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THE INFLUENCE OF DIETARY COMPONENTS ON ACNE; A CASE-CONTROL SURVEY

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Acne vulgaris affects millions of adults.Despite extensive research, its food related etiology remains elusive. The objective was to assess the correlation between dietary intake and acne through a case-control survey of 300,15-25 year old respondents living in Pakistan. 50 acne patients and 150 age-and ethnicity-matched controls completed a questionnaire.Cases and controls were separated using SPSS-22 and univariate analysis was performed using the chi-square test. p value < 0.05 was considered statistically significant. We used adjusted odds ratios to assess the strength of associations with 95% confidence intervals. Most of the respondents were females (91.3%).Most (48.7%) acne patients were 20-25 years old. Acne severity was mild in 50%,moderate in 34%,severe in14%and very severe in 2%.Frequent low-fat foods(p<0.001)(OR=3.22),fat intake(p=0.03)(OR = 1.629),sweet snacks i.e. biscuits and candies etc. (p=0.013) (OR=1.9254), soft drinks(p= 0.045)(OR= 1.9091),butter(p<0.001) (OR= 1.8185),dairy products(p=0.043)(OR=0.624),salty foods(p= 0.011)(OR=1.961),chocolate (p=0.028)(OR=1.669), were associated with increased acne risk.No association was found with consumption of fried foods, desserts, fruit juices, raw fruit, fast food, vegetables, cheese, soy products, salt, and corn. Increased butter and chocolate consumption were linked to more severe forms of acne(p=0.049 and p=0.005 respectively).Most respondents (n=218) considered themselves to have healthy eating habits, indicating they were not educated about the nutritional aspects of acne treatment.Certain food item intake was significantly higher in acne patients to give an association between the two. Further studies must be conducted to develop a causative relationship. Nutrition aawareness is critical to reduce acne.

Keywords: Correlation between acne and diet, Dietary habits, Acne

INTRODUCTION

Acne is one of the most common skin condition, affecting millions of young adults worldwide (Tan JKL et al.2015). Excess sebum, hormonal alterations, *Propionibacterium acnes* proliferation in the pilosebaceous unit and abnormal follicular keratinization are the main etiologic factors in acne. The influence of diet on these factors for the development of acne has been widely believed in the patient population and is now supported by scientific evidence (Smollich M, et al. 2022). Patients' diet can influence insulin, IGF-1, FoxO1, mTORC1,PPAR,leptin receptors, which can directly impact sebocytes,augment mitogenic down stream signaling pathways, and androgen levels thereby altering acne pathogenesis.(Dréno B. 2017, Baldwin H. et al. 2021,Melnik et al.2013.)

The relationship between diet and acne is controversial.1960's studies showed no correlation between diet and acne. In 1969, study by Fulton et al. showed no effect of chocolate on acne, but was criticized for having no difference in the glycemic index of chocolate and the placebo used (Fulton JE Jr et al.1969,Mackie BS et al.1974).Another study by Anderson(P. C. Anderson.1971) also denied any association between intake of milk and hazelnut chocolate and acne. However, it too had limitations as it did not take the full dietary details of the subjects into account. The landscape has changed since then. A recent review of literature (Dall'Oglio Fet al. 2021) showed that acne-promoting factors included high GI/GL food, dairy products, and chocolate, whereas acne-protective factors included fatty acids, fruit, and vegetable intake. A study (Aghasi M et al. 2019) found an association between milk consumption and acne. This was attributed to the high carbohydrate content of milk in addition to the fact that many dairy cows in the United States are treated with bovine growth hormone to increase their milk supply, which leads to higher levels of IGF-1 in milk(Danby FW. 2010).In

addition, Western diets are associated with acne compared to non-Westernized populations(Suda KM. 2018). A study (Burris J et al.2018) compared the effect of low glycemic-load diet with high glycemic-load diet on acne vulgaris and suggested that low glycemic index reduces IGF -1 among acne patients .Another study showed that an acne patient had a significantly higher daily intake of sodium chloride (NaCl) than a control group(El Darouti MA et al. 2016). A wide variety of food items have been implicated in acne such as cheese, chocolate, sweets, soft drinks, beer, wine and alcohol, fatty foods, corn, fried beef, salty food, soy products, dairy, fruits and vegetables (Aksu AEK et al. 2012,Okoro EO et al. 2016,Saleh NF et al. 2011)

The role that specific dietary constituents play in relation to different foods remains an unsolved issue and the subject of future research, and preliminary results need to be corroborated by further research.This study will evaluate the correlation between dietary components of acne patients when compared to age and ethnicity matched controls so as to determine the role of diet in acne. This would allow physicians to introduce appropriate dietary interventions in teenagers to reduce the severity of acne lesions. The confirmation of multimodal pathophysiology of acne would also offer numerous opportunities for appropriate pharmacologic intervention.

MATERIALS AND METHODS

It was a case-control study using quantitative method to collect and analyze the data. The study used a questionnaire which was filled by 150 acne patients and 150 age and ethnicity matched healthy people who attended Dermatology OPD from February 2022 to March 2022 which were selected via Stratified Random Sampling. After approval of Institutional Review Board (IRB) KEMU, Lahore (IRB NO. 347/RC/KEMU) dated 22/2/2022; administrative permission from all authorities was obtained. Prior to collection research design was explained to the on-call physician. Consent was taken from respondents. A questionnaire comprising items enquiring into the respondent's dietary habits (adapted from The Adolescent Food Habits Checklist) and acne severity using Hayashi lesion counting chart (Hayashi N, et al. 2008) was distributed. Patient-physician interaction was not intervened.

SAMPLE SIZE:

Sample size of 150 patients is estimated by usingthe expected proportion exposed in control as 0.05,assumed odds ratio as 3 , confidence interval of 0.9, and desired power as 0.8.

$$n = \frac{(\bar{p}(1-\bar{p})(Z_{\alpha} + Z_{\beta})^2}{E^2}\left[\frac{r+1}{r}\right]$$ where $E = P_1 - P_2$ and r is ratio of controls to cases.

n=sample size

Z_1^2-α/2= confidence level 90%

Z β= power 80%

r= assumed odds ratio

E=expected proportion in controls

Strict inclusion criterion to include consenting patients with and without acne aged 15-25 years living in Pakistan was used**.**

DATA ANALYSIS:

Data was done by entering it in SPSS-22.The cases and controls were separated and the intake frequency of each food item was calculated.Univariate analysis between the cases and controls was done by using the chi-square test to find co-relation between the diet of the two groups. p value < 0.05 was considered statistically significant. Binary Logistic Regression was used to calculate the adjusted odds ratio with 95% confidence interval which was used to assess the strength of association between dependent and independent variables.

ETHICAL CONSIDERATIONS:

All ethical issues such as maintaining confidentiality and avoiding harm were strictly observed during the study.

RESULTS

DEMOGRAPHIC DATA :

The case group consisted of137 (91.3%) females and 13(8.7%) males while the control group consisted of 109 females (72.7%) and 41 males (27.3%) (Table 1). The cases included 24(16%) people aged 15-20, 73(48.7%) people aged 20- 25, and 53(35.3%) people aged 25-30 while the healthy people had the distribution of 7(4.7%), 54(36%) and 89(59.3%) people respectively. Acne severity was assessed using the Hayashi lesion counting method;75(50%) had mild acne, 51(34%) had moderate acne,21(14%) people with severe acne, and 3(2%) had very severe acne.

ACNE SEVERITY:

MILD	MODERATE	SEVERE	VERY SEVERE
75(50%)	51(34%)	21(14%)	3(2%)

CORRELATION:

Chi-square test was used to calculate correlations between variables and odds ratios were used to determine the degree of association (Table 2).The participants without acne had healthier dietary habits than those with acne. Our study linked low-fat foods, increased fat intake, frequent sweet snacks i.e. biscuits and candies etc., soft drinks, butter, dairy products, salty foods, chocolate to acne .

Fat and butter intake was higher in the acne group(p=0.03)(OR = 1.629 (95% CI [1.030, 2.577])) and(p<0.001) (OR= 1.8185 (95% CI [1.1474, 2.8820])) respectively.Although fats increased the chances of acne,

strangely low-fat food intake also rose the odds of developing acne by three times (p<0.001)(OR=3.221, (95% CI [1.984, 5.228]))Similarly, high glycemic load foods were also associated with the acne group.

TABLE 1: Characteristics of the Study Population

Variable	Total population N(%)	Acne status YES	NO
No.(%)	300(100%)	150(50%)	150(50%)
SEX			
WOMEN	246(82%)	137(91.3%)	109(72.7%)
MEN	54(18%)	13(8.7%)	41(27.3%)
AGE			
15-20	31(10.3%)	24(16%)	7(4.7%)
20-25	127(42.3%)	73(48.7%)	54(36%)
25-30	142(47.3%)	53(35.3%)	89(59.3%)

TABLE 2: Corelation between Acne and Food Groups:

	CASE N/150 (%)	CONTROL N/150 (%)	P value	OR (95% CI)
Low-fat foods	83(55%)	41(27.3%)	<0.001	OR=3.221, (95% CI [1.984, 5.228])
Fat intake	76(50.7%)	58(38.7%)	0.037	OR = 1.629(95% CI [1.030, 2.577])
Fried foods	95(63.3%)	84(56%)	0.195	OR=1.357(95% CI [0.854, 2.156]).
Desserts at end of meal (cakes, pastries etc.)	61(40.7%)	50(33.3%)	0.188	OR=1.371(95% CI [0.856, 2.194]).
Sweet snacks (biscuits,candies etc.)	58(38.7%)	37(24.7%)	0.013	OR=1.9254(95%CI [1.1727, 3.1611])
Fruit juices	88(58.7%)	82(54.7%)	0.485	OR=1.177(95% CI [0.745, 1.859]).
Fresh fruit (raw) intake as a snack Three times per day	52(34.7%) 34(22.7%)	61(40.7%) 30(20.0)	0.562 0.573	OR=1.172(95% CI [0.674, 2.039]).
Fast foods (sausages , burgers ,take away meals)	58(38.7%)	57(38.0%)	0.763	OR=1.0289(95% CI [0.6458, 1.6384]).
Soft drinks	126(84.0%)	110(73.3%)	0.045	OR=1.9091 (95% CI [1.0829, 3.3658]).
Vegetables	79(52.7%)	69(46.0%)	0.18	OR=1.364(95% CI [0.864, 2.152]).
Butter	78(52%)	56(37.3%)	<0.001	OR=1.8185 (95% CI [1.1474, 2.8820]).
Cheese Mozerella Cheddar Combined Others	44(29.3%) 5(3.3%) 10(6.67%) 19(12.7%) 3(2%)	36(24.0%) 9(6%) 6(4%) 14(9.3%) 3(2%)	0.280	OR=1.327(95% CI [0.794,2.219]).
milk low-fat Skimmed full fat	64(42.7%) 24(16%) 39(26%) 36(24%)	60(40%) 41(27.3%) 19(12.7%) 63(42.0%)	0.639	OR=1.116(95% CI [0.705, 1.768]).
Dairy products yoghurt icecream milk	85(56.7%) 44(29.3%) 36(24%) 4(2.7%)	68(45.3%) 55(36.6%) 10(66.6%) 3(2%)	0.043	OR=1.576 (95% CI [0.9998, 2.4872]).
Soy product	34(22.7%)	25(16.7%)	0.191	OR=1.466(95% CI [0.825, 2.604]).
Salt intake	118(78.7%)	99(66%)	0.011	OR=1.961(95% CI [1.166, 3.299]).
Corn	70(46.7%)	61(40.7%)	0.295	0R=1.277(95% CI [0.808, 2.017]).
Chocolate Cocoa Dark Milk	79(52.7%) 18(12%) 5(3.3%) 72(48%)	60(40%) 17(11.3%) 15(10%) 65(43.3%)	0.028	OR=1.669(95% CI [1.056, 2.638]).

Frequent snacking on sweet foods doubled the odds of developing acne (p=0.013) (OR=1.9254(95%CI [1.1727, 3.1611])) butit was noted that consumption of dessert at the end of a meal was not associated with acne. Soft drinks correlated with acne formation (p=0.045)(OR= 1.9091 (95% CI [1.0829, 3.3658])).

Chocolate consumptionwas higher in the acne group when compared to controls, with milk chocolate being consumed the most (p=0.028)(OR=1.669(95% CI [1.056, 2.638])).Regarding dairy products, use ≥3 times per week was observed in acne patients (p=0.043)(OR=0.624(95% CI [0.395, 0.986])),while intake of one glass of milk daily was seen in similar frequencies in both groups.In terms of the type of dairy product, it was noted that yogurt consumption was higher in the control group while icecream was more consumed by the acne patients. Acne patients took salty foods more frequently and a positive association was found between the two.(p=0.011)(OR=1.961(95% CI [1.166, 3.299])).

No significant differences were found in terms of frequencies of fried foods, desserts (cakes, pastries, etc.),fruit juices, fresh fruit (raw) intake,fast foods (sausages, burgers, takeaway meals), vegetables, cheese, soy product, salt intake, corn($p > 0.05$).

Butter and chocolate were associated with acne severity and those consuming them had more severe forms of acne (p=0.049 and p=0.005 respectively).

Most of the respondents said they tried to have a healthy diet but this was not in accordance with the finding from the detailed questionnaire, showing that they were not educated on the basics of a healthy diet for acne. (N=217)

DISCUSSION

MAIN FINDINGS:

Our study included 300 subjects; most of them being women aged 20-25 years. This was conisitent with data collected through a previous study on acne by Penso in 2019 where most of the subjects were females (Penso L et al. 2020).This highlights the fact that females are most likely to suffer from acne (Noorbala M et al. 2013) although selection bias might also affect this. Older patients suffer less from acne (Skroza N et al. 2018); acne patients were predominantly between 20-25 years old while the controls were most prevalent in 25-30 years age group.

High-fat consumption, including butter, was associated with acne.Previous studies have also established this relationship. This is due to altered delivery of lipophilic vitamins A and D to sebaceous gland,changes inlipid oxidation pathways,lack of essential linoleic and α-linolenic acid in saturated fats,high ratio of omega-6 to omega-3 fatty acids where proinflammatory omega 6 fatty acids are thought to induce acne vulgaris (Pappas A . 2009). In addition, deficient ω-3 polyunsaturated fatty acids (PUFAs) which change the proportion of monounsaturated fatty acids in sebum triglyceridescan cause acne (Melnik BC. 2015).These findings are the basis for studies that revealed that non-Western diets correlated with the absence of acne(Pappas A . 2009).In our study the reason for correlation of low-fat foods to acne formations probably because of their high sugar content(Nguyen PK et al. 2016)

High glycemic index foods were associated with higher likelihood of acne. These include low-fat foods, frequent snacking on sugary foods, soft drinks, and chocolate. All of these foods have a high glycemic index which elevates serum insulin concentrations thereby stimulating sebocyte proliferation and sebum production, suppress SHBG concentrations and raise androgen concentrations(Melnik BC et al.2009) contributing to acne. This research showed that the frequency of snacking also influences acne prevalence as those consuming sweet foods as part of dessert at the end of a meal had no association with acne formation but those who had multiple sweet snacks in a day developed acne.This might be due to higher insulin and IGF-1released with more frequent snacking on sweet foods (Chapelot D. 2011). We could not find any previous researches which specifically correlated glycemic index of foodsand insulin levels after their consumption to acne severity and could be subject for further research.

Acne patients consumed dairy products greater than 3 times per week; the most associated was skimmed milk. This result was in accordance with a previous cross-sectional study in which women, who consumed two or more servings of skimmed milk every day, were 22% more likely to suffer from severe acne than those who consumed only one glass of skimmed milk a day (Juhl CR et al. 2018). This shows endocrine factors are involved in acne because milk is an insulinotropic nutrient and has a high glycemic index which increases serum insulin and IGF-1 levels. Other mechanisms for the dairy-induced impact of acne include IGF-1 which is a forceful mitogen that promotes proliferation of sebaceous glands and sebaceous lipogenesis. Itcauses overproduction of androgens and oncogenic phosphoinositide -3-kinasewhich causes acne(Zubair N. 2011).IGF-1 down regulates Fox -O1 which increases oxidative stress and hence promotes acne (Adebamowo CA et al.2005).Our study found that yogurt consumption was lower in acne vulgaris patients and is consistent with the findings by several studies(Kang SH et al. 2006). When added to milk during the fermentation process, probiotic bacteria (specifically Lactobacilli) utilize IGF-1 and lower IGF-1 levels in fermented milk. This might explain the association of milk with acne vulgaris occurrence as opposed to fermented dairy products such as yogurt.(Ismail NH et al.2012)

We also found a link between salty foods and acne. A

study conducted on salty food showed that people with acne consumed significantly higher daily amounts of sodium chloride ($P < 0.001$) (El Darouti MA et al. 2016)

Although there are many studies on diet and acne, the understanding of the mechanism of the association between acne and sodium is somewhat limited and remains a topic for future research.

In the present study, we could not find the association in terms of frequencies of the following food items and acne ($p > 0.05$); fried foods, desserts(cakes, pastries etc.) at end of meal, fruit juices, raw fresh fruit intake, fast foods (sausages, burgers, take away meals), vegetables, soy product, salt intake, corn. Further studies could investigate this association in different populations.

Butter and chocolate were associated with more severe forms of acne. This is confirmed by a previous study where the odds ratio for butter consumers was more as compared to other dietary products(Afnan BH et al. 2021).Researches done previously also found that chocolate was closely linked to acne due to its high glycemic index(Delost GR et al. 2016)

Lastly, the majority of respondents in both groups said that they tried to follow a healthy diet even though their eating habits were not in accordance with the diet recommended by previous researches.

LIMITATIONS AND STRENGTHS:

The strengths of this study are: Acne was assessed by a dermatologist, demographic characteristics of selected groups were similar, and the data were collected through a face-to-face interview. The severity of acne vulgaris condition was also considered through acne lesion counts on patients to relate severity to specific types of food and the frequency of their consumption. The main limitation was a small sample size due to which the groups couldn't be matched on basis of age and gender using SPSS, hence, a higher proportion of women with acne might have led us to overestimate certain associations. Moreover, our findings reflect an association and not a causal role of dietary components in the establishment of acne due to the nature of the study design used. Confounding factors such as stress, sleep, smoking, alcohol consumption, and facial hygiene were not taken into account and must be assessed in future studies. Limitations in human ability to accurately remember and recall their exposure with accuracy might have affected the results. Despite these limitations, the findings from our study have provided further support to the role of certain foods in acne formation.

INTERPRETATION:

In view of these findings, patients must be educated on the basics of healthy eating habits for acne. High glycemic index foods, fat, dairy, and salty foods must be reduced as an adjunct to therapy to treat acne faster. Moreover, randomized control trials must be arranged to find a causative association between acne and dietary components.

CONCLUSION

In summary, our case-control study is one of the few studies that used formal epidemiological methodology to assess the association between acne and food. Our research showed that low-fat foods, frequent sweet snacks i.e. biscuits and candies etc., soft drinks, butter, increased fat intake, dairy products, salty foods, and chocolate were all associated with acne.Findings from this study further support the hypothesis that dietary factors play a fundamental role in acne vulgaris occurrences. Randomized clinical trials are needed to confirm the role of these food items in acne occurrence.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

Atiya Mahmood; conceived, designed, did statistical analysis, editing of the manuscript, and is responsible for the integrity of the research. Mubasharah Hanif; did data collection and manuscript writing. Ghazala Butt and Mahwish Zahoor; did review and final approval of the manuscript

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