

# Diet and Acne Update: Carbohydrates Emerge as the Main Culprit

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## ABSTRACT

The prevalence of adult acne in the US appears to be increasing over the last few decades. But what's behind the rise: is it nature or nurture? We are well aware that genetics can strongly influence a patient's risk of developing acne. However, significant changes in germline genetic variants are unlikely to have occurred over the last 20 years. Consequently, we are forced to examine environmental variables, including diet. This review article presents the most updated evidence supporting a link between refined carbohydrates and acne. Based on the data summarized here, dermatologists should encourage their acne patients to minimize their intake of high glycemic index foods.

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## INTRODUCTION

Acne vulgaris is a common skin condition, particularly in developed Western nations. More than 85% of adolescents suffer from this ubiquitous and psychologically debilitating disease, which is moderate to severe in about 15–20% of patients.<sup>1</sup> Acne often persists into adulthood with 64% of individuals in their 20s and 43% of individuals in their 30s showing signs of visible acne.<sup>2,3,4</sup> Another study of more than 2000 adults showed that 3% of men and 5% of women still had definite mild acne at the age of 40 to 49 years.<sup>5</sup>

Pathogenesis of acne is characterized by androgen-stimulated overproduction of sebum, follicular hyperkeratinization, inflammatory mediators, and colonization by organisms such as *Propionibacterium acnes*.<sup>6</sup> These generally agreed on factors have guided treatment towards hormone control, antimicrobial therapy, and vitamin A derivatives. We are well aware that genetics can strongly influence a patient's risk of developing acne. However, with the prevalence of adult acne in the US increasing over the last few decades<sup>7</sup>, significant changes in germline genetic variants are unlikely. Consequently, elucidating the relationship of environmental factors such as nutrition and diet have become more important in the recent study of acne.

The relationship between diet and acne, however, has been historically controversial. In the 1930s through the 1960s, patients were regularly counseled regarding their dietary habits, as dietary triggers were thought to play a major role in acne. Following two critically impactful studies<sup>8,9</sup> dietary restrictions were deemed no longer necessary. The idea that diet affected acne was relegated to myth. In 2007, one of the authors<sup>10</sup> published a review in the JAAD re-implicating certain dietary factors in acne based on emerging evidence. This article concluded that refined carbohydrates and certain dairy products, in particular skim milk, appeared to be associated with acne.

Since that review, several studies have been conducted, further elucidating which dietary factors play the largest role when it comes to acne. In this update, we present those studies and confirm our initial suspicion that refined carbohydrates are indeed the main dietary contributors to acne. This article is meant to serve as a follow up to that original JAAD publication, providing an update on the evidence linking diet and acne with a specific focus on carbohydrate intake.

## Study Selection

PubMed - Medline database was used to allow for a thorough literature search. An attempt was made to also include published abstracts in order to broaden the search for available information. Articles published over a 4-year period (2009-2013) that reported results relating to diet and acne were incorporated. Medical Subject Headings (MESH) were used to search articles and free text to search article abstracts that contained (1) a term related to acne and (2) a term related to diet and nutrition. Prospective controlled trials, prospective and retrospective cohort studies, case-control studies, and large case series examining the role of diet in acne, published in the English language and on humans were included in this review. See Table 1.

## RESULTS

### Influence of Carbohydrate Intake on Acne Severity

The glycemic index (GI) is a measure of the relative potential of food to raise blood glucose levels as compared to equal amounts of carbohydrates within the food. It gives a sense of the quality of the carbohydrates present in food as it reflects the rate of carbohydrate absorption. Glycemic load (GL) determines the potential of a food to raise blood glucose as well as insulin as it accounts for the glycemic index of a particular food (quality) as well as the amount of food consumed (quantity).<sup>11</sup>

TABLE 1.

## Studies Investigating Relationship Between Carbohydrates and Acne

Study	Study Design	Subjects	Sample Size	Intervention	Acne Assessment	Study Length	Conclusions and Limitations
<b>Kwon et al., 2012</b>	RCT, investigator-blind	Korean subjects with mild to moderate acne	LGL Diet n=17 Control Diet n=15	LGL group adhered to a diet of 45% calories of low GI carbs, 25% protein, 30% fats. Control group was instructed to eat carbohydrate rich foods daily.	Leeds Revised Acne Grading System, 2 Dermatologists; Photographs; Self-assessment; Immunohistochemical analysis of acne punch biopsy.	10 weeks	Subjects adhering to a LGL diet resulted in clinical and histopathological improvements of acne. Limitations: Use of a self reporting food diary may have prevented accurate calculation of the nutritional composition and amount of food consumed. Other dietary factors were not considered including milk/dairy, saturated fat, fiber, zinc, and iodine. Relatively short duration (10 weeks as compared to 12 weeks in Smith et al.)
<b>Reynolds et al., 2010</b>	RCT, investigator-blind	Boarding school adolescent male students, mean age 16.6 +/- 1.1years, mean BMI 23.6 +/- 3.8 kg/m <sup>2</sup>	n=58, 43 completed the study	Low Glycemic or High Glycemic Diet	Dermatologist	8 weeks	Facial acne severity improved more on the low GI diet, but the difference between diets did not reach significance. Additionally, insulin sensitivity did not differ between the two diets. Limitations were numerous and included short study duration (8 weeks), use of a non-validated and insensitive acne grading method, inconsistency with regards to acne grader, and only a mild difference in GI between the two diets (10 points).
<b>Jung et al., 2010</b>	Case - Control Study	Korean subjects with Acne, mean age 24 years	Subjects with Acne affected by Food = 420, Subject with Acne not affected by food = 363, control subjects without Acne = 502	Validated Food Frequency Questionnaire, Blood work (hormonal and growth factor, Insulin sensitivity)	Dr. Cunliffe's Grading System, 2 independent dermatologists	Food frequency questionnaire analyzed after 1 week.	Acne associated with high GL, dairy, high saturated fat, and iodine intake. IGF-1 and IGF-1R3 showed sex-dependent differences. Limitations: observational design (no intervention to prove causal relationship), confounders such as topical or oral medications for acne, skin care, and stress were not accounted for.
<b>Ismail et al., 2012</b>	Case - Control Study	Malaysian subjects with acne, ages 18-30	Acne subjects=44 (66% female), controls = 44 (66% female)	Validated questionnaire and food interviews, three day food diary	Comprehensive Acne Severity Scale (CASS), Dermatologist	Three day food diary	Glycemic load and frequency of milk and ice cream ingestion were positively associated with acne. No significant differences in BMI or fat percentage in cases vs. controls. Limitations: observational study design, short food diary duration, confounders such as topical or oral medications for acne, skin care, and stress were not accounted for.

Study	Study Design	Subjects	Sample Size	Intervention	Acne Assessment	Study Length	Conclusions and Limitations
<b>Skroza et al., 2012</b>	Case - Control Study	Italian subjects, median age 16-17	Cases n= 93; Controls n = 200	Validated food frequency questionnaire to assess dietary pattern and adherence to the Mediterranean diet.	Dermatologist - Cases were recruited from an outpatient Dermatology Clinic that had been diagnosed with mild/mod/severe acne for the first time.	Food Frequency Questionnaire used to assess food consumption within the past year.	Adhering to a Mediterranean diet plays a protective role in the pathogenesis of acne. This could be secondary to the increased intake of omega-3 fatty acids in olive oil and fish as compared to Western diets. Familial diabetes, hypercholesterolemia, and hypertension also represented risk factors for acne. Limitations: BMI and psychological state was not recorded. Questionnaire evaluated food intake for the past year allowing for recall bias and information bias.
<b>Rouhani et al., 2009</b>	Cross - Sectional Study	Subjects adhering to a low glycemic South Beach Diet	n=2528	World Wide Web Based questionnaire	Self- report	Single point in time (survey)	Subjects reported improvement of acne and ability to wean off of acne treatment while adhering to low-glycemic South Beach diet. Limitations include self-report of acne, presence of confounding factors such as weight loss and exercise, recall bias, and selection bias.
<b>Kim et al., 2010</b>	Interventional Study: Double Blind, Placebo Controlled	Subjects with mild to moderate acne, ages 18-30	Lactoferrin group n=18, Placebo group n=18	Daily ingestion of a Lactobacillus-fermented dairy beverage plus 200mg of Lactoferrin, or Lactobacillus-fermented dairy beverage alone.	Acne lesion counts and revised Leeds Acne Grading System, Dermatologist; (condition of skin was also assessed at baseline and 12 weeks including sebum, hydration, pH, skin surface lipids)	12 weeks	Lactoferrin (an anti-inflammatory milk protein) group showed a significant decrease in acne grading, inflammatory and total lesion counts, and sebum production (both triacylglycerols and free fatty acids). Placebo group (probiotic drink alone, without lactoferrin) showed significant improvement in total lesion counts and a decrease in sebum production. A trend towards improvement in the other outcomes (including inflammatory lesion counts and acne grade) were noted even in this group, although statistical significance was not reached. Limitations: This study would have benefited from the addition of a 3rd control group: a group consuming a probiotic-free, lactoferrin-free beverage.

Study	Study Design	Subjects	Sample Size	Intervention	Acne Assessment	Study Length	Conclusions and Limitations
<b>Halvorsen et al., 2009</b>	Cross - Sectional Study	Norwegian subjects, ages 18-19	n=3775	Self Report of 5 dietary variables (Assessment of Diet); Hopkins Symptom Checklist 10 (measure of Mental Distress); Self Report of Lifestyle variables	Self- report (In validation study, self report was compared to dermatologists assessment with 74% overall agreement, 93% sensitivity and 43% specificity)	Single point in time (survey)	Among late adolescents in Norway, self-reported acne was significantly associated with mental distress. Self-reported acne was also associated with infrequent consumption of raw vegetables among girls. Limitations: Diet questionnaire was a major limiting factor in that food items were limited solely to five broad range groups and broad categorical classifications may lead to misclassification or generalized food intake estimations rather than precise calculations. Self reporting of acne brings into question the accuracy of the severity of acne. Cross-sectional design.
<b>Law et al., 2009</b>	Cross - Sectional Study	Hong Kong University students with acne.	n=332	Traditional Chinese Medicine (TCM) Yin and Yang body constitution scores, Validated Youth Risk Behavior Questionnaire	Global Acne Grading System	Validated food frequency questionnaire was asked in reference to food consumption within the past week.	When considering acne as a <i>homogenous/ undifferentiated</i> diagnosis, no significant associations between diet and acne were found. However, when using the TCM method to classify acne diagnoses based on Yin vs. Yang body type, acne was positively associated with certain high GI foods such as desserts, ice cream, and fresh fruit juices in subjects with "Yang" characteristics (relating to the exterior, hyperactivity, bright color, hot red tongue, superficial rapid and forceful pulse). Limitations: Cross Sectional design suggests association not causation. Food frequency questionnaire assessed food consumption within the past week and not usual intake of food. Details concerning how a diagnosis of Yin/Yang deficiencies were not given.
<b>Ghodsi et al., 2009</b>	Cross - Sectional Study	Iranian High school students	n=1002	Questionnaire	Lesion counts and Global Alliance to Improve Outcomes in Acne Classification system, Examination team of Dermatologist, 2 Dermatology residents, and 2 general practitioners.	Single point in time (survey)	Regular consumption of sweets, nuts, chocolate, and oily foods were recognized as risk factors for moderate to severe acne while spicy foods and fasting were not associated with acne severity. Limitations: Lack of a validated questionnaire, Recall Bias.

Study	Study Design	Subjects	Sample Size	Intervention	Acne Assessment	Study Length	Conclusions and Limitations
<b>Mueller et al., 2011</b>	Interventional Study: open label, single arm	Subjects with mild to moderate acne, ages 14 - 30	n=39	Daily ingestion 100mg bovine lactoferrin chewable tablets BID for 8 weeks	Acne Lesion counts, skin status assessment as per subject and dermatologist using a 5 point scale, overall acne severity relative to baseline questionnaire as per subject using a 5 point scale, photographs evaluated by a panel of 6 experts.	8 weeks	Lactoferrin supplementation may have a treatment benefit for adolescence and young adults with mild to moderate acne. Limitations: this study did not provide a control group, was open label, many of the visual assessments were based on photographs of mild acne lesions or few acne lesions which may have affected overall outcome rankings,
<b>Aksu et al. 2012</b>	Cross-sectional study	Subjects ages 13 - 18	n=2300	Questionnaire (The Adolescent Food Habits Checklist)	Objective evaluation by dermatologist and resident using Pillsbury's diagnostic criteria	Single point in time (survey)	Acne was related with dietary habits. Fat, sugar and fast food consumption was found to be positively correlated with acne prevalence.
<b>DiLandro et al., 2012</b>	Case - Control Study	Cases: Italian subjects with new dx of moderate to severe acne seeking treatment at 1 of 15 dermatology outpatient clinics, ages 10-24. Controls: no or mild acne seeking treatment for a derm condition other than acne	Cases n= 205; Controls n= 358	Short version of a validated Food Frequency Questionnaire; Standardized Questionnaire assessing Personal Habits, Menstrual History, and relevant Medical History; Anthropometric measures to calculate BMI.	Photographs of the face graded using Validated Global Score Acne Severity Scale (Cunliffe), Dermatologists	Food Frequency Questionnaire used to assess 'usual' food consumption as well as 'food consumed the week prior to interview.'	Weekly consumption of cakes, sweets, and chocolate was not associated with a higher risk of acne. Family history, higher BMI, and milk consumption were all associated with a higher risk of acne while fish consumption was associated with a protective effect. Limitations: Use of mild acne patients in the control group may have underestimated risk estimates; recall bias concerning dietary questionnaire (perhaps use of a food diary may have been more accurate).

In the previous Diet & Acne JAAD review, Bowe et al suggested that high glycemic load (HGL) diets might exacerbate acne. Recent studies appear to lend support to this conclusion, implicating high glycemic index foods even further in the exacerbation of acne. To place these recent findings into context, it is necessary to briefly review two key studies that were described in the initial Diet and Acne review. In a cross-sectional study, Cordain et al noted an absence of acne cases in non-Westernized societies. After comparing the differences in dietary habits of these societies with the typical Western diet, these authors chose to focus on the glycemic load of the diets, concluding that diet-induced hyperinsulinemia was to blame for acne in Westernized societies.<sup>12</sup> Bowe et al further identified the Smith et al studies to be ground breaking studies in elucidating the relationship between carbohydrate intake and acne severity. In a series of three randomized control trials and a nonrandomized clinical trial, Smith et al tested the hypothesis that diet-induced hyperinsulinemia could result in IGF-1 and androgen imbalances, causing changes in

sebum composition and resulting in an increase in acne in male patients.<sup>13-16</sup> Low GI foods, on the other hand, resulted in weight loss and ultimate improvements in acne. However, as noted in Bowe et al, there were a few limitations to these studies, including the use of only adolescent males and failure to account for weight loss as a possible confounding variable. Such limitations brought into question whether it was a decrease in GI or a decrease in BMI that led to improvements in acne, and whether such findings could be extrapolated to female patients as well.<sup>10</sup> We follow with a summary of more recent studies exploring the link between carbohydrates and acne, starting with the most rigorous of study designs and ending with studies that suffer from serious design flaws. Although not chronological, the authors felt this approach led to a more meaningful analysis of the available data.

Since the Cordain and Smith studies, the strongest evidence to implicate high GI diets in acne has been a randomized control trial conducted by Kwon et al, which showed that subjects adhering to

a low glycemic load diet resulted in both clinical and histopathological improvements in acne.<sup>17</sup> Kwon et al recruited thirty-two Korean subjects with mild to moderate acne and randomly assigned them to either a Low Glycemic Load (LGL) Diet or a Control diet. The authors defined the LGL diets as follows: 45% calories from low GI carbohydrates, 25% protein, 30% fats; subjects in the control group were instructed to eat carbohydrate rich foods daily. Two dermatologists then assessed acne using the Leeds Revised Acne Grading System. A self-assessment, photographs, and immunohistochemical analyses of punch biopsies were also used to assess the impact of the LGL on the skin.

Subjects adhering to the LGL diet showed significant clinical improvements in the number of non-inflammatory and inflammatory acne lesions as compared to the control group. Histopathological evaluation showed that the size of sebaceous glands was significantly reduced in those following the LGL diet. Furthermore, the authors noted a decrease in the number of inflammatory cells seen on H&E, and a decrease in the expression of inflammatory cytokines such as IL-8. These findings not only further bolstered the arguments made by Smith et al, but they provided even greater insights into the timeline over which one might appreciate these changes (Kwon et al saw results in 10 weeks, while Smith et al study lasted 12 weeks). The Kwon et al study had several strengths worth mentioning here. Confounding variables in the Smith et al trial such as BMI were eliminated in the Kwon et al study as total energy intake and BMI were maintained throughout the study. Rigorous nutritional counseling and reinforcement of diet adherence through daily food records, nutritionist consults, and personalized eating plans for each subject were provided. Furthermore, histopathology assessment using 2mm punch biopsies stained with H&E to evaluate inflammation, size of sebaceous glands, and stained for inflammatory markers like IL-8. This study was the first of its kind to confirm a decrease in clinical inflammation on a microscopic scale. The inclusion of females (though only eight in total), allowed for results to be universally applicable to both male and females. Additionally, a wash out period for patients previously on prescription treatment regimens was included and acne assessments utilized a validated grading system and two independent dermatologists as graders.

Despite breakthrough progress with this study, it did have several limitations. First, the use of a self-reporting food diary may have prevented accurate calculation of the nutritional composition and amount of food consumed. Second, other dietary factors were not considered including milk/dairy, omega-3 fatty acids, antioxidants, probiotic consumption, saturated fat, fiber, zinc, and iodine.

The results of a study conducted by Reynolds et al in 2010 are not as straight forward.<sup>18</sup> This was an 8-week randomized controlled trial looking at 43 Australian males, mean age 16.6,

attending boarding school. In those who followed a LGL diet, there was a trend towards greater improvement in acne severity, but it did not reach statistical significance. Furthermore, no change in insulin sensitivity was detected in this group. However, this study suffered from major design flaws. First, the LGL did not differ much from the control group (only a difference of 10 points in GI), as the LGL was far from strict. Second, the study duration was very short- only 8 weeks total. Given the natural history of comedogenesis, one would not expect to see a significant result in such a short time frame. Additionally, the authors used non-validated and insensitive grading method and noted inconsistencies to the acne grader. Minimal efforts were taken to ensure dietary compliance. Despite all of these limitations, there was clearly a greater improvement in facial acne severity from week 0 to week 8 in the LGL group. Although this trend didn't reach statistical significance, it is hard to ignore when you see the raw data. Although suffering from a number of limitations, we listed this study after the Kwon study simply because of its RCT design.

Jung et al conducted a cross-sectional study on 1,285 male and female Korean patients.<sup>19</sup> Acne triggers were evaluated using a validated food frequency questionnaire and blood levels of insulin, IGF-1, insulin-like growth factor binding protein-3 (IGFBP-3), post-prandial 2 hours blood glucose, dehydroepiandrosterone sulphate were measured. Two independent dermatologists using Dr. Cunliffe's Grading System conducted acne assessment.

Subjects were categorized into three groups: acne patients affected by food (AF), acne patients not affected by food (NAF), and a control group. 54% of acne patients reported that their acne was aggravated by food. It was found that acne severity was positively associated with high GL, dairy, high saturated fat, and iodine intake as acne patients showed a greater preference for hamburgers, doughnuts, instant noodles, carbonated drinks, processed cheeses, high fat foods (nuts, fried chicken, pork), and foods with high iodine levels such as seaweed. Furthermore, blood levels of IGF-1 and IGFBP-3 showed sex-dependent differences as males in the AF group showed increased levels of IGF-1 and females in the AF group showed decreased levels of IGFBP-3, both allowing for increased free and active IGF-1 to be circulating in the blood. Control subjects without acne showed more regularity of meal habits and increased intake of vegetables and fish, which may prove to be protective against the pathogenesis of acne.

The study had numerous advantages, including a large sample size (783 patients and 502 controls), sensitive assays for insulin resistance (postprandial 2-hour blood glucose test), validated Food Frequency Questionnaire and objective dermatologist assessments of acne severity. It also included female participants, which was a strength compared to the Smith et al studies. With that said, numerous limitations were also observed. The use of

an observational design such as a cross-sectional study does not establish a causal relationship between diet and acne. Additionally, confounders such as topical or oral medications for acne, skin care, and stress levels were not accounted for.

In 2012, Ismail et al conducted a case-control study on forty-four Malaysian subjects with acne and forty-four subjects without acne.<sup>20</sup> The subjects evaluated included adolescents as well as adults, ages 18-30, with both males and females represented. Validated questionnaire on food perceptions and beliefs, food interviews using an adapted validated questionnaire on milk and dairy product intake, and a three-day food diary to assess dietary patterns were used. Dermatologists used a Comprehensive Acne Severity Scale (CASS) to evaluate acne severity.

Ismail et al concluded that glycemic load and frequency of milk and ice cream ingestion were positively associated with acne. Adults and females were included, whereas most prior studies were limited to adolescent males, giving further applicability of the results to a broader patient population affected by acne. Furthermore, there were no significant differences in BMI or fat percentage in cases vs. controls, providing support that the effects seen in the Smith et al trials was due to GI and not weight loss. However, limitations to this study were also noted. The observational study design prevented a causal relationship from being determined and short food diary duration may not have been accurately reflective of "usual" dietary habits. Additionally, confounders such as topical or oral medications for acne, skin care, and stress were not accounted for.

We conclude with two studies that deserve a brief mention, as they indirectly address the role of carbohydrates in acne. The Mediterranean diet refers to a food model lifestyle consisting of increased intake of olive oil, fish and antioxidants, and low glycemic load foods as compared to Western diets. It is believed to be protective with regards to the development of cardiovascular disease and metabolic syndrome. Skroza et al was one of the first studies to examine whether the Mediterranean diet serves a protective role in acne.<sup>21</sup> In a case-control study of 93 Italian subjects with acne and 200 controls without acne, Skroza et al concluded that adhering to a Mediterranean diet appeared to play a protective role when it comes to the development of acne. This could be attributed to the LGL, lack of dairy, or increased intake of omega-3 fatty acids (olive oil and fish) as compared to Western diets. In this study like many of the others, patients with acne showed increased consumption of high glycemic foods and more milk and dairy as compared to their Mediterranean diet-adhering controls. Furthermore, familial diabetes, hypercholesterolemia, and hypertension also associated with acne and may represent risk factors.

Similar to the Mediterranean diet, the South Beach diet is also a low glycemic food model as it advocates carbohydrate restriction and consists of unprocessed, fresh fruits, vegetables and

lean meats, fish, and seafood. In 2009, Rouhani et al conducted a cross-sectional study using internet-based survey, showing that the South Beach Diet resulted in the improvement of acne.<sup>22</sup> A total of 2528 self-proclaimed "active dieters" completed the online survey. Subjects with acne reported improvement and ability to wean off of acne treatment while adhering to low-glycemic South Beach diet. And while the self-report survey showed strength in number of subjects (n=2528), there were several major limitations. Acne was self-reported, meaning that results went unverified by a physician.<sup>23</sup> Furthermore, numerous confounding factors went unaccounted for, such as weight loss and exercise, which are often seen in active dieters. The study also suffered from multiple biases including recall bias, selection bias, and misclassification bias. Of note, this study was presented as a poster and not published in a peer-reviewed journal.

Various cross-sectional studies continued to show a positive association between high glycemic load foods and acne severity, however were limited in clinical significance due to major design flaws. Consequently, we have not included them in our discussion but did include them in our Table. See Table 1 for details.

## CONCLUSION

This review serves to examine the evidence supporting the influence of nutrition on acne, with a particular focus on the role of carbohydrates. While a few preliminary studies suggested an association between low GI diets and acne improvement a few years ago, there now exists sufficient evidence to confirm that such an association exists. While we still do not have a firm grasp on the exact mechanism behind this association, we do have enough of an epidemiological link to provide dietary counseling to our acne patients. Based on our current knowledge, dermatologists can encourage acne patients to substitute high glycemic index foods for low glycemic index foods, and avoid refined carbohydrates whenever possible.

## DISCLOSURES

The authors have not disclosed any relevant conflicts.

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