

Nutrition, Obesity and Seborrheic Dermatitis: A Systematic Review

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Nutrition, Obesity and Seborrheic Dermatitis: A Systematic Review

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Abstract

Background: Pathogenesis of seborrheic dermatitis (SD) involves lipid secretion by sebaceous glands, *Malassezia* colonization and an inflammatory response with skin barrier disruption. Each of these pathways could be modulated by diet, obesity, and nutritional supplements. Current treatment options provide only temporary control of the condition; thus, it is essential to recognize modifiable lifestyle factors that may play a role in determining disease severity.

Objective: To summarize published evidence on diet, nutritional supplements, alcohol, obesity, and micronutrients in SD patients and to provide useful insights into areas of further research.

Methods: A literature search of Scopus, PubMed, and Medline (OVID interface) for English language articles published between 1993-2023 was conducted on 16th April 2023. Case-control studies, cohort studies, and randomized controlled trials with 5 or more subjects conducted on adult participants (>14 years) were included, case reports, case series and review papers were excluded.

Results: 13 studies, eight case-control, three cross-sectional and two randomized control trials, involving 13,906 patients were included. SD patients had significantly increased copper, manganese, iron, calcium, and magnesium concentrations and significantly lower serum zinc and vitamin D and E concentrations compared to controls. Adherence to the Western Diet was associated with a higher risk for SD in female patients and an increased consumption of fruit was associated with a lower risk of SD in all patients. The prebiotic Triphala improved patient satisfaction and decreased scalp sebum levels over eight weeks. Most studies find associations between regular alcohol use and SD but the association with BMI and obesity on SD severity and prevalence is mixed.

Conclusions: This review sheds light on specific promising areas of research that require further study, including the need for interventional studies evaluating serum zinc, vitamin D, and vitamin E supplementation for SD. The negative consequences of a western diet, alcohol use, and obesity, and the benefits of fruit consumption are well known; however, to fully understand their specific relationships to SD, further cohort or interventional studies are needed. Clinical Trial: This protocol was registered and can be accessed at Prospero with the registration number CRD42023417768.

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Original Manuscript

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I.W. conceived the presented idea, synthesized the data and wrote the preliminary manuscript. I.W. and M.A. verified the search terms and methods. I.W. and E.W. screened and assessed all studies for eligibility. N.K, A.P., M.A. and R.D. provided feedback and edited the manuscript. All authors discussed the results and contributed to the final manuscript.

Abstract

Background: Pathogenesis of seborrheic dermatitis (SD) involves lipid secretion by sebaceous glands, Malassezia colonization and an inflammatory response with skin barrier disruption. Each of these pathways could be modulated by diet, obesity, and nutritional supplements. Current treatment

options provide only temporary control of the condition; thus, it is essential to recognize modifiable lifestyle factors that may play a role in determining disease severity.

Objectives: To summarize published evidence on diet, nutritional supplements, alcohol, obesity, and micronutrients in SD patients and to provide useful insights into areas of further research.

Methods: A literature search of Scopus, PubMed, and Medline (OVID interface) for English language articles published between 1993-2023 was conducted on 16th April 2023. Case-control studies, cohort studies, and randomized controlled trials with 5 or more subjects conducted on adult participants (>14 years) were included, case reports, case series and review papers were excluded due to insufficient level of evidence.

Results: 13 studies, eight case-control, three cross-sectional and two randomized control trials, involving 13,906 patients were included. SD is correlated with significantly increased copper, manganese, iron, calcium, and magnesium concentrations and significantly lower serum zinc and vitamin D and E concentrations compared to controls. Adherence to the Western Diet was associated with a higher risk for SD in female patients and an increased consumption of fruit was associated with a lower risk of SD in all patients. The prebiotic Triphala improved patient satisfaction and decreased scalp sebum levels over eight weeks. Most studies find associations between regular alcohol use and SD but the association with BMI and obesity on SD severity and prevalence is mixed.

Conclusion: This review sheds light on specific promising areas of research that require further study, including the need for interventional studies evaluating serum zinc, vitamin D, and vitamin E supplementation for SD. The negative consequences of a western diet, alcohol use, and obesity, and

the benefits of fruit consumption are well known; however, to fully understand their specific relationships to SD, further cohort or interventional studies are needed.

This protocol was registered and can be accessed at Prospero with the registration number CRD42023417768.

Keywords: Seborrheic Dermatitis; Systematic Review; Diet; Nutritional Supplements; Alcohol; BMI

Key Points

- Multiple studies found significantly lower serum zinc, Vitamin E and Vitamin D levels in seborrheic dermatitis (SD) patients compared to controls. Interventional studies evaluating whether normalization of these levels could contribute to decreasing SD severity and prevalence are needed.
- Triphala (a prebiotic) supplementation for 8 weeks led to significant improvement in both subjective SD severity and mean scalp sebum levels in a small randomized controlled trial.
- Weak evidence supports that patients with a higher fruit intake have a decreased prevalence of SD and that higher adherence to the western diet in females is associated with an increased prevalence of SD.
- Regular alcohol use was shown to be associated with SD across numerous studies, however, significant confounders exist. Conflicting evidence exists on the association between BMI and SD with the majority of evidence supporting no association between the two.

Introduction

Seborrheic dermatitis (SD) is a chronic inflammatory skin disease that commonly presents on the face, scalp, and chest [1]. Seborrheic dermatitis, affects approximately 5% of the global population, while its non-inflammatory form affects closer to 50% of individuals [2]. SD prefers males of all ethnicities and peaks in the first three months of life and again at puberty, where it then reaches an apex at 40-60 years and later declines [3,4]. Risk factors for SD includes immunodeficiency, neurological diseases including Alzheimer's and Parkinson's, increased sebaceous gland activity, and exposures to drug treatment, including lithium, immunosuppressants, and dopamine antagonists [5]. SD has no definitive cause; however, evidence suggests the pathogenesis begins with androgens and adrenal corticosteroids that stimulate sebaceous gland activity [4]. These hormones are modulated by obesity; therefore, nutrition and BMI may play a role in influencing the SD clinical course. Several studies suggest that nutrition can influence other inflammatory skin diseases such as acne vulgaris, hidradenitis suppurativa, and psoriasis [6,7,8]. However, the magnitude of effect on each disease may be small, and nutritional studies are inherently limited by recall bias. Typical treatment includes antifungals in combination anti-inflammatories including topical corticosteroids and calcineurin inhibitors. However, long term use of these corticosteroids can cause adverse effects such as telangiectasia and current treatments cannot eliminate this chronic disease. Therefore, other options like dietary modifications could assist with management and prevent recurrence [9]. Currently, there is no review evaluating the effects of

nutrition and obesity on SD disease severity.

The goal of this review is to incorporate studies looking at diet, nutritional supplements, alcohol, obesity, and micronutrients in SD patients into an organized framework that can be used by clinicians to make evidence-based recommendations and to provide useful insights into specific areas of further study. We aim to answer the question of how diet, nutritional supplements, alcohol, obesity, and micronutrients affect SD prevalence, clinical course, severity, and subjective improvement in patients.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement was used to create this study. Case-control studies, cross-sectional studies, cohort studies, and randomized controlled trials with five or more subjects conducted on adult participants (>14 years) were included. Exclusion criteria were no case reports, case series, and review papers, as those did not provide a sufficiently high level of evidence. We also excluded studies which included any dietary or supplement intervention evaluated in the context of purposeful concurrent medication use. Eligible literature was any study evaluating BMI, waist circumference, micronutrients, alcohol use, or diet in relation to SD and any dietary or nutritional supplement intervention for SD. Eligible methodology to measure changes in SD severity included the SD Area and Severity Index (SDASI) score, sebum levels, subjective SD severity, or SD severity evaluated by a physician.

We searched Scopus, PubMed, and Medline (OVID interface) for English language articles published between 1993-2023. The final search was conducted on 16th April 2023. The search terms consisted of (seborrheic dermatitis OR seborrheic eczema) AND (diet OR dietary patterns OR dietary activities OR nutrition OR supplements OR fruit OR vegetables OR gluten OR dairy OR sugars OR meat OR carbohydrates OR protein OR fats OR vitamin OR micronutrients OR minerals OR alcohol OR calorie OR weight loss OR weight changes OR obesity OR obesity reduction OR

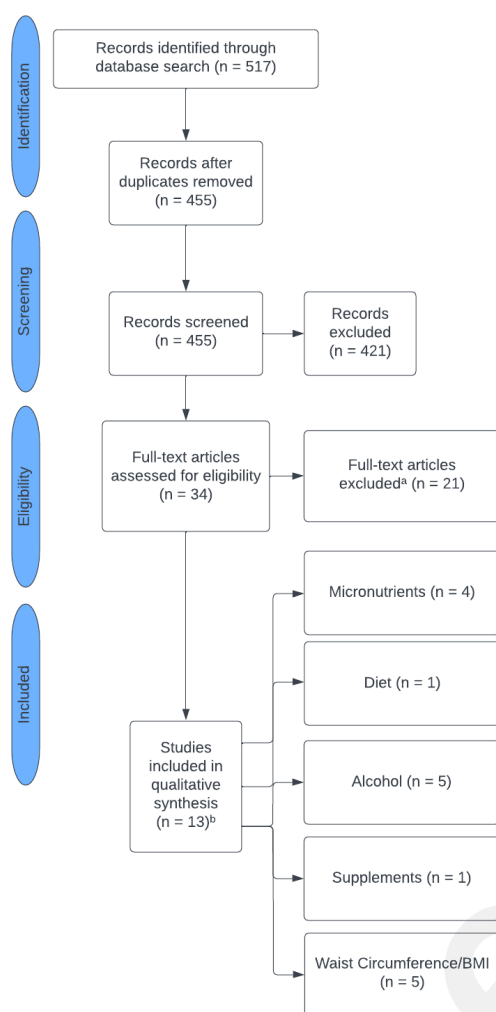
waist circumference OR body mass index OR BMI).

Literature search results were conducted by one person and exported to Cadima to remove duplicates and review articles. This tool was employed to ensure articles were uploaded to one place and so that reviewers could independently review included articles. 455 unique studies were screened and assessed for eligibility by two reviewers working independently. Disagreements were resolved by a third reviewers' decision. After applying inclusion and exclusion criteria, 13 studies (eight case-control, three cross-sectional, two randomized control trials (RCT's)) involving 13,906 patients were selected for inclusion. Multiple studies included results that fit into more than one category, including three studies evaluating both BMI and alcohol use (Figure 1).

Table 1. Search Strategy for Systematic Review

Database	Search Strategy
Scopus, PubMed, OVID (Medline interface)	(seborrheic dermatitis OR seborrheic eczema) AND (diet OR dietary patterns OR dietary activities OR nutrition OR supplements OR fruit OR vegetables OR gluten OR dairy OR sugars OR meat OR carbohydrates OR protein OR fats OR vitamin OR micronutrients OR minerals OR alcohol OR calorie OR weight loss OR weight changes OR obesity OR obesity reduction OR waist circumference OR body mass index OR BMI)

Figure 1. Study Selection.



^aAll full text articles were excluded due to lack of inclusion criteria eligibility

^bThree studies included results that evaluated both BMI and alcohol use

Table 2 summarizes the included studies' findings and evidence levels according to the ratings of Oxford Centre for Evidence-based Medicine [10]. Levels of evidence are defined as: level 1, randomized trials or systematic reviews of randomized trials, cross-sectional studies, inception cohort studies, or nested case-control studies; level 2, systematic review of surveys, randomized trials, individual cross-sectional studies with consistent reference standards and blinding, inception cohort studies, or (exceptional) observational studies with dramatic effect; level 3, Cohort studies, local nonrandom sample, nonconsecutive studies or studies without a consistently applied reference standard; level 4, case series, case-control study or historically controlled studies; and level 5,

mechanism-based reasoning. Level 1 represents evidence generally considered to be stronger, and level 5 represents evidence generally considered to be weaker. The Cochrane Collaboration's tool for assessing risk of bias was used to evaluate randomized control trials [11].

Although the intention of these tools is to reduce bias in selected studies, bias can be transferred from the tools themselves. The Cochrane Collaboration's tool specifically assesses for the risk of bias, rather than for bias itself, and is more likely to miss bias associated with incomplete data and selective reporting [11]. Oxford-based Medicine levels of evidence help readers prioritize studies, but they should be used as a guide, rather than absolute, when determining the validity of a study [10].

Table 2. Summary of included studies.

Author/s (year)	Study Design	Subjects	Sample	Intervention	Findings	Limitations	Evidence Level [10]
an et al/2021 [12]	Case Control Study	Dermatologist diagnosed SD patients Controls: age/sex matched healthy patients	151	Evaluate serum trace elements, micronutrients, antioxidants, malondialdehyde, and immunoglobulins in SD patients	Mean \pm SEM for: Serum Zinc (mg/L) SD patients: 1.430 ± 0.11 , HC's: 1.308 ± 0.09 , $P = .289$ Serum Copper (mg/L) SD patients: 2.136 ± 0.10 , HC's: 0.950 ± 0.05 , $P < .001$ Serum Manganese (mg/L) SD	Did not measure these parameters after the remission of SD This study received	

					<p>patients: 15.830 ± 0.85 HC's: 7.022 ± 0.46, $P < .001$</p> <p>Serum Iron (mg/L) SD patients: 2.248 ± 0.14 HC's: 1.130 ± 0.11, $P < .001$</p> <p>Serum Calcium (mg/L) SD patients: 185.040 ± 5.89 HC's: 99.580 ± 1.77, $P = .001$</p> <p>Serum Magnesium (mg/L) SD patients: 29.640 ± 0.55 HC's: 20.640 ± 0.27, $P < .001$</p> <p>Serum Vitamin A ($\mu\text{mol/L}$) SD patients: 0.403 ± 0.07 HC's: 0.374 ± 0.03, $P = .707$</p> <p>Serum Vitamin E ($\mu\text{mol/L}$) SD patients: 5.564 ± 0.39 HC's: 7.074 ± 0.37, $P = .009$</p>	<p>funding from the Cerebral Palsy Alliance Research Foundation, Sydney Medical School Foundation, and internal funding from CSF Global in Nepal, Indonesia, and Bangladesh</p>	
Shimi et al/2021 [14]	Case Control Study	<p>Patients aged 18-65 referred to the general outpatient clinic of Imam Sajjad Hospital and seen by a single dermatologist</p> <p>Controls: healthy adults attending clinic for cosmetic consultations</p>	289	<p>Determine serum level of 25-hydroxyvitamin D (25(OH)D) in patients with clinically manifested facial or scalp SD</p>	<p>25(OH)D was significantly lower in the case group compared to the control group (20.71 ± 8.16 vs. 23.91 ± 7.78, $P = .007$)</p> <p>Vitamin D insufficiency: more prevalent among healthy individuals</p> <p>Vitamin D deficiency: more prevalent in cases (Difference was statistically significant among groups, $P = .013$)</p>	<p>Lack of follow-up to see if supplementation of Vitamin D improved SD</p> <p>This study received funding from Mazandaran University for Medical Sciences Vice Chancellor of Research.</p>	
Arabay & Arman/2019 [15]	Case Control Study	<p>Patients diagnosed with SD by clinical or histopathological examination from dermatology outpatient clinic</p> <p>Controls: healthy age/sex matched patients with no evidence of SD from hospital staff volunteers</p>	84	<p>Determine the association between SD and serum zinc levels</p> <p>SD was graded according to SDASI</p>	<p>Significantly lower serum zinc levels in SD patient's vs control group (79.16 ± 12.17 vs. 84.88 ± 13.59, $P = .045$)</p> <p>No correlation found between serum zinc levels and disease duration ($P = .658$) or SDASI scores ($P = .273$)</p>	<p>Small sample size</p> <p>Only patients with mild/moderate SD included</p> <p>This study did not declare funding source</p>	

Smith et al/2002 [13]	Double Blind Placebo Controlled Study	Patients 20-77 with dermatologist diagnosed SD and a minimum of 20% affected scalp, face or combined surface area Controls: age/sex matched patients with diagnosed SD	41	Evaluate therapeutic potential of low-dose oral administration of weight based dosage (<100 pounds = 2.0 mL/day, 100-200 pounds = 4.0 mL/day, >200 pounds = 8.0 mL/day) of potassium bromide (3.5 mg/mL), sodium bromide (2.0 mg/mL), nickel sulfate (0.6 mg/mL) and sodium chloride (0.6 mg/mL) on SD severity over 10 weeks SD severity measured by SDASI	Percent improvement in SDASI at 10 weeks: Placebo = -10.82% Active = 38.5% ($P = .0302$) Significant improvement in SD due to active treatment after crossover did not occur until 10 weeks of dosage ($P = .0035$) Three patients lost to dropout due to intervention side effects (placebo: nausea, flu-like symptoms; active: stomach problems) but no significant difference in frequency of side effects for active vs placebo ($P = .80$)	Small sample size This study did not declare funding source
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TABLE 2

Wenders et al/ 2019 [16]	Cross Sectional Study	Rotterdam study participants that underwent FBSE by a dermatologist and had complete nutrition data Controls: participants without SD	4379	Evaluate whether total dietary antioxidant intake (Using FRAP score) or specific defined dietary patterns (Using an FFQ) were associated with SD	No association between antioxidant intake and SD (quartile 1 vs quartile 4: adjusted odds ratio = 0.94; 95% confidence interval = 0.73–1.19, $P = .88$) Western diet: associated with a higher risk for SD (quartile 1 vs quartile 4: adjusted odds ratio = 1.34, 95% confidence interval = 1.03–1.75, $P = .07$) Stratification of Western diet and sex: Males - No significance association between Western pattern and SD Females - Higher adherence to Western pattern was associated with an increased risk of SD Adherence to the fruit pattern: associated with a lower risk for SD (quartile 1 vs. quartile 4: adjusted odds ratio = 0.75, 95% confidence interval = 0.58–0.97, $P = .03$) Vegetable or fat patterns: No	Cross-sectional design does not allow for causal inferences The study covers only the middle-aged and elderly population thus generalizability to younger patients is limited The disease severity and distribution of SD was not specifically documented
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					association with presence of SD	<p>during the FBSE so no relationship between location or severity of the disease and the associations with the diet components can be determined</p> <p>Use of an FFQ to assess dietary intake is prone to measurement error</p> <p>This study was funded by Erasmus Medical Center and Erasmus University Rotterdam; Netherlands Organization for the Health Research and Development (ZonMw); the Research Institute for Diseases in the Elderly (RIDE); the Ministry of Education, Culture and Science; the Ministry for Health, Welfare and Sports; the European Commission (DG XII); and the Municipality of Rotterdam</p>
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ALCOHOL

Arma et al/2017 [17]	Case Control Study	Subjects fulfilling criteria of Royal College of Psychiatry for chronic drinking (> 200 ml of pure alcohol/week) Controls: age/sex matched patients in the dermatology outpatient department	196	Correlate the spectrum of dermatoses in chronic alcoholics with the quantum/duration of alcohol intake and raised liver transaminases	Prevalence of SD in cases vs controls: 11.2% vs 1% (OR: 12.26, $P < .001$) SD was inversely related to duration of alcohol intake (12 ± 6.094 vs. 21.02 ± 9.179 years, $P < .001$), i.e., more in those with lesser years of intake and of lesser age (35.68 ± 5.093 vs. 44.26 ± 8.852 years; $P < .001$)	Small sample size Nonreliable history of alcohol intake Inability to eliminate the confounding bias due to factors such as smoking, tobacco, and HIV infection
o/2004 [18]	Case Control Study	Patients attending alcohol deaddiction camps underwent detailed skin exam Controls: age/sex matched non alcoholics	200	Determine cutaneous changes in chronic alcoholics	Prevalence of SD in cases vs controls: 11.5% vs 2.5% ($Z=3.6$, $P < .001$)	Small sample size No standardized history of alcohol intake Inability to completely eliminate the confounding bias due to factors such as smoking, tobacco, and HIV infection This study did not use funding.

SUPPLEMENTS

reie et al/2022 [21]	RCT	Participants with scalp seborrhea aged 14–50 were randomized to Triphala or placebo groups	80	1 g of Triphala (standardized as 91.82 ± 0.5 mg gallic acid) or placebo (wheat flour) was administered BID for 8 weeks Scalp sebum levels were detected using	Triphala group: experienced 25.34 scores (95% CI, 0.39–50.29: $P = .047$) more improvement in scalp sebum levels compared with placebo group Mean percentage of patients' satisfaction: ($P = .001$) 37.91 in the Triphala group 17.89 in the placebo group	Small sample size This study did not declare funding source
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				Sebumeter VR sm 815			
				Treatment satisfaction was measured using a score between 0 and 100			

OBESITY/BMI

Logan et al/2022 [23]	Case Control Study	Participants were > 18 and diagnosed with SD Controls: age/sex/BMI matched healthy patients	103	Evaluate MS and glucose metabolism disorders in patients with SD graded by SDASI score and subjective disease severity score	Waist circumference ($P = .007$): Significantly higher in the SD group compared with the control group Significantly positive relationship between the SASI score and BMI ($r = 0.298$, $P = .030$) No relationship between subjective disease severity score and BMI ($P = .62$)	Small sample size This study did not declare funding source	
Bas et al/2022 [22]	Case Control Study	Participants were > 18 and without known diabetes mellitus, hypertension, and coronary artery disease who were clinically diagnosed with SD in clinic Controls: healthy individuals who came to clinic for general care	101	Investigate the relationship between the presence of MS parameters, SD severity graded by SDASI score and duration of disease	SD patients: Mean BMI was 26.9 (standard deviation: 7.2) Control patients: Mean BMI was 23.5 (standard deviation: 4.1) BMI of SD patients was significantly higher compared to the controls ($P = .002$) Waist circumference of SD patients was significantly higher than the control group ($P = .001$)	Small sample size This study did not receive funding	
Anders et al/2018 [3]	Cross Sectional Study	Rotterdam study participants that underwent a FBSE by a dermatologist	5498	Evaluate lifestyle and physiological determinants associated with SD	No association between BMI and SD (Adjusted OR for BMI (95% CI): 25-30 = 1.05 (0.87-1.27), >30 = 1.12 (0.90-1.39)) No association between alcohol and SD (Adjusted OR for alcohol consumption (95% CI) = 1.01 (0.99-1.01))	Cross-sectional design does not allow for causal inferences Study covers only the middle-aged and elderly population thus generalizability to	

						<p>younger patients is limited</p> <p>This study is funded by Unilever. The parent Rotterdam Studenten is funded by Erasmus Medical Center, Erasmus University Rotterdam, Netherlands Organization for Health Research and Development, the Research Institute for Diseases in the Elderly, the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports the European Commission, and the Municipality of Rotterdam</p>	
s et al/2016 [19]	Cross Sectional Study	Family Medicine patients > 20 years of age that reflected the population demographics of Tokat Provincence	2325	Determine the prevalence and frequently encountered risk factors associated with SD and Psoriasis	<p>BMI and SD: No significant association</p> <p>Alcohol use and SD: Significant difference between participants ($P = .011$)</p>	<p>Cross-sectional design does not allow for causal inferences</p> <p>This study did not declare funding source</p>	
ncar et al/2020 [20]	Case-Control	Case-Control Study: Patients	Case Control	Evaluate risk factors for SD	<p>BMI and SD: No significant relationship ($P = .52$)</p>	Confounding due to lack	

	and Crossover Study	with either a past history of or an active form of SD Control patients: age/sex matched outpatients seen during the same period Cross Over Study: Patients who visited the same dermatologist for a second time and had presented with active SD during the first visit and inactive SD during the second visit or vice versa	Study: 378 Crossover Study: 81	flares in a population of French patients consulting the same office-based dermatologist	Regular alcohol consumption and SD: OR = 10.2, 95% CI = 2.0-52.6, $P = .01$ Risk of SD flares and higher consumption of alcohol: OR = 5.4, CI = 0.8–34.9, $P = .08$	of controls for ethnic background, socioeconomic status, and lifestyle factors This study received funding from pharmaceutical companies but did not specify amount.
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II, Body Mass Index; CI, Confidence Interval; FBSE, Full Body Skin Exam; FFQ, food frequency questionnaire; FRAP, ferric-reducing ability; HC, healthy controls; MS, Metabolic Syndrome; OR, Odds Ratio; P , p value; RCT, Randomized Control Trial, SDASI, Seborrheic Dermatitis Area and Severity Index; SD, seborrheic dermatitis; SEM, Standard Error of the Mean.

Results

Micronutrients

Three studies evaluated micronutrient concentrations in patients with SD. Jahan *et al.* measured levels of vitamins and minerals in SD patients ($n = 75$) compared to controls ($n = 76$) in a case-control study, and concluded SD patients had increased copper, manganese, iron, calcium, and magnesium concentrations ($P < .001$) and lower Vitamin E concentrations ($P = .009$) [12]. Unfortunately, the study did not re-measure micronutrient concentrations after remission of SD, so it is not possible to conclude whether normalizing them is clinically beneficial. Another 10-week,

randomized double-blind, placebo-controlled trial by Smith *et al.* (n = 41) studied the impact of supplementation with weight-based, low-dose oral potassium bromide (3.5 mg/mL), sodium bromide (2.0 mg/mL), nickel sulfate (0.6 mg/mL) and sodium chloride (0.6 mg/mL) in a vehicle of purified water and 20% ethyl alcohol on SD severity measured by SDASI [13]. This study found an improvement in participants SDASI score at 10 weeks of treatment ($P = .0302$), with no significant difference in the frequency of adverse events between active and placebo groups [13].

Rahimi *et al.* evaluated serum levels of 25-hydroxyvitamin D (25(OH)D) in SD patients (n = 118) compared to healthy controls (n = 171) in another case-control study [14]. They found that vitamin D deficiency was more prevalent in patients with SD than in controls ($P = .013$) [14]. This team neither obtained follow-up serum levels of vitamin D nor determined if subsequent supplementation resulted in SD improvement, thus it is difficult to conclude if supplementation is clinically beneficial. A separate case-control study evaluated serum zinc levels in SD patients (n = 43) compared to age and sex-matched, healthy controls (n = 41) [15]. This study found lower serum zinc levels in SD patients ($P = .045$); however, there was no correlation between serum zinc levels and SD duration or SDASI score [15]. Though it evaluated the relationship between micronutrients and disease duration and severity, the study is limited by small sample size and exclusion of severe SD patients, limiting generalizability of the data.

One study in the literature evaluates the association between SD and diet. This cross-sectional study by Sanders *et al.* (n = 4,379) examined if specific dietary patterns were associated with SD using participants of the Rotterdam Study (a prospective population-based cohort study of chronic

diseases in the middle aged and elderly population in the Netherlands) with a skin exam performed by a dermatology trained physician and a food frequency questionnaire with 389 questions evaluating the consumption of food over the past month [16]. They found that the Western diet, characterized by meat, potato, and alcohol consumption, was associated with a higher risk for SD (Adjusted odds ratio = 1.34, $P = .07$) but only in female patients [16]. They also found that an increased amount of fruit in the diet was associated with a lower risk of SD (Adjusted odds ratio = 0.75, $P = .03$) [16]. Both associations compared the highest quartile of those most adherent to the dietary pattern with the lowest quartile of adherent participants [16]. Despite popularity in recommending dietary changes, it is difficult to establish concrete conclusions about the viability of dietary manipulation as an adjunctive treatment due to limited data.

Alcohol

Numerous studies found significant associations between regular alcohol use and an increased prevalence of SD [17,18,19,20]. Further, increased alcohol consumption is associated with a greater risk of SD flares (OR = 5.4, $P = .08$) [20]. Sharma *et al.* evaluated quantity of alcohol consumed in a week, duration of alcohol intake, and SD duration in 196 males, who reported drinking ≥ 200 mL of pure alcohol weekly, that were referred for a dermatologic consult [17]. They found an inverse relationship between SD prevalence and duration of alcohol intake, SD prevalence is inversely related to the duration of alcohol intake, meaning those with fewer years of alcohol use ($P < .001$) were more likely to have SD [17].

One cross-sectional study by Sanders *et al.* ($n = 5498$) utilized Rotterdam study participants who underwent a full body skin exam by dermatologists, and it compared patient characteristics for those with and without SD [10]. They found no association between alcohol and SD; however, this study only included middle-aged and elderly patients, making it difficult to generalize to younger patients [10]. In addition, according to findings by Sharma *et al.*, SD would be more prevalent in younger patients who use alcohol, and this could account for the lack of association found by Sanders *et al.*

when looking at an older population [17].

These studies are limited by their survey-based design, which inherently include self-reported alcohol intake, which may be unreliable. In addition, there are numerous uncontrolled, confounding factors, including smoking, tobacco use, and HIV, making it difficult to draw accurate conclusions about the effects of alcohol alone. Data related to alcohol and SD found in this review has weak and contradictory evidence, warranting further study.

Supplements

Few nutritional supplements have been evaluated as an intervention for SD. One evaluated in an 8-week, randomized, placebo-controlled trial by Zaeie *et al.* (n = 80) was Triphala: a prebiotic [21]. Patients with SD received 1 gram of Triphala twice a day for 8 weeks, then rated subjective symptomatic improvement from 1-100[21]. Researchers assessed scalp sebum levels using a sebumeter [21]. The Triphala group experienced both improvement in patient satisfaction (mean percentage of patients' satisfaction was 37.91 in the Triphala group and 17.89 in the placebo group, $P = .001$) and scalp sebum levels (103.67 ± 70.37 , Triphala group; 128.45 ± 73.90 , placebo group; $P = .047$) [21].

This study is limited by small sample size, which prevents generalizability to broader populations and introduces doubt surrounding data reproducibility. More trials are necessary to elucidate if there is true efficacy of oral nutritional supplements on SD.

Obesity

Some studies demonstrate no relationship between SD and BMI [10,19,20]; however, a case-control study by Akbas *et al.* (n = 101) compared SD patients with age and sex matched controls and found that SD was associated with higher BMI when compared to controls ($P = .002$) [22]. Erdogan *et al.* (n = 103) also evaluated the relationship between BMI, subjective SD severity, and SDASI score in a case control study with SD patients and age, sex, and BMI matched controls [23]. Results

showed a positive relationship between the SDASI score and BMI ($r = 0.298$, $P = .030$) but no relationship between subjective disease severity score and BMI ($P = .62$) [23]. Though there are studies to the contrary, most evidence indicates no relationship between BMI and SD severity [10,19,20,24]. Studies that suggest a causal relationship between the two are limited by numerous confounders, including ethnic background, socioeconomic status and lifestyle factors.

Erdogan *et al.* ($n = 103$) and Akbas *et al.* ($n = 101$) conducted case-control studies comparing waist circumference in SD patients to age, sex, and BMI-matched healthy controls. Both found that waist circumference was higher in the SD groups ($P = .007$, $P = .001$ respectively) [22,23]. These studies are limited by small sample size. [24].

Discussion

The pathophysiology of SD is still not entirely understood; however, colonization of *Malassezia*, a fungus present on normal skin, is strongly associated with this condition [25]. *Malassezia* is found on sebum-rich skin and functions as a lipophilic yeast [25]. The metabolites of *Malassezia* induce inflammation, causing infiltration of NK cells and macrophages, and increased inflammatory cytokines such as interleukin 1α , 1β , and 6, and tumor necrosis factor α [26]. These inflammatory mediators can stimulate keratinocyte differentiation, resulting in dysfunction in the stratum corneum, disruption of the epidermal barrier, and perpetuation of an inflammatory response. This creates a cycle of skin barrier disruption which manifests the clinical features of SD [15,25].

Inflammation and oxidative stress are closely linked: oxidative stress causes inflammation, and inflammation precipitates oxidative stress [27]. Increased serum iron, copper, and manganese cause oxidative stress by catalyzing the creation of reactive oxygen species, which in turn lends to development of inflammatory skin diseases like atopic dermatitis and psoriasis [28,29,30]. Systemic oxidative stress is also higher in SD patients than in healthy subjects, suggesting a role in the pathogenesis of this disease [31]. Thus, Jahan *et al.* findings of elevated levels of serum iron, copper,

and manganese in SD patients may contribute to the cycle of oxidative stress, inflammation, and skin barrier disruption [12].

One study found dietary supplementation with low dose oral potassium bromide, sodium bromide, nickel sulfate and sodium chloride, reduced SD severity [13]. This compound consists of inorganic soluble mineral salts, but no evidence exists in the literature to explain this compound's mechanism of action. More research is needed to determine the function these mineral salts play in modulating the epidermal barrier.

Zinc is an essential trace element that both assists in cell growth, development, and differentiation; and plays catalytic and structural roles in transcription factors, receptors, growth factors, cytokines, and enzymes [32]. It also possesses anti-inflammatory properties, including inhibiting polynuclear neutrophils chemotaxis and altering production of interleukin-6 and tumor necrosis factor α , two pro-inflammatory cytokines produced by keratinocytes [33,34]. It also possesses antiandrogen activity by inhibiting 5 alpha-reductase type I expression [35]. These inflammatory and androgenic pathways are essential to pathogenesis of SD, therefore lower serum zinc levels in SD patients may represent a precipitating factor to disease development [15]. Importantly, there was no correlation between serum zinc levels and disease severity graded by SDASI, so it may only be involved in development of the disease rather than progression [15]. The authors postulated that this is due to the study's small sample size and their inclusion of only mild SD. More studies are needed to identify if this relationship holds true for severe SD and if oral zinc supplementation is of clinical benefit.

Vitamin E is a fat-soluble vitamin and important antioxidant that helps protect cell membranes from lipid peroxidation, minimizing oxidative damage [36]. Therefore, the low levels of vitamin E in SD patients may contribute to an increased oxidative burden [12]. Supplementation with oral Vitamin E showed early promising results in improving other inflammatory skin diseases, including atopic dermatitis and psoriasis [36]. Further research is needed to elucidate the role of Vitamin E

supplementation as an adjunctive therapy in SD.

Vitamin D plays a role in multiple skin processes, ranging from keratinocyte proliferation, differentiation, and apoptosis to immunoregulatory processes and barrier maintenance [37]. Vitamin D enhances synthesis of structural proteins and mediates immunosuppressive action in the skin [37]. Thus, the lower 25-hydroxyvitamin D levels in SD patients found by Rahimi *et al.* may decrease these protective functions, generating the epidermal barrier dysfunction in SD [14,25]. Vitamin D deficiency also plays a role in other inflammatory skin pathologies, such as psoriasis and atopic dermatitis; supplementation of Vitamin D3 and vitamin D analogs are effective against psoriasis [37]. Further research is needed to determine the significance of Vitamin D deficiency in SD and the efficacy of interventional supplementation.

Prebiotics and probiotics possess antimicrobial properties and play a role in the inflammatory response and skin barrier function [38]. Probiotics are live microorganisms while prebiotics are non-digestible carbohydrates that induce growth of probiotic bacteria [38]. Pre- and probiotics are beneficial for several dermatologic conditions, including dandruff and seborrhea, but their use in SD is limited [39]. Triphala, a polyphenol-rich prebiotic, is one of the few dietary supplements that has been tested as an SD treatment [21]. It has antioxidant properties and acts as a skin protectant for human skin cells in vitro [40]. The study was limited by small sample size, but Triphala is a potential adjunctive treatment for SD, but more extensive clinical trials are necessary to fully understand its efficacy and safety.

Through assessment with the Cochrane tool for assessing risk bias, a tool validated for randomized controlled trials, some biases were observed [11]. Authors denoted a small sample size as a limitation which could inherently give the trial attrition bias. Of the 81 patients originally starting the trial, 80 completed it as participants could abandon it at any time. Patients were blinded due to placebo intervention being used in half of the group. Assessors were blinded to if the subject had the active or the placebo. Authors stated that use of a Sebumeter made the data objective, which

could have led to some detection bias to overestimate the validity of the results. Additionally, performance bias could be at risk due to overconfidence in blinding of the capsules. Researchers claimed that capsules were matched to size, color and consistency [21].

The Western diet is high-volumes of meat, potato, and alcohol, and low volume of foods rich in fiber, vitamins, and minerals; its popularity has grown substantially over the past few decades. Long-term consumption of foods popular in the Western Diet can negatively impact health by promoting weight gain, activating the immune system, and causing pathological changes in lipids and metabolism [41]. Only one study evaluates adherence to specific dietary patterns and their association with SD. This study found that patients with higher fruit intake had a decreased likelihood of SD [16]. These results parallel research on other inflammatory skin diseases, including eczema incidence, which is negatively associated with increased fruit intake [42]. Fruits contain high levels of vitamins and flavonoids, which reduce inflammation and may modulate the inflammatory response in SD that contributes to skin barrier dysfunction [42].

This same study found that higher adherence to the Western Diet in females was associated with an increased prevalence of SD, possibly due to increased chronic inflammation associated with the diet [16,43]. This association was not present in males, which may be explained by known differences in dietary response between the sexes [44,45].

It should be further highlighted that the use diet to mitigate disease severity is popular in the mainstream, but existing literature suggests a tenuous relationship. A 2015 study assessed the validity of memory-based dietary assessment methods (B-BMs) on informing dietary policies and found that they are inherently flawed, as they necessarily involve subjective memory recall with no objective data [49]. Therefore, retrospective studies of food consumption are prone to bias and generally limited.

Chronic alcohol use is linked to a variety of skin conditions and the earliest clinical manifestations of alcohol use disorder are cutaneous [46]. There is a known association between

regular alcohol use and SD, likely resulting from immunosuppression, malnutrition, poor hygiene, vitamin B deficiency, and other confounders [17,18,19,20]. One study did not find an association between regular alcohol use and SD adjusted for possible confounders, including demographic, socioeconomic, and medical information, calling into doubt conclusions drawn from unadjusted studies [10]. A separate crossover study found that more recent consumption of alcohol was associated with SD flares; however, this also correlated with increased reported stress levels, introducing an additional confounder [20]. Given the conflicting nature of this data, it is unclear whether alcohol is an independent determinant of SD clinical course, thus controlled interventional studies are necessary.

Current literature on the association between BMI and SD is mixed, though larger studies indicate no association [10,19,20,22,23]. The conflicting nature of these data may reflect BMI's poor predictive value in judging metabolic health, which is associated with SD [22,47].

An arguably more accurate indicator of obesity is waist circumference, with multiple case-control studies showing waist circumference significantly higher in SD patients compared to controls [22,23,24]. Numerous inflammatory markers are higher in those with obesity, which may contribute to initiating or aggravating SD[49]. Abdominal obesity can also lead to dyslipidemia: another factor associated with SD [22,23,47].

Conclusion

More studies are needed to determine how micronutrients, diet, supplements, and obesity affect SD. This review sheds light on promising areas of research that require further study but highlight that current data is limited. Low levels of serum zinc, vitamin D, and vitamin E in SD patients suggest a role for interventional studies evaluating benefits of supplementation. The prebiotic Triphala may be also improve SD; however, though larger studies with more severe SD are needed to evaluate its true potential.

The negative consequences of a western diet, alcohol use, and obesity, and the benefits of fruit

consumption are well known; however, to fully understand their specific relationships to SD, further cohort or interventional studies are needed. As it stands, information on diet-based therapy for SD is conflicting and limited, thus future studies are warranted.

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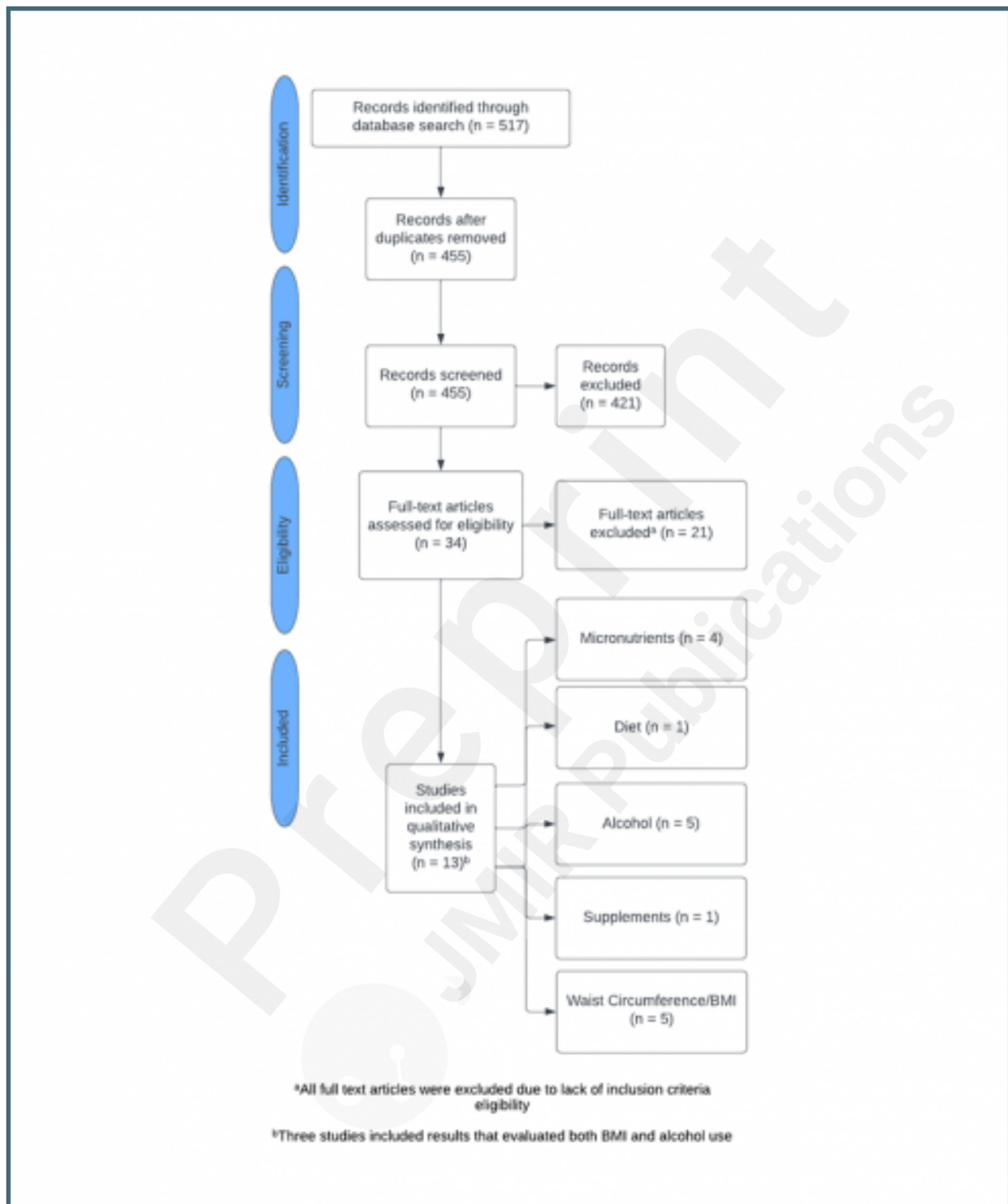
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