkey	35	13	22	42.54 ± 13.7	24	10	14	44 ± 13.04
M. Asefi	2012	Iran	100	43	57	35.3 ± 10.9	100	44	56	35.7 ± 13.2
E. Attwa	2011	Egypt	25	16	9	42.54 ± 13.69	31	14	17	43.00 ± 13.04
M Yildirim	2003	Turkey	22	10	12	33	22	10	12	37
P.ROCHA-PEREIRA	2004	Portugal	70	40	30	45.9 ± 12.2	40	22	18	47.4 ± 13.3

(I^2 = 91.08%, p < 0.001). Random-effects modeling of the combined results revealed a significant difference in the TOS levels between psoriasis patients and controls (WMD = 2.196 μmol/L, p < 0.001, 95% CI = 1.667 to 2.726, Fig. 2).

Meta-analysis of the association of malondialdehyde with psoriasis

The meta-analysis revealed a significant level of between-study heterogeneity for MDA among the available studies (I^2 = 98.20%, p < 0.001). Random-effects modeling of the combined results revealed a significant difference in the MDA levels between psoriasis patients and controls (WMD = 1.854 nmol/L, p < 0.001, 95% CI = 1.494 to 2.215, Fig. 2).

Meta-analysis of the association of catalase with psoriasis

The meta-analysis revealed a significant level of between-study heterogeneity for CAT among the available studies (I^2 = 78.17%, p = 0.010). Random-effects modeling of the combined results revealed a significant difference in the CAT levels between psoriasis patients and controls (WMD = − 22.341 kU/L, p = 0.008, 95% CI = − 38.934 to − 5.748, Fig. 2).

Meta-analysis of the association of total antioxidant status, malondialdehyde, and catalase with severity of psoriasis

The meta-analysis revealed a significant level of between-study heterogeneity for TAS, MDA, and CAT among the

Table 2 Newcastle–Ottawa Scale (NOS) quality assessment table

Study	Selection	Comparability	Outcome	Overall Star Rating
M Hashemi	4	2	3	9
Nemati Houshang	4	2	3	9
Marta Wacewicz	4	2	3	9
Petronila Rocha-Pereira	4	2	3	9
Kumari Asha	4	2	3	9
Medha Rajappa	4	2	3	9
Ufuk Sezer	4	2	3	9
Norina Gavan	3	1	2	6
Birgül Vanizor Kural	4	2	3	9
Fatih Karababa	4	2	3	9
Vijaykumar M. Pujari	2	1	3	6
Hacer Altın Sürücü	4	2	3	9
Susana Coimbra	4	2	3	9
Sami A. Gabr	4	2	3	9
Dipali P. Kadam	2	1	2	5
Aysun Toker	4	2	3	9
Sirje Kaur	4	2	3	9
K.H. Basavaraj	2	1	2	5
S. Emre	4	2	3	9
Serap Utas	4	2	3	9
I~brahim Ko¨kc¸am	4	2	3	9
Vineet Relhan	3	1	3	7
A. S¸ ikar Aktu¨ rk	3	1	2	6
Kiymet Baz	4	2	3	9
M. Asefi	4	2	3	9
E. Attwa	4	2	3	9
M Yildirim	4	2	3	9
P.ROCHA-PEREIRA	4	2	3	9

available studies (TAS [mild vs. moderate $I^2 = 98.04\%$, $p < 0.001$; moderate vs. severe $I^2 = 99.84\%$, $p < 0.001$]; MDA [mild vs. moderate $I^2 = 90.07\%$, $p < 0.001$; moderate vs. severe $I^2 = 96.32\%$, $p < 0.001$]; CAT [mild vs. moderate $I^2 = 95.34\%$, $p < 0.001$; moderate vs. severe $I^2 = 89.02\%$, $p < 0.001$]). Random-effects modeling of the combined results revealed a significant difference in the TAS, MDA, and CAT levels between the patients with mild vs. moderate psoriasis and moderate vs. severe psoriasis (Fig. 3, Table 4).

Analysis of publication bias

Funnel plots and Egger's test were used to analyze the publication bias in our current meta-analysis. Only a slight asymmetry was observed in the funnel plots, except for CAT (Fig. 4). Egger's test revealed no publication bias in our current meta-analysis (TAS $t = 0.59$, $p = 0.57$, 95% CI = − 2.66 to 4.65; TOS $t = 2.32$, $p = 0.146$, 95% CI = − 3.63 to 12.13; MDA $t = 0.86$, $p = 0.407$, 95% CI = − 3.92 to 9.02), except for CAT ($t = 115.72$, $p = 0.0055$, 95% CI = − 9.79 to − 7.85). In the mild, moderate, and severe subgroup analysis, only a slight asymmetry was observed in the funnel plots (Fig. 5). Egger's test showed no publication bias in the meta-analysis (TAS [mild vs. moderate $t = 0.87$, $p = 0.47$, 95% CI = − 38.45 to 25.31; moderate vs. severe $t = 0.41$, $p = 0.72$, 95% CI = − 146.66 to 121.01]; MDA [mild vs. moderate $t = 1.14$, $p = 0.32$, 95% CI = − 4.04 to 9.64; moderate vs. severe $t = 2.24$, $p = 0.09$, 95% CI = − 1.58 to 14.73]; CAT [mild vs. moderate $t = 0.42$, $p = 0.74$, 95% CI = − 82.61 to 88.31; moderate vs. severe $t = 1.28$, $p = 0.42$, 95% CI = − 14.23 to 11.62]).

Sensitivity analysis

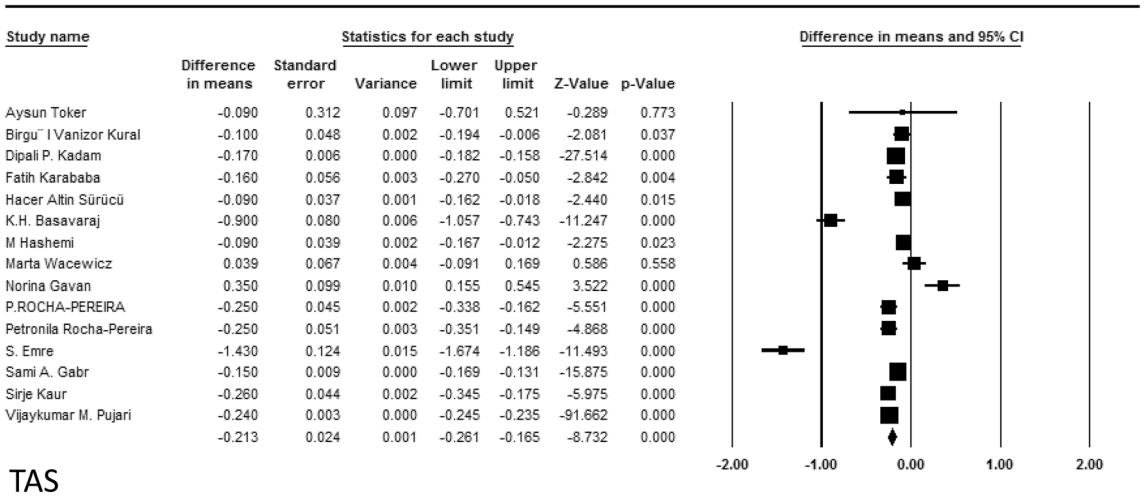
For the meta-analysis of the association of TAS, TOS, MDA, and CAT with psoriasis, sensitivity analysis was performed using the leave-one-out strategy. The removal of any single study during the sensitivity analysis of TAS, TOS, and MDA did not change the overall statistical significance, suggesting that this meta-analysis was relatively stable and credible (Table 5). However, two studies affected the meta-analysis results in the context of the association between CAT and psoriasis (Table 5).

Table 3 Comparison of the level of TAS, TOS, MDA, and CAT in psoriasis and control group

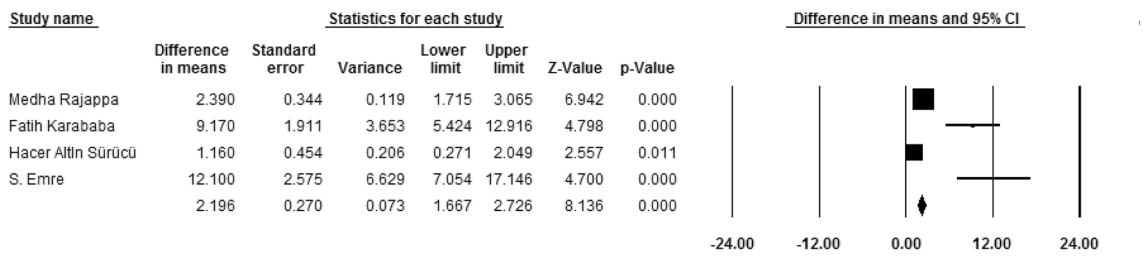
Study	Psoriasis group			Control group		
	Mean	SD	Number	Mean	SD	Number
TAS						
Aysun Toker	1.94	1.21	30	2.03	1	23
Birgül Vanizor Kural	1.52	0.18	35	1.62	0.22	35
Dipali P. Kadam	0.79	0.028	90	0.96	0.033	30
Fatih Karababa	1.03	0.19	39	1.19	0.26	25
Hacer Altın Sürücü	1.09	0.13	40	1.18	0.2	47
K.H. Basavaraj	0.29	0.206	30	1.19	0.257	10
M Hashemi	0.685	0.177	40	0.775	0.187	46
Marta Wacewicz	1.892	0.395	60	1.853	0.323	58
Norina Gavan	2.25	0.22	7	1.9	0.11	6
P.ROCHA-PEREIRA	1.38	0.25	70	1.63	0.18	40
Petronila Rocha-Pereira	1.41	0.28	48	1.66	0.18	40
S. Emre	2.14	0.12	28	3.57	0.65	46
Sami A. Gabr	0.82	0.033	55	0.97	0.044	20
Sirje Kaur	1.28	0.19	60	1.54	0.26	47
Vijaykumar M. Pujari	1.49	0.019	90	1.73	0.016	90
TOS						
Medha Rajappa	8.54	1.94	60	6.15	1.83	60
Fatih Karababa	26.92	7.82	39	17.75	6.85	25
Hacer Altın Sürücü	12.05	2.66	40	10.89	1.49	47
S. Emre	24.52	4.7	28	12.42	13.09	46
MDA						
A. Sikar Aktu¨ rk	4.33	1.2	23	2.03	1.28	23
Aysun Toker	9.5	3.5	30	9.47	5	23
Dipali P. Kadam	3.11	0.24	90	1.54	0.19	30
E. Attwa	4.78	0.51	25	3.4	0.96	31
I~brahim Ko¨kc¸am	1.47	0.36	34	1.39	0.26	34
Kiymet Baz	4.7	2.9	35	2.7	1.9	24
Kumari Asha	3.67	0.74	150	1.84	0.37	150
M Yildirim	13.9	2.8	22	13.2	3.2	22
M. Asefi	4.01	0.872	100	2.22	0.557	100
Nemati Houshang	17.6	3.7	100	10.1	2.4	100
Sami A. Gabr	4.24	0.57	55	1.32	0.5	20
Serap Utas	2.29	0.76	20	1.26	0.32	15
Vijaykumar M. Pujari	3.98	0.28	90	2.51	0.16	90
Vineet Relhan	3.85	0.21	40	2.7	0.17	40
CAT						
Nemati Houshang	42.4	18.1	100	56.1	56.1	100
Sami A. Gabr	24.92	6.73	55	69.54	69.54	20
Dipali P. Kadam	42.02	3.92	90	55.44	55.44	30

Discussion

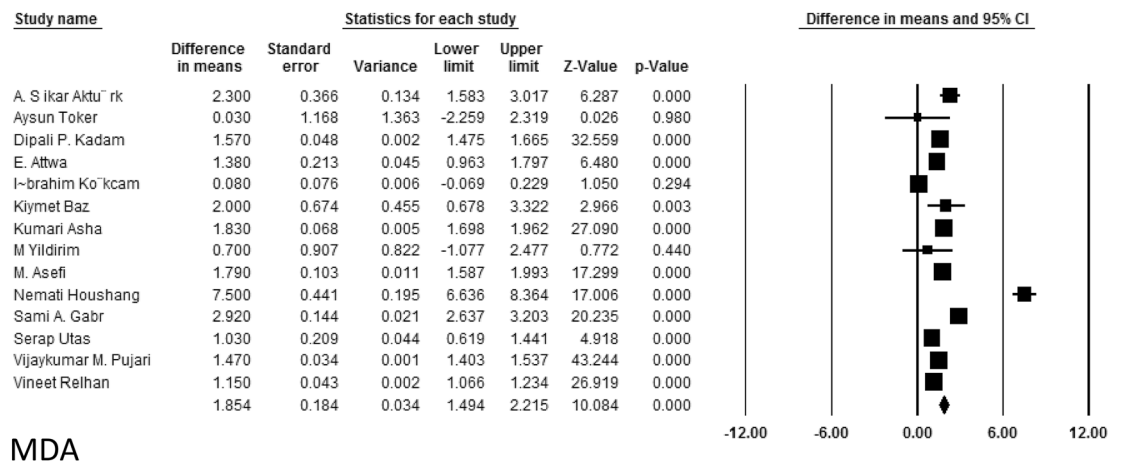
Although many studies in the literature have indicated that oxidative stress is involved in the pathogenesis of psoriasis [37], the association between oxidative stress biomarkers and psoriasis in humans remains unclear. To the best of our knowledge, this study is the first systematic review and meta-analysis to evaluate the available evidence on the association of TAS, TOS, MDA, and CAT levels in patients with psoriasis. The results from our meta-analysis showed that the TAS and CAT levels in psoriasis patients are significantly lower than



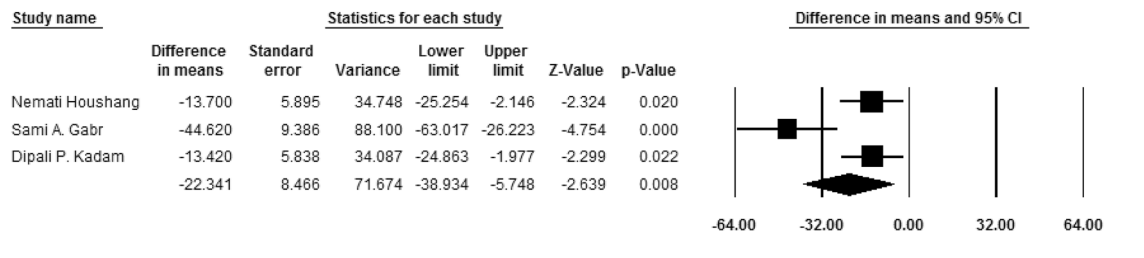
TAS



TOS



MDA



CAT

Fig. 2 Forest plot of the random effects in meta-analysis, showing the association of total antioxidant status, total oxidant status, malondialdehyde, and catalase levels with psoriasis

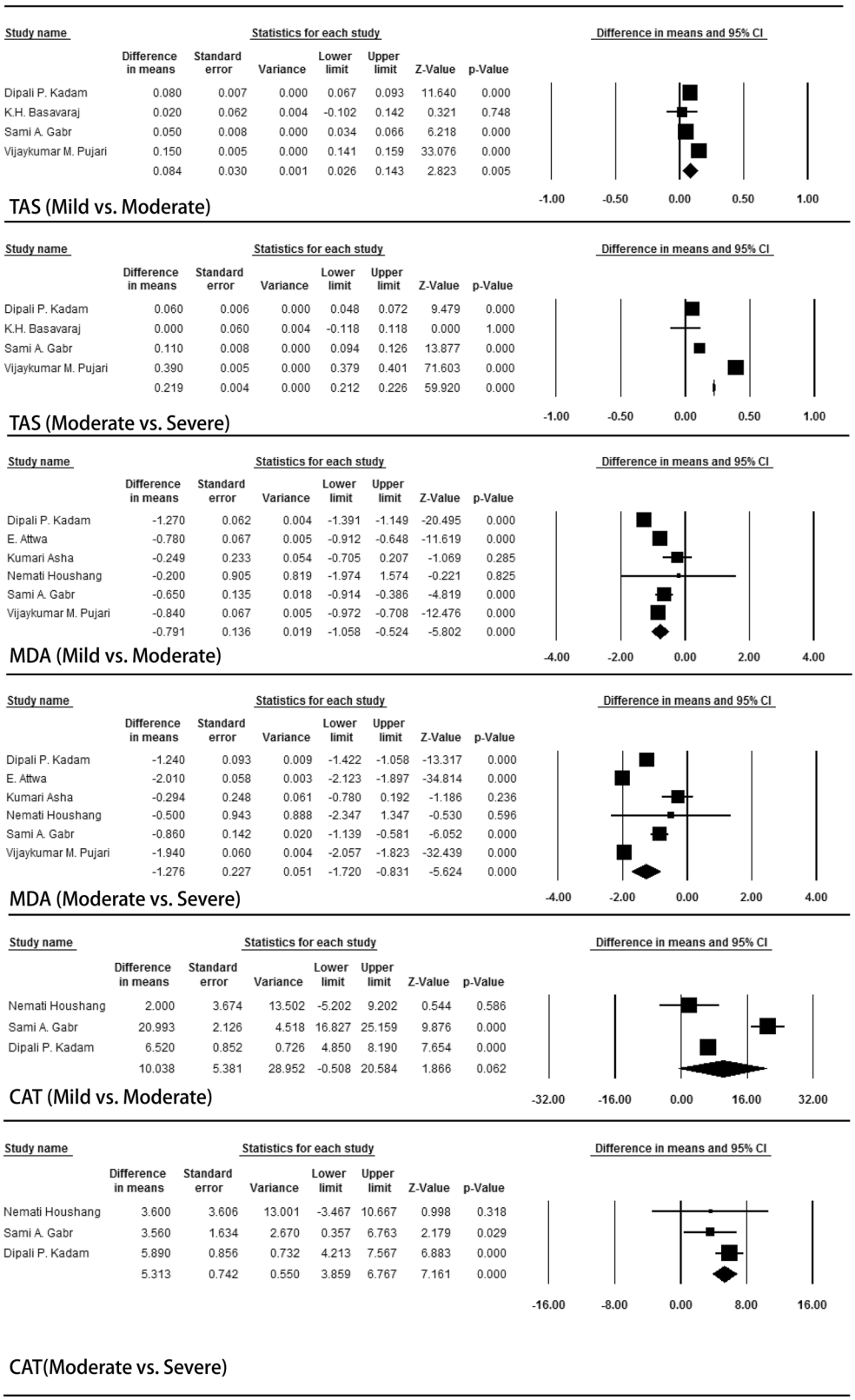


Fig. 3 Forest plot of the random effects in meta-analysis, showing the association of total antioxidant status, total oxidant status, malondialdehyde, and catalase levels with severity of psoriasis

in healthy controls, whereas TOS and MDA levels in psoriasis patients are significantly higher than in healthy controls. Moreover, the TAS, MDA, and CAT levels are associated with the severity of disease. These results suggest that oxidative stress imbalances play a vital role in the pathogenesis of psoriasis.

Table 4 Comparison of the level of TAS, TOS, MDA, and CAT among mild, moderate, and severe psoriasis

Study	Mild psoriasis		Moderate psoriasis		Severe psoriasis	
	Mean	SD	Mean	SD	Mean	SD
TAS						
Dipali P. Kadam	0.88	0.024	0.8	0.029	0.74	0.019
K.H. Basavaraj	0.14	0.225	0.12	0.257	0.12	0.207
Sami A. Gabr	0.87	0.028	0.82	0.034	0.71	0.027
Vijaykumar M. Pujari	1.64	0.016	1.49	0.019	1.1	0.023
TOS	None					
MDA						
Dipali P. Kadam	1.84	0.24	3.11	0.24	4.35	0.45
E. Attwa	3.19	0.26	3.97	0.26	5.98	0.18
Kumari Asha	2.436	0.84	2.685	0.96	2.979	0.96
Nemati Houshang	17.4	3.3	17.6	3.7	18.1	3.6
Sami A. Gabr	3.59	0.47	4.24	0.57	5.1	0.53
Vijaykumar M. Pujari	3.14	0.24	3.98	0.28	5.92	0.17
CAT						
Nemati Houshang	44.4	8.8	42.4	18.1	38.8	7.9
Sami A. Gabr	45.913	9.5	24.92	6.73	21.36	5.9
Dipali P. Kadam	48.56	2.53	42.04	3.92	36.15	2.57

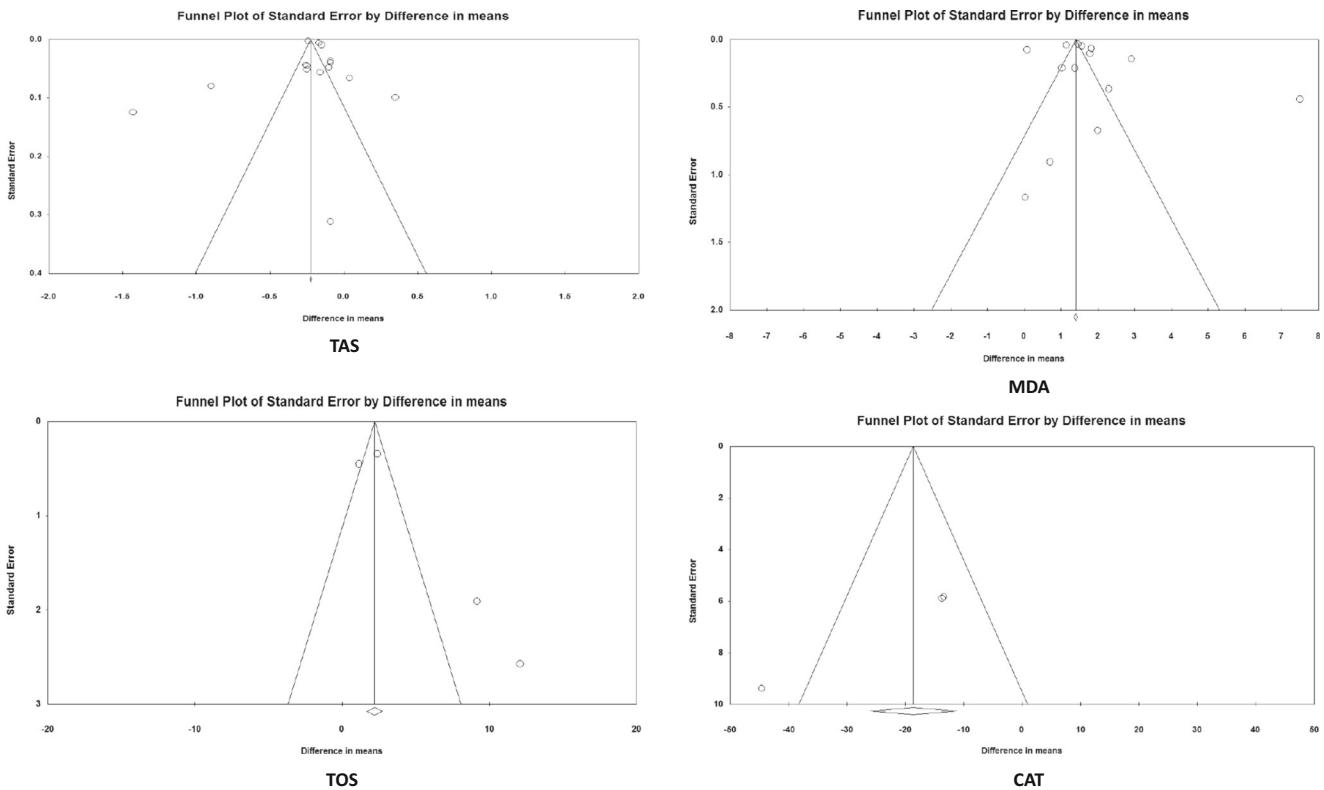


Fig. 4 Funnel plot analysis to detect the publication bias, total oxidant status, total antioxidant status, malondialdehyde, and catalase levels in patients with psoriasis

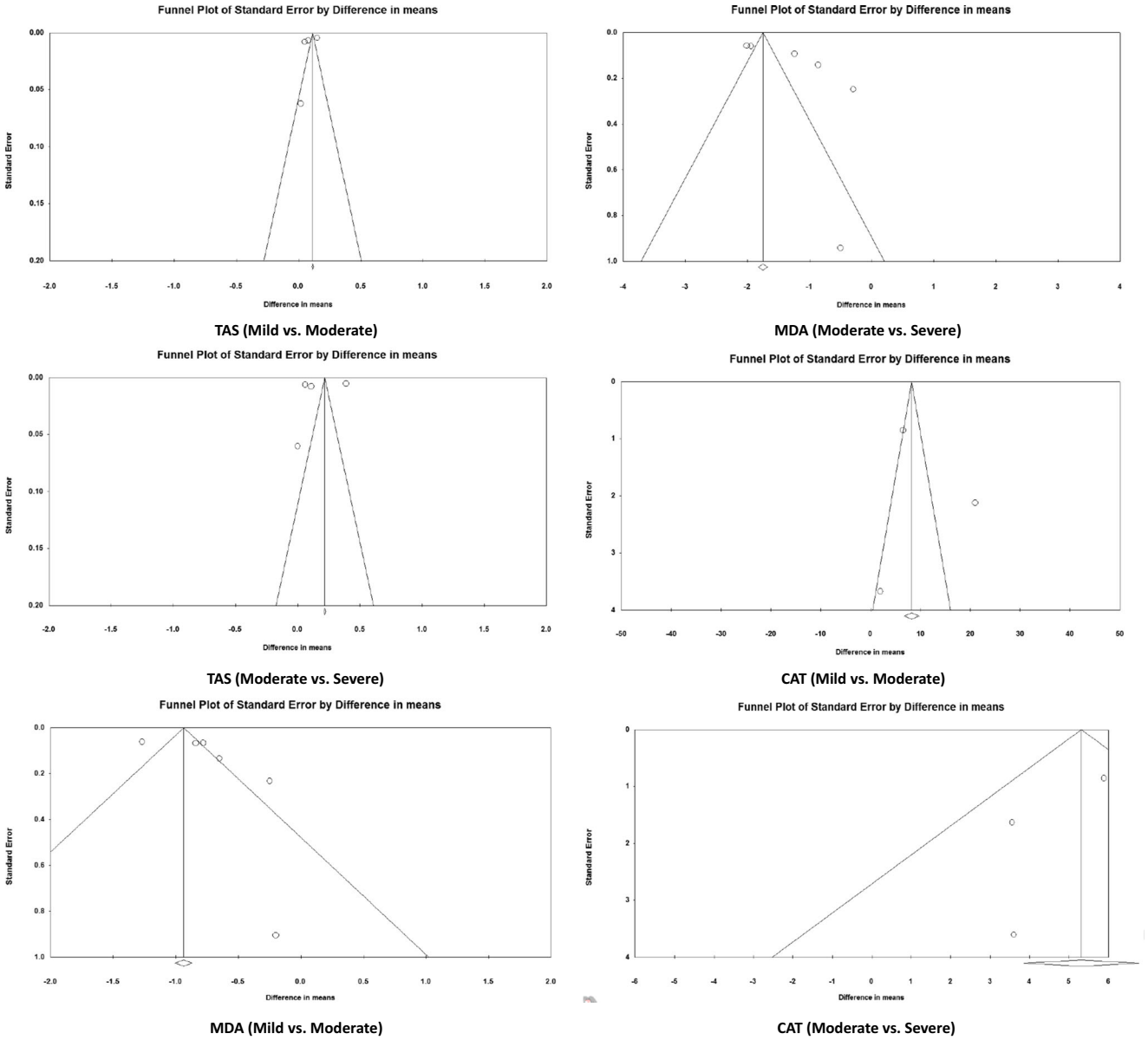


Fig. 5 Funnel plot analysis to detect the publication bias, total oxidant status, total antioxidant status, malondialdehyde, and catalase levels in patients with mild, moderate, and severe psoriasis

Total antioxidant status in psoriasis

Many efforts have been made to investigate the relationship between TAS and psoriasis. Rocha-Pereira et al. [24], based on a case-control study, reported that the TAS levels are significantly decreased in patients with psoriasis. Similarly, Kaur et al. [33] found that patients with psoriasis had significantly lower TAS levels than healthy controls ($p < 0.0001$). However, contrasting results, with significantly higher TAS levels in psoriasis patients than in healthy controls, have also been reported by Gavan et al. [8]. Meanwhile, Wacewicz et al. [20] suggested that the levels of TAS were not significantly different between psoriasis patients and control individuals. Our current meta-analysis revealed that the levels of TAS were significantly lower in psoriasis patients compared with those in controls. However, we detected a significant level of heterogeneity in psoriasis research concerning TAS among the available studies. The marked heterogeneity in the outcomes may be partially explained by the differences in populations studied (e.g., Turkey vs. India), as well as the different measures and units employed. However, the sensitivity analysis for TAS revealed no change in the overall statistical significance, and Funnel plots and Egger's test confirmed no publication bias in our current meta-analysis, suggesting that this meta-analysis was relatively stable and credible.

Table 5 Sensitivity analysis using the leave-one-out strategy

Study	Point	95% CI		*t* value	*p* value
TAS					
Aysun Toker	−0.21	−0.26	−0.17	−8.73	< 0.001
Birgül Vanizor Kural	−0.22	−0.27	−0.17	−8.77	< 0.001
Dipali P. Kadam	−0.23	−0.29	−0.16	−6.91	< 0.001
Fatih Karababa	−0.22	−0.27	−0.17	−8.57	< 0.001
Hacer Altın Sürücü	−0.22	−0.27	−0.17	−8.83	< 0.001
K.H. Basavaraj	−0.18	−0.22	−0.13	−7.60	< 0.001
M Hashemi	−0.22	−0.27	−0.17	−8.83	< 0.001
Marta Wacewicz	−0.23	−0.28	−0.18	−9.17	< 0.001
Norina Gavan	−0.23	−0.28	−0.19	−9.67	< 0.001
P.ROCHA-PEREIRA	−0.21	−0.26	−0.16	−8.25	< 0.001
Petronila Rocha-Pereira	−0.21	−0.26	−0.16	−8.29	< 0.001
S. Emre	−0.18	−0.22	−0.13	−7.95	< 0.001
Sami A. Gabr	−0.22	−0.28	−0.17	−8.23	< 0.001
Sirje Kaur	−0.21	−0.26	−0.16	−8.21	< 0.001
Vijaykumar M. Pujari	−0.22	−0.29	−0.16	−6.84	< 0.001
TOS					
Medha Rajappa	1.89	1.03	2.74	4.34	< 0.001
Fatih Karababa	2.05	1.52	2.59	7.53	< 0.001
Hacer Altın Sürücü	2.76	2.11	3.42	8.23	< 0.001
S. Emre	2.09	1.55	2.62	7.69	< 0.001
MDA					
A. S¸ ikar Aktu¨ rk	1.40	1.36	1.44	68.91	< 0.001
Aysun Toker	1.40	1.36	1.44	69.17	< 0.001
Dipali P. Kadam	1.36	1.32	1.41	61.13	< 0.001
E. Attwa	1.40	1.36	1.44	68.85	< 0.001
I~brahim Ko¨kc¸am	1.50	1.46	1.54	71.45	< 0.001
Kiymet Baz	1.40	1.36	1.44	69.10	< 0.001
Kumari Asha	1.36	1.32	1.40	63.98	< 0.001
M Yildirim	1.40	1.36	1.44	69.16	< 0.001
M. Asefi	1.39	1.34	1.43	67.07	< 0.001
Nemati Houshang	1.39	1.35	1.43	68.45	< 0.001
Sami A. Gabr	1.37	1.33	1.41	66.98	< 0.001
Serap Utas	1.40	1.36	1.44	69.00	< 0.001
Vijaykumar M. Pujari	1.36	1.31	1.41	54.03	< 0.001
Vineet Relhan	1.47	1.43	1.52	64.05	< 0.001
CAT					
Nemati Houshang	−28.15	−58.68	2.37	−1.81	0.071
Sami A. Gabr	−13.56	−21.69	−5.43	−3.27	0.001
Dipali P. Kadam	−28.30	−58.55	1.96	−1.83	0.067

Total oxidant status in psoriasis

In this meta-analysis, the level of TOS in psoriasis patients was significantly higher than that in healthy controls. A total of four case-control studies of TOS were used in this meta-analysis, all of which claimed that the TOS levels were higher in psoriasis patients than in healthy controls. Even though there was a marked heterogeneity among the available studies concerning TOS, the sensitivity analysis suggested that our meta-analysis was relatively stable and credible. The literature regarding the association of TOS levels with psoriasis is rather limited. Thus, multi-center studies with a larger sample size should be conducted to confirm these results.

Malondialdehyde in psoriasis

Some studies have claimed the association of MDA with psoriasis. Kadam et al. [12] carried out a case-control study, showing that the serum MDA levels were significantly increased in psoriasis patients than in healthy controls. Relhan et al. [19] also reported significantly increased levels of plasma MDA in patients with acute psoriasis than in controls. However, several other studies have reported an absence of significant difference in MDA between psoriasis and normal controls [10, 18, 36]. The combined results from our meta-analysis revealed that psoriasis patients have higher serum MDA levels than normal controls. The meta-analysis revealed a significant between-study heterogeneity for MDA among the available studies. This marked heterogeneity in the outcomes might be due to the lack of standardization in case selection or data collection. In spite of the marked heterogeneity concerning MDA among the available studies, sensitivity analysis and publication bias analysis suggested that the meta-analysis was relatively stable and credible.

Catalase in psoriasis

Only three case-control studies have reported the relationship between CAT and psoriasis. Although the combined results showed a significant difference in the CAT levels between psoriasis patients and controls, the sensitivity analysis showed that two studies in particular affected this result of the meta-analysis. Moreover, publication bias was also observed. Therefore, further studies with larger sample size are needed to verify our results.

Although a standard search strategy and a thorough computerized search method were applied in the current meta-analysis, our study has some limitations. First, we included case-control studies with differences in population characteristics (e.g., age, gender, country). Second, different measures and units are usually employed in the included studies, which may lead to between-study heterogeneity and publication bias. Third, it is important to assess the relationship between TOS, TAS, MDA, and CAT levels with psoriatic arthritis, but most of the literature included in the search did not clarify how many psoriatic patients had psoriatic arthritis. Last, the relationship between different clinical types of psoriasis (vulgar, inverted, pustular, and erythrodermic) and oxidative stress markers may be different, but most of the included literature did not clarify the clinical type of skin psoriasis.

Treatment approaches to psoriasis

Psoriasis has a considerable impact on the patients and the health care system. Therapeutic approaches to psoriasis may be varied because a number of issues in psoriasis research have not been definitively addressed. Furthermore, therapeutic paradigms are continuously changing. Methotrexate, a classic immunomodulator, has been used in the treatment of psoriasis for more than 50 years. West et al. [38] performed a meta-analysis and reported that 45.2% of patients achieve PASI75 at primary endpoint, against a calculated PASI75 of 4.4% (95% CI of 3.5–5.6%) for placebo, yielding a relative risk of 10.2% (95% CI 7.1–14.7%), suggesting that methotrexate is effective and remains the cornerstone of systemic treatment of psoriasis. Rajappa et al. [22] reported that methotrexate treatment results in a significant decline of both the inflammatory and oxidative stress parameters. Moreover, Wacewicz et al. [20] reported that the TAS level decreased upon NB-UVB treatment in psoriasis patients. With the continuously changing therapeutic paradigms, highly selective biological therapies (interleukin-17 inhibitors, tumor necrosis factor-α inhibitors) have been approved for the treatments of psoriasis [39]. Bacchetti et al. [40] reported that treatment with tumor necrosis factor-α inhibitors is associated with a reduction in lipid peroxidation and an improvement in HDL antioxidant and anti-inflammatory properties. Moreover, Caso et al. [41] reported that the levels of visfatin were higher in patients with psoriatic arthritis and suggested that visfatin may mediate a complex cellular signaling process stimulated by oxidative stress, resulting in vascular endothelial inflammation. Thus, visfatin may be a novel biomarker of psoriasis and a potential therapeutic target.

Conclusions

The meta-analysis provides evidence that the TAS and CAT levels in psoriasis patients are significantly lower than in healthy controls, whereas the TOS and MDA levels in psoriasis patients are significantly higher than in healthy controls. In addition, TAS, MDA, and CAT levels were associated with the severity of the disease. However, drawing a definitive conclusion on the association of CAT and TOS with psoriasis is difficult, owing to the limited number of available studies so far. Therefore, further studies should be carried out to strengthen this evidence, especially on the association of CAT and TOS with psoriasis.

Authors' contributions YC Z and Z M designed the study; YC Z, ZS L, Y M, and Z M collected the data; YC Z, ZS L, Y M, and Z M performed the statistical analysis; YC Z and Z M wrote the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Disclosures None.

Abbreviations WMD, weighted mean difference; CI, confidence interval; TOS, total oxidant status; TAS, total antioxidant status; MDA, malondialdehyde; CAT, catalase

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