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Meta-analyses

Dairy intake and acne development: A meta-analysis of observational studies

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SUMMARY

Background & aims: In the past, some observational studies have been carried out on the relationship between milk and dairy intake and risk of acne occurrence; however, their results were conflicting. This study is a meta-analysis and dose–response analysis designed to evaluate the relationship between milk and dairy products and acne development.
Materials & methods: Data of the study were searched and collected from Pubmed/Medline, Scopus, Web of Science, and Embase databases. Study design, sex, age, exposure (i.e. dairy, milk, yogurt, cheese), dietary assessment method, acne ascertainment, total sample size, number of total subjects and cases in each category of exposure intake, OR, RR and PR with 95% CI in each category of exposure intake and adjusted variables were extracted.
Results: Highest compared with lowest category of dairy (OR: 2.61, 95% CI: 1.20 to 5.67), total milk (OR: 1.48, 95% CI: 1.31 to 1.66), low-fat milk (OR: 1.25, 95% CI: 1.10 to 1.43) and skim milk (OR: 1.82, 95% CI: 1.34 to 2.47) intake significantly was associated with the presence of acne. Results of dose–response analysis revealed a significant linear relationship between dairy, whole milk and skim milk and risk of acne and nonlinear association between dairy, milk, low-fat milk and skim milk intake and acne.
Conclusion: In this meta-analysis we found a positive relationship between dairy, total milk, whole milk, low-fat and skim milk consumption and acne occurrence. In contrary, no significant association between yogurt/cheese and acne development was observed.

1. Introduction

Acne vulgaris is a dermatosis that affects 50–95% of adolescents aged 12–18 years [1–6] and is diagnosed through the presence of comedones, papules, and pustules in the region abundant in sebaceous glands [7]. Acne is developed in all ages, and sexes, but it is common among males and adolescent especially during puberty [8]. The main method of acne development is through the over-production of sebum by sebaceous glands which then results in hyperliferation and blockage of follicle opening [9]. Acne has social and emotional adverse effects; hence, identification of factors causing acne is very important. Several factors are involved in pathogenesis of acne and they include: genetic, sex-hormonal disorders especially androgen, immunological dysfunction, psychological factors, and environment [10].

It has been proposed that dietary habits especially western dietary pattern, high glycemic index (GI) diet, and diet-rich in omega-6 fatty acids contribute to the development of acne [7,11–13]. Regardless of low GI, cow's milk and dairy products are the main components of western diet that has been suggested to play a role in pathogenesis of acne [14–16]. Milk and dairy products contain casein and whey protein that raise insulin-like growth factor-1 (IGF-1) and insulin concentrations, respectively [8,17]. IFG-1 is an important hormone that increased mammalian target of rapamycin (mTOR) activity and sebaceous lipogenesis; hence result in acne development [18,19]. Studies have shown that patients suffering from acne have higher IGF-1 level than subjects without acne [20–22]. In addition, they have sex-hormones such as androgen

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which both IGF-1 and androgens are involved in sebaceous hyperplasia and comedogenesis [8,23]. In the past, some observational studies have been carried out on the relationship between milk and dairy intake and risk of acne occurrence; however, their results are yet to be concluded. Results of a large retrospective study on 47,355 nurses have shown that the frequency of milk intake is significantly associated with increased risk of acne occurrence during adolescence [24]. Burris et al. [25] reported that the consumption of milk was higher in patients with mild to severe acne than in subjects with no acne. On the contrary, LaRosa et al. [26] reported that there was no significant difference on dairy intake between acne group and control group. In another study on 2201 adolescents, there was no relationship between the consumption of milk, yogurt and cheese and the presence of acne [27]. To the best of our knowledge, no systematic review and meta-analysis was found in the literature search for the present meta-analysis that determined the relationship between milk and dairy products and risk of acne. Therefore, this meta-analysis and dose–response analysis of observational studies was designed to evaluate the relationship between milk and dairy products and acne development.

2. Methods

2.1. Article source and literature search

This meta-analysis was conducted according to MOOSE's guideline [28]. A comprehensive literature search was carried out in Pubmed/Medline, Scopus, Web of Science and Embase databases for all studies that investigated the relationship between dairy products and acnes up to August 2017 by an investigator. The searched keywords were: “dairy products”, “milk”, “yogurt”, “cheese”, “cream”, “butter”, “ice cream”, “dairy”, “yoghurt”, “buttermilk”, “acne” and “*Acne vulgaris*”. There was no limit for date of publication and language. The reference list of the retrieved studies was reviewed to find relevant studies. When the need arises, the investigators of the current study contacted the authors for more details. The population, intervention/exposure, comparison, outcome, and setting (PICOS) criteria were used to define the research question (Table 1).

2.2. Study selection

Two researchers (M.A and M.G) reviewed the retrieved articles according to the inclusion and exclusion criteria individually. Inclusion criteria included: a) prospective, case–control and cross-sectional designs, b) reported odds ratio (OR), relative risk (RR) or prevalence ratio (PR) with 95% confidence interval (CI) for the highest vs. lowest category of exposure intake or provided number of cases and total participants in each category of dairy products to calculate OR and 95% CI, c) English language, d) considered dairy, total milk (comprised of low-fat, whole and skimmed milk), yogurt, cheese, butter and ice cream as exposure, and e) considered acne as outcome. Exclusion criteria included: a) randomized clinical trial (RCT) design and b) comment, editorial, review, meta-analysis and animal studies. Newcastle-Ottawa Scale (NOS) was used to assess the quality of observational studies [29].

Table 1
PICOS criteria.

Population	Children, adolescent and adults
Intervention/Exposure	Dairy, total milk, whole milk, low-fat milk, skim milk, yogurt and cheese
Comparison	Highest vs. lowest categories of exposure
Outcome	Acne development
Setting	Observational studies
Research question	Are milk and dairy products associated with acne development

2.3. Data extraction

Data extraction was done according to the predefined form. The following data were extracted: first author, date of publication, country, study design, duration of follow-up, sex, age, exposure (that is, dairy, milk, yogurt, cheese, butter and ice cream), dietary assessment method, acne ascertainment, total sample size, number of total subjects and cases in each category of exposure intake, OR, RR and PR with 95% CI in each category of exposure intake, and adjusted variables.

2.4. Statistical analysis

Stata software version 12 (StataCrop, College Station, Texas, USA) was used to carry out the meta-analysis. ORs (95% CI) for the highest vs. lowest category of dairy and dairy products were used to calculate log OR and its standard error. All results were reported as ORs (95% CI) in order to homogenize risk estimate. If studies have reported several statistical models, the last model with the most adjusted variable was included. According to the heterogeneity between studies, fixed and random model was performed for the pooled ORs (95% CI). Heterogeneity was evaluated using the I-squared (I^2).

Dose–response analysis was performed to assess linear and nonlinear relationship between exposures of intake and risk of acne. Cross-sectional studies were excluded from both linear and nonlinear dose–response analyses and studies with <3 categories of exposure intake only from nonlinear dose–response analysis. The median or mean intake of exposure for each category was estimated. If the study reported a range for a category, the average of lower and upper band was calculated. When the lowest or highest category was open ended, it was assumed that the range was similar to the adjacent category. If exposure was reported as serving size, then it was converted to g/day as follows: 177 g for dairy, 244 g for total milk, low-fat, whole, and skimmed milk, and yogurt, and 43 g for cheese. Nonlinear dose–response analysis was carried out using restricted cubic splines with four knots at fixed percentiles (5, 35, 65, and 95%) of the distribution. The linear dose–response was performed using generalized least squares trend according to Greenland and Longnecker method [30]. Linear trend (95% CI) in each study was calculated, then results of studies were pooled together with random-effect meta-analysis. The linear dose–response was expressed on 177 g dairy and 244 g milk, low-fat, whole, and skimmed milk.

Sensitivity analysis was used to assess impact of studies on the pooled ORs (95% CI). Egger's test was run to show publication bias among included studies.

3. Results

Figure 1 shows the flow chart of the study. A total of 1750 articles were included in the study by initial search from Pubmed/Medline (n = 407), Scopus (n = 696), Web of Science (n = 573), and Embase (n = 74) databases. Duplicated articles were removed and the remaining 1233 articles were reviewed based on title and abstract and 1143 articles were excluded owing to no sufficient data (n = 7), inappropriate design (n = 50) and non-English language (n = 9). The remaining studies were screened for eligibility based on the inclusion and exclusion criteria. Finally, 14 relevant studies were selected to be included in the meta-analysis [24,27,31–42].

Table 2 shows the characteristics of the included studies. Four studies were prospective design [24,31,32,41], seven studies were case–control [33–37,39,42] and three studies were cross-sectional framework [27,38,40]. Age of participants ranged from 9 to 30 years. Four and three studied reported PR (95% CI) [24,27,31,32] and OR (95 %CI) [35,37,41] for the highest vs. lowest category of intake, respectively. The remaining articles provided the number of cases and total participants in each category of exposure to calculate ORs (95% CI) [33,34,36,38–40,42]. Six studies used food frequency questionnaire (FFQ) [24,31,32,35,36,38], two studies used food records questionnaire [34,37] and six studies used dietary habit questionnaire [27,33,39–42] to evaluate dairy and dairy products intake. The presence of acne was diagnosed by physician in eight studies [24,27,33–38] and the remaining studies were self-reported [31,32,39–42]. Among included studies, three studies had quality score ≥6 [24,32,37].

3.1. Meta-analysis on dairy intake and acne

Five studies were evaluated the relationship between dairy intake and the presence of acne [33,39–42]. The Forest plot of the relationship between dairy intake and acne is shown in Fig. 2. A significant relationship was observed with the presence of acne when the highest category of dairy intake is compared with the lowest (OR: 2.61, 95% CI: 1.20 to 5.67). There was a severe heterogeneity between the studies (I^2 = 75.6%, P-heterogeneity = 0.003).

Of the five included studies, three were included in dose–response analysis [40–42], two were excluded because one study has cross-sectional design [39] and the other one did not report the dose of dairy intake in each category [33]. Linear dose–response analysis showed that a 177 g/d increment in dairy intake was positively associated with the risk of acne (OR: 1.83, 95% CI: 1.14 to 2.96) with significant heterogeneity (I^2 = 95.8%, P-heterogeneity < 0.001). In addition, evidence of nonlinear dose–response association was observed between dairy intake and acne (P-nonlinearity = 0.0007). Risk of acne was elevated by 80% with increasing intake of dairy between 250 and 450 g/d (goodness-of-fit = 58.4) (Fig. 3).

Sensitivity analysis showed that none of the studies had significant effect on the pooled effect size. No evidence of publication bias was found among the included studies (Egger's test = 0.10).

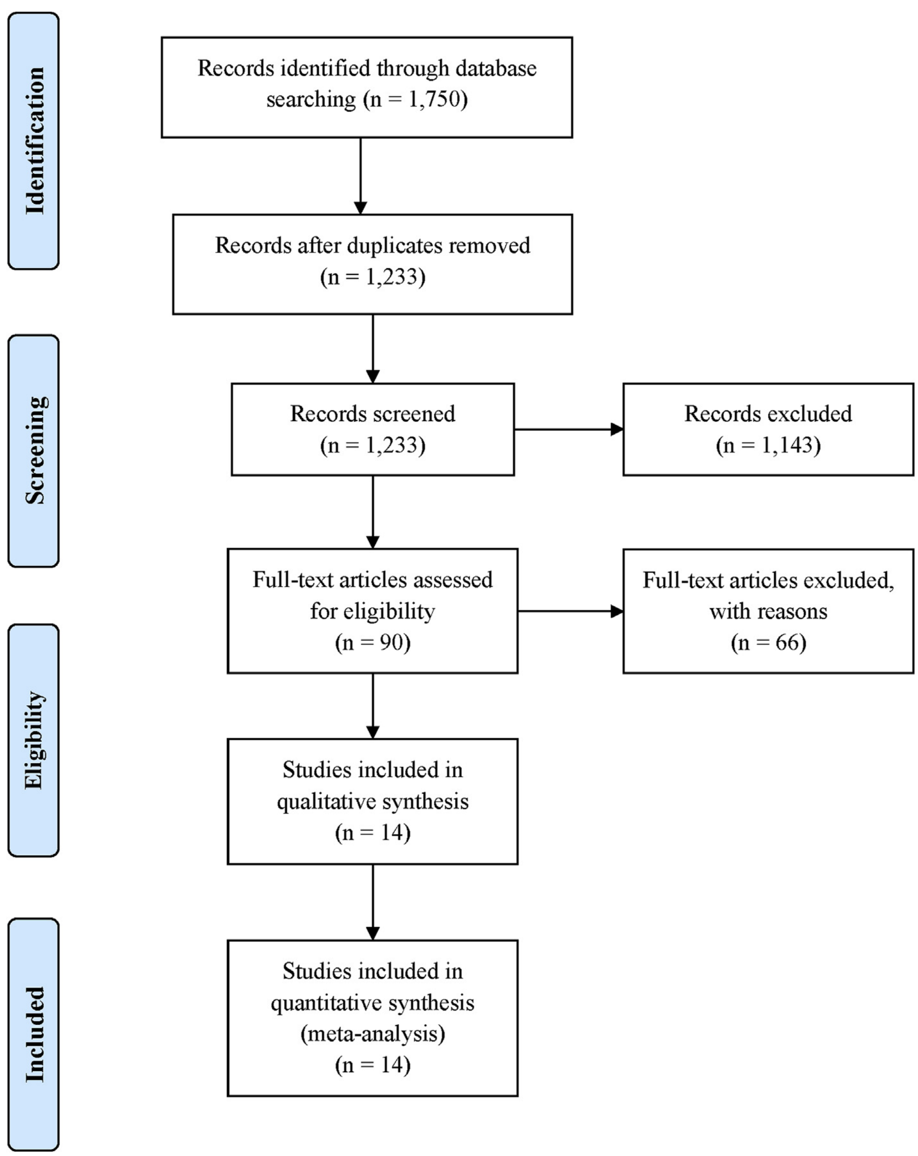

Fig. 1. Flow chart of retrieved studies.

Table 2
Characteristics of included studies based on exposure type.

Exposure	Study, year	Country	Study deign	Age (yr)	Case/total	Exposure assessment	Acne ascertainment	Exposure category	OR (95% CI)
Dairy	Agamia, 2016 [33]	Egypt	Case–control	17–29	40/60	Diet questionnaire	By physician	Low vs. high intake	2.25 (0.43–11.75)
	Tsoy, 2013 [39]	Kazakhstan	Case–control	17–18	431/523	Diet questionnaire	Self-reported	Never vs. daily	10.16 (3.00–34.43)
	Tsoy, 2013a [40]	Kazakhstan	Cross-sectional	–	90/182	Diet questionnaire	Self-reported	Never vs. daily	12.50 (2.11–73.74)
	Wolkenstein, 2014 [42]	France	Case–control	15–24	1375/2266	Diet questionnaire	Self-reported	Never vs. 4 d	1.10 (0.67–1.83)
	Ulvestad, 2016 [41]	Norway	Cohort	15–16	331/2718	Diet questionnaire	Self-reported	Never vs. ≥2 d	1.47 (0.96–2.23)
Total milk	Abedamowo, 2005 [24]	USA	Cohort	13–18	3412/46,879	FFQ	By physician	<1 wk vs. 2–3 d	1.31 (1.09–1.56)
	Abedamowo, 2006 [32]	USA	Cohort	9–13	2588/3756	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.45 (1.12–1.88)
	Abedamowo, 2008 [31]	USA	Cohort	9–13	1856/2759	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.90 (1.33–2.72)
	Di Landro, 2012 [35]	Italy	Case–control	10–24	125/298	FFQ	By physician	≤3 wk vs. >3 wk	1.78 (1.22–2.59)
	Ismail, 2012 [37]	Malaysia	Case–control	18–30	44/88	Food record	By physician	<1 wk vs. ≥1 wk	3.98 (1.39–11.43)
	Okoro, 2015 [38]	Nigeria	Cross-sectional	10–17	292/450	FFQ	Self-reported	No vs. yes	1.62 (1.03–2.55)
	Cerman, 2016 [34]	Turkey	Case–control	15–22	50/86	Food record	By physician	≤3 wk vs. >3 wk	0.95 (0.40–2.24)
	Grossi, 2016 [36]	Italy	Case–control	10–24	204/560	FFQ	By physician	Never vs. >3 wk	1.49 (0.92–2.41)
Low-fat milk	Abedamowo, 2005 [24]	USA	Cohort	13–18	1116/15,268	FFQ	By physician	<1 wk vs. >1 d	1.24 (1.07–1.44)
	Abedamowo, 2006 [32]	USA	Cohort	9–13	977/1421	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.39 (0.94–2.05)
	Abedamowo, 2008 [31]	USA	Cohort	9–13	498/765	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.58 (0.97–2.58)
	Pereira Duquia, 2016 [27]	Brazil	Cross-sectional	18	241/2201	Diet questionnaire	By physician	No vs. yes	0.91 (0.52–1.58)
Whole milk	Abedamowo, 2005 [24]	USA	Cohort	13–18	2306/33,185	FFQ	By physician	<1 wk vs. >1 d	1.16 (1.03–1.31)
	Abedamowo, 2006 [32]	USA	Cohort	9–13	1694/1133	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.37 (1.00–1.88)
	Abedamowo, 2008 [31]	USA	Cohort	9–13	826/1279	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.69 (1.12–2.53)
	Di Landro, 2012 [35]	Italy	Case–control	10–24	42/104	FFQ	By physician	≤3 wk vs. >3 wk	1.64 (0.81–3.33)
	Pereira Duquia, 2016 [27]	Brazil	Cross-sectional	18	241/2201	Diet questionnaire	By physician	No vs. yes	0.69 (−0.52–0.92)
Skimmed milk	Abedamowo, 2005 [24]	USA	Cohort	13–18	682/9492	FFQ	By physician	<1 wk vs. ≥2 d	1.53 (1.26–1.85)
	Abedamowo, 2006 [32]	USA	Cohort	9–13	1049/1521	FFQ	Self-reported	≤1 wk vs. ≥2 d	1.45 (1.02–2.07)
	Abedamowo, 2008 [31]	USA	Cohort	9–13	687/1006	FFQ	Self-reported	≤1 wk vs. ≥2 d	3.11 (1.84–5.26)
	Di Landro, 2012 [35]	Italy	Case–control	10–24	75/170	FFQ	By physician	≤3 wk vs. >3 wk	2.20 (1.18–4.10)
Yogurt/cheese	Di Landro, 2012 [35]	Italy	Case–control	10–24	76/213	FFQ	By physician	≤3 wk vs. >3 wk	0.94 (0.64–1.37)
	Ismail, 2012 [37]	Malaysia	Case–control	18–30	44/88	Food record	By physician	<1 wk vs. ≥ 1 wk	1.83 (0.82–4.10)
	Grossi, 2016 [36]	Italy	Case–control	10–24	204/561	FFQ	By physician	Never vs. >3 wk	1.29 (0.62–2.69)
	Pereira Duquia, 2016 [27]	Brazil	Cross-sectional	18	241/2197	Diet questionnaire	By physician	No vs. yes	0.76 (0.57–1.00)

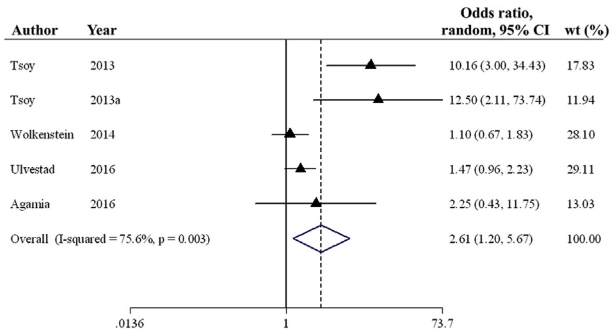

Fig. 2. Forest plot of association between dairy intake and acne.

3.2. Meta-analysis on milk intake and acne

Generally, eight effect sizes from eight studies [24,31,32,34–38] were included. Results of the meta-analysis showed that there was a significant relationship with acne in the highest vs. lowest total milk intake (OR: 1.48, 95% CI: 1.31 to 1.66) (Fig. 4) with no significant between-study heterogeneity ($I^2 = 23.6\%$, P-heterogeneity = 0.24).

Seven [24,31,32,34–37] and four [24,31,32,36] studies were included for linear and nonlinear dose–response analyses, respectively. No significant linear dose–response relationship was found between total milk intake and acne (OR for every 244 g increase per day was 1.10, 95% CI: 0.97 to 1.24, $I^2 = 81.5\%$, P-heterogeneity < 0.001). The dose–response analysis showed a positive nonlinear relationship between total milk and risk of acne (P-

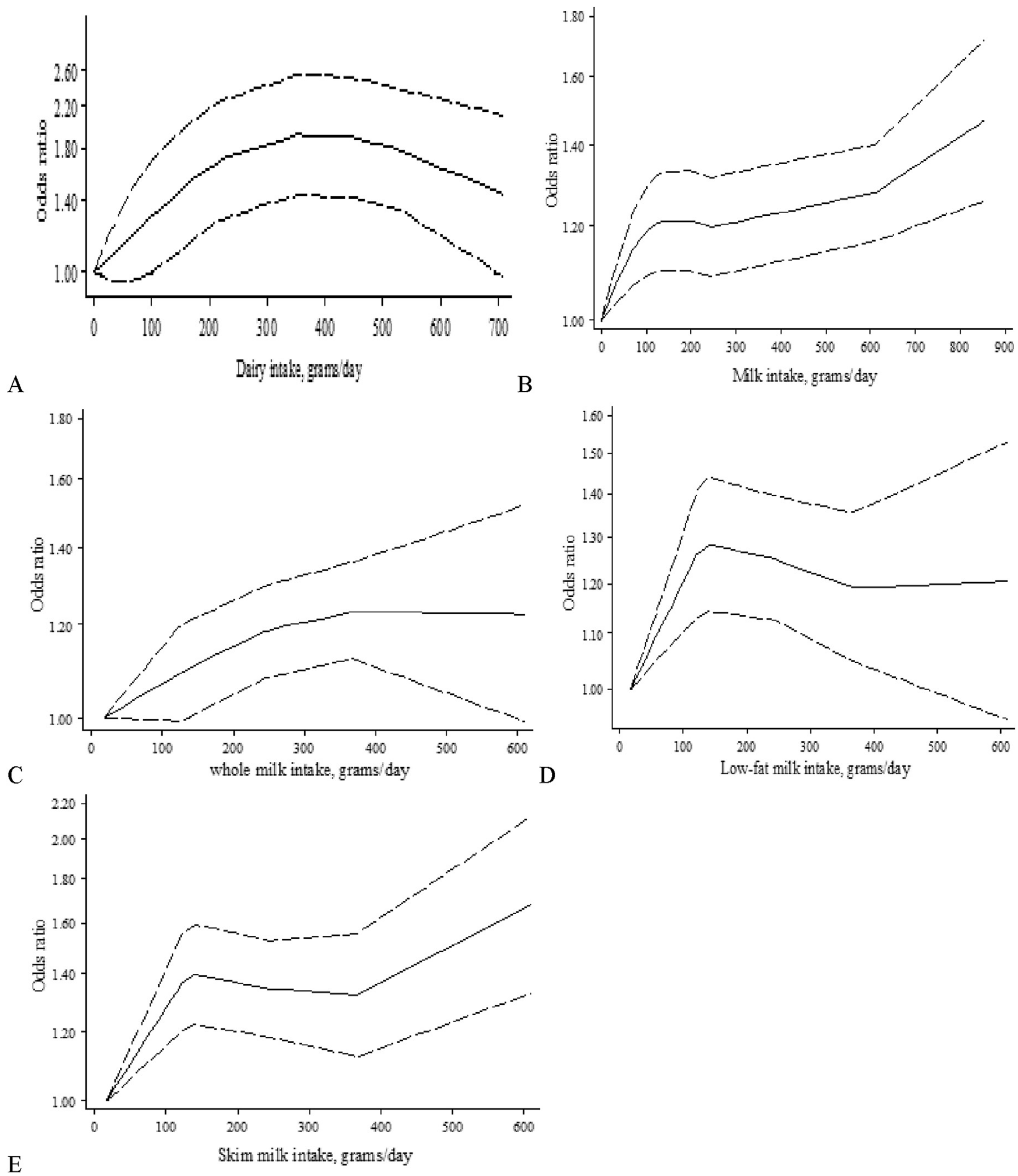

Fig. 3. Nonlinearity dose–response of association between A. dairy intake (P-nonlinearity = 0.0007), B. total milk intake (P-nonlinearity = 0.004), (C) whole milk intake (P-nonlinearity = 0.33), (D) low-fat milk intake (P-nonlinearity = 0.0004) and (E) skimmed milk intake (P-nonlinearity = 0.0007) and acne.

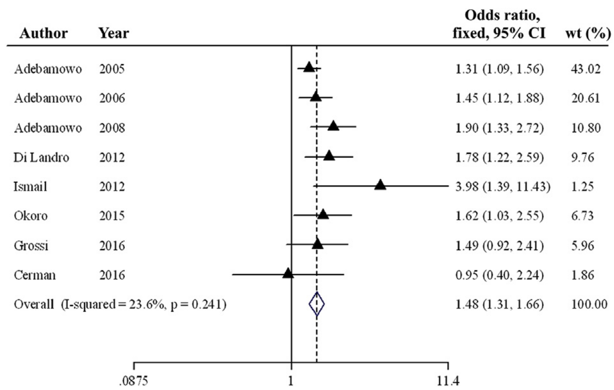

Fig. 4. Forest plot of association between total milk intake and acne.

Table 3
Association between different type of milk intake and acne.

Type of milk	Model	Odds ratio (95%CI)	P value	Heterogeneity (%)
Whole milk	Random	1.18 (0.89–1.57)	0.001	77.6
Low-fat milk	Fixed	1.25 (1.10–1.43)	0.48	0.0
Skimmed milk	Random	1.82 (1.34–2.47)	0.05	60.1

nonlinearity = 0.004, goodness-of-fit = 58.4) with the strongest risk of elevation at the higher amount of total milk intake (Fig. 3).

The Relationship between consumption of whole milk, low-fat milk and skimmed milk was investigated in five [24,27,31,32,35], four [24,27,31,32] and four [24,31,32,35] studies, respectively. The relationship between different types of milk intake and acne is shown in Table 3. The highest vs. lowest intake of whole milk showed no association with acne (OR: 1.18, 95% CI: 0.89 to 1.58). On the contrary, there was a positive relationship between the highest vs. lowest intake of low-fat milk (OR: 1.25, 95% CI: 1.10 to 1.43) and skimmed milk (OR: 1.82, 95% CI: 1.34 to 2.47) and presence of acne.

Dose–response meta-analysis showed whole milk (OR: 1.13, 95% CI: 1.06 to 1.20, $I^2 = 0.1\%$, P-heterogeneity = 0.39) and skimmed milk intake (OR: 1.26, 95% CI: 1.02 to 1.56, $I^2 = 79.9\%$, P-heterogeneity = 0.002) were linearly associated with risk of acne. However, there was no statistically significant difference between the linear relationship of low-fat milk intake and acne (OR: 1.08, 95% CI: 0.97 to 1.21, $I^2 = 51.0\%$, P-heterogeneity = 0.13). Nonlinear dose–response relationship between whole, low-fat and skimmed milk intake and acne is shown in Fig. 3. Low-fat milk (P-nonlinearity = 0.0004, goodness-of-fit = 12.4) and skimmed milk intake (P-nonlinearity = 0.0007, goodness-of-fit = 26.4) were associated with risk of acne in a nonlinear fashion. There was no evidence of a nonlinear dose–response trend between whole milk intake and acne (P-nonlinearity = 0.33, goodness-of-fit = 16.1).

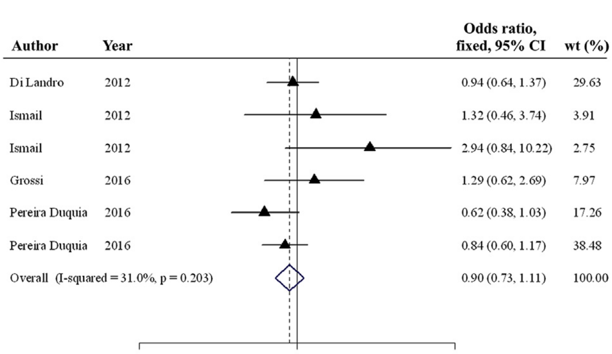

Fig. 5. Forest plot of association between yogurt/cheese intake and acne.

Results of the sensitivity analysis showed that no study from the analysis changed the pooled effect size. There was no publication bias amongst studies on total milk (Egger's test = 0.17), whole milk (Egger's test = 0.77), low-fat milk (Egger's test = 0.92) and skimmed milk (Egger's test = 0.25).

3.3. Meta-analysis on yogurt/cheese intake and acne

Findings of meta-analysis on the association between yogurt/cheese intake and acne are shown in Fig. 5. Six effect sizes from four studies [27,35–37] were included in the meta-analysis. No significant relationship was found between yogurt/cheese intake and acne (OR: 0.90, 95% CI: 0.73 to 1.11). There was no heterogeneity between studies ($I^2 = 31.0\%$, P = 0.20). Three studies [35–37] were included for linear dose–response analysis and one study [27] was excluded due to cross-sectional design. No significant linear dose–response was found between yogurt/cheese intake and risk of acne development (OR: 0.72, 95% CI: 0.35 to 1.47, $I^2 = 39.5\%$, P-heterogeneity = 0.19). Nonlinear dose–response relationship between yogurt/cheese intake and acne were no evaluated, because the included studies had <3 exposure category.

According to the sensitivity analysis, no study had influence on the pooled effect size. Results of Egger's test showed no publication bias among the included studies (Egger's test = 0.12).

4. Discussion

In the present meta-analysis, 14 observational studies that investigated the relationship between dairy, total milk, whole milk, low-fat milk, skimmed milk and yogurt/cheese and acne development were included. In the present meta-analysis, showed that dairy, total milk, whole fat milk, low-fat milk and skimmed milk consumption was associated with the presence of acne. Linear dose–response analysis showed that each additional serving of dairy, whole milk and skimmed milk significantly increased the risk of acne by 83, 13 and 26%, respectively. Findings of the nonlinear dose–response analysis showed a nonlinear relationship between consumption of dairy, total milk, low-fat milk and skimmed milk and development of acne. There was no relationship between yogurt/cheese intake and risk of acne. Results of the current meta-analysis support the hypothesis that dairy products are positively associated with acne development.

The present study had several strengths and limitations. To the best of our knowledge, this is the first meta-analysis that evaluated the relationship between dairy products and acne occurrence. In this meta-analysis, a broad range of dairy products were included. Use of linear and nonlinear dose–response analyses was the other strength of the present study. The main limitation of the current study was that few numbers of studies were included in the meta-analysis and dose–response analysis according to each exposure. In addition, subgroup and meta-regression analyses were not conduced due to few numbers of included studies. Residual confounders are the main limitations that can affect the results, because observational studies were used to conduct the current meta-analysis. Moreover, in six studies validated, dietary questionnaire was not used and diagnosis of acne was self-reported and this may cause measurement bias. As well as, included studies in the present meta-analysis considered total milk as sum of whole, low-fat and skimmed milk and assessed its association with acne development, while proportion of total milk from different type of milk was unclear. The last limitation of the current study was lack of data on thermal and bacterial method applied during preparation of milk and dairy products. It seems boiling and ultra-heat treatment (UHT) techniques decline milk and dairy microRNA and have a protective effect against acne [43].

The relationship between dairy and acne was investigated in observational studies. Nevertheless, the relationship between milk and dairy products intake with acne creation is yet to be investigated through systematic review and meta-analysis. In this study, results for the highest vs. lowest total milk and different type of milk intake were in agreement with the findings of four large prospective studies that have shown positive relationship between total milk and skimmed milk and acne development, but their results on whole milk and low-fat milk were inconsistent [24,31,32,41]. The results of case–control and cross-sectional studies were inconsistent. In addition, findings of the present meta-analysis have shown similar findings with the observational studies in which dairy intake was collected using food frequency questionnaire. However, results of the current study were not in agreement with some observational studies that used dietary habit questionnaire to assess dairy intake.

Milk and dairy products are the main sources of protein, calcium, potassium, magnesium, vitamin A and B12 recommended as a part of healthy dietary pattern by guidelines. Evidence has shown that milk and dairy products have paradoxical effect on health. Previous meta-analyses have revealed that milk and dairy products were inversely associated with the risk of hypertension [44], gastric cancer [45], stroke [46,47], colorectal cancer [48]. On the contrary, they increased the risk of prostate cancer [49], non-Hodgkin lymphoma [50] and Parkinson [51,52] with no relationship with hip fracture [53], mortality, cardiovascular disease (CVD) and coronary heart disease (CHD) [54,55]. The association between milk and dairy products and risk of diabetes is contradictory and is dependent on the type of dairy [56–59].

Acnegenic properties of milk and dairy products were explained via several mechanisms. Results of a meta-analysis conducted by Harrison et al. [60] have shown that milk and dairy significantly elevate IGF-1 concentration. Milk and dairy products contain IGF-1 that is not hydrolyzed by gut enzymes and lead to plasma IGF-1 elevation [24]. In addition, casein content of milk and dairy products stimulates hepatic IGF-1 release [61], subsequently raise plasma IGF-1 level that in a way that both exogenous and endogenous IGF-1 stimulate sebocytes resulting to acne development [24]. Studies have shown that milk and dairy intake through IGF-1/phosphinositide-3-kinase (PI3K)/Akt pathway modulates Forkhead box transcription factor (Fox) O1 expression and causes acne occurrence [25,26,33,34]. FoxO1 is responsible for regulation of acne-related genes and sebaceous gland secretion and upregulation of FoxO1 play an important role in acne management [33]. Moreover, FoxO1 is a modulator of mTOR complex 1 (mTORC1) which in involved in sebocytes activation and acnegenesis. Moreover, milk augments branched-chain amino acid (BCAA) levels that stimulate mTOR activity [61]. IGF-1 also increases androgen receptors and testosterone and dihydrotestosterone (DHT) production that leads to greater androgen activity and stimulation of follicle cells growth, and subsequently acne occurrence [14,62,63]. Moreover, milk and dairy products contain sex-hormones derivatives such as estrogen, progesterone, androgen, androstenedione, dihydrotestosterone (DHT), dehydroepiandrosterone-sulfate and 5α-reduced steroids that have acnegenesis properties. They are rich in glucocorticoides, transforming growth factor-β (TGF-β) and neutral thyrotrophin-releasing hormone like peptides that may influence on sebocytes [8,11,64]. It has also been stated that iodine exist in milk and dairy may agitate acne creation [8].

U.S. Department of Agriculture (USDA) guideline recommends three serving milk and dairy products per day for subjects >9 years with emphasis on fat-free and low-fat milk and dairy products [65]. However, in the present study, low-fat milk and especially skimmed milk has stronger relationship than whole milk with acne development. Some studies have shown the beneficial effects of whole milk intake on risk of hypertension [66] and colorectal cancer [67]. However, several investigations have indicated that whole milk intake augments risk of prostate cancer [68,69]. There are several mechanisms that may explain this phenomenon. Milk and dairy products comprised of casein (80%) and whey protein (20%) that attribute to IGF-1 (by 15%) and insulin (by 21%) elevation, respectively [14]. These effects were reinforced when milk undergo fat-reducing processes; stating development of acne is independent of milk-fat content. It has been hypothesized that fat-reducing process possibly raises functional molecules concentration of milk and dairy products which are responsible for development and progression of acne [8]. In addition, whole milk contains more estrogen concentration than skimmed milk and low-fat milk which suppress acne creation. On the contrary, skimmed milk and low-fat milk have higher amount of α-lactalbumin when compared with the whole milk that stimulates acne occurrence [24].

In this meta-analysis, the consumption of yogurt/cheese had no relationship with the risk of acne and this was in agreement with two previous case–control studies [35,37]. No meta-analysis, cohort study and RCT has been carried out to assess the relationship between yogurt/cheese and acne occurrence. Unlike the results for milk and dairy, no meta-analysis has reported adverse effects of yogurt and cheese intake on health. Previous meta-analyses have shown that the consumption of yogurt decreased the risk of diabetes [56], all-causes mortality [54], breast cancer [70] and hip fracture [53] and cheese intake is associated with lower risk of CVD, CHD, stroke [47,70] and hip fracture [53]. Also, milk and dairy, yogurt and cheese are good source of protein, some vitamins, and minerals. The lack of relationship between yogurt/cheese and acne may be as a result of fermentation process. Milk contains several microRNA especially micrRNA-148a that suppresses DNA methyltransferase 1 (DNMT1) and promote androgen signaling and androgen receptor activity. Fermentation process by enhancement probiotic bacteria which destroys milk exosomes reduces milk microRNAs and prevents acne development [43]. In addition, it is likely that this process alters functional molecules and hormones concentration of yogurt and cheese that may attenuate acne development [32]. Fermentation process reduces IGF-1 level of yogurt and cheese which may show the absence of relationship between yogurt/cheese and acne occurrence [37].

5. Conclusion

In this meta-analysis, a positive relationship was found between dairy, total milk, whole fat, low-fat and skimmed milk consumption and acne occurrence. On the contrary, there was no significant relationship between yogurt/cheese and acne development. Results of the present meta-analysis recommend the consumption of yogurt/cheese to avoid acne creation. Further investigations especially RCT are needed to confirm the effect of milk and dairy products on acne development.

Statement of authorship

M.A designed the study and conducted initial searches. M.A and M.G contributed to screen retrieved articles and data extraction. Data were analyzed and interpreted by M.G and S.S-B. M.G, A.A and M.O wrote a first draft of the manuscript. M.A, M.G, S.S-B and F.T prepared final draft. All authors read the manuscript and approved it.

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Conflicts of interest

The authors declare there is no conflict of interest.

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