Assessment of the Frequency of Gastrointestinal Symptoms in Patients with Acne in Dermatology Department of Bu-Ali-Sina Hospital in Qazvin from 2014 to 2015

Akram Beheshti[1], Ameneh Barikani[2], and Zohreh Ahmadi*[3]

[1,2]Associate Professor, Qazvin University of Medical Sciences, Qazvin, Iran

[3]Qazvin University of Medical Sciences, Qazvin, Iran

Corresponding author: Zohreh Ahmadi, Qazvin University of Medical Sciences, Qazvin, Iran, E-mail: zohrehahmadi2015@yahoo.com

Abstract

Many years ago, two dermatologist named H. Stokes and Donald M. Pillsbury presented a mechanism to explain the pathophysiology of acne as the gut-brain-skin axis. In 2008 Hang Zhang In a study of 13,215 adolescents, represented gastrointestinal symptoms such as halitosis, gastric reflux, abdominal bloating and constipation in patients with sebaceous gland diseases such as acne, are more common than in healthy controls. He also noted that gastrointestinal dysfunction is an important risk factor for diseases of the sebaceous glands and is associated with their occurrence and progression. In a study conducted in 2014 by H. Ismaeili, a strong correlation between gastrointestinal dysfunction including bloating and constipation, and acne severity, was mentioned.

In this cross sectional, case-control study, we sought to evaluate the frequency of gastrointestinal symptoms in acne patients compared with healthy individuals. In this study, 221 person including 112 patients and 109 healthy for any skin disorder and acne disease, all referred to the dermatology department of Bu-Ali hospital in the city of Qazvin were randomly participated over a one year period (2014-2015). The frequency of the severity of gastrointestinal disorders in patients were compared with controls. The relationship between the severity of acne in patients with severity of gastrointestinal disorders, and factors such as gender, age, education and marital status were examined. The two groups were matched for their member's age, sex, education and marital status.

In people with acne, severity of the gastrointestinal tract disorders, including "gastric dysfunction", "GI inflammation", "Small intestine and pancreas disorder" and "colon disorder" is higher compared to healthy controls (p value amounts are respectively 0.03, 0.02, 0.01 and 0.04).There is a direct correlation between severity of acne and severity of gastrointestinal disorders, including "gastric dysfunction", "GI inflammation" and "colon disorder"(p value amounts are respectively 0.02, 0.01 and 0.03). In addition, the acne disease is more severe in women than men (p= 0.03); moreover "GI inflammation" and "colon disorder" in women with acne is more severe than men with acne (p value levels are 0.001 and 0.007 respectively). Also in patients with acne, severity of the "Small intestine and pancreas disorder" increases with age (P=0.009).

Keywords: *Acne vulgaris*; Gastrointestinal dysfunction; Gastric dysfunction; GI inflammation; Small intestine and pancreas disorder and colon disorder

Introduction

ACNE is a papular or pustular eruption, involving the face, chest, and back. Acne may occur at any age, but is more common in the teenage years, and may persist well into adulthood. Plugged follicles, increased sebum production, *Propionibacterium acnes*, and inflammation are thought to promote acne.

The role of diet in the pathogenesis of acne remains unclear, although consumption of dairy production and simple sugars has been implicated in some studies [1]. At present, the pathogenesis of sebaceous gland diseases remains unknown, but, nevertheless, it is known that their occurrence and development are affected by multiple factors [2-4]. For example, seborrheic dermatitis is significantly related to disruption of the normal gastrointestinal flora [5]. Furthermore, the pathogenesis and development of acne is associated with gastrointestinal dysfunction, bacterial infection and psychological factors [6-8]. Some patients with rosacea have been found to have *Helicobacter pylori* infection [9]. It has previously been reported that gastrointestinal dysfunction increases sebaceous secretion [6]. For example, one study involving over 13,000 adolescents showed that those with acne were more likely to experience gastrointestinal symptoms such as constipation, halitosis, and gastric reflux. In particular, abdominal bloating was 37% more likely to be associated with acne and other seborrheic diseases [10]. Studies show that 85% of adolescents ages 12 to 24 years have acne while acne is much more common in adolescents; 8% of adults aged 25 to 34 years and 3% of those aged 35 to 44 years are affected by acne [11]. In adolescence, acne is more common in boys than girls, but the incidence is higher in young women. nodulocystic acne is more common in whites than blacks [12]. In the study by Whitney P Bowe and Alan C Logan entitled "*Acne vulgaris*, probiotics and the gut-brain-skin axis-back to future?" that proposed a gastrointestinal mechanism for the overlap between depression, anxiety and skin conditions such as acne, hypothesized that emotional states might alter the normal intestinal microflora, increase intestinal permeability and contribute to systemic inflammation. Among the remedies advocated by them were Lactobacillus acidophilus cultures. The ability of the gut microbiota and oral probiotics to influence systemic inflammation, oxidative stress, glycemic control, tissue lipid content and even mood itself, may have important implications in acne. The intestinal microflora may also provide a twist to the developing diet and acne research.They also found a historical perspective to the contemporary investigations and clinical implications of the gut-brain-skin connection in acne [13].

Hong Zhang and colleagues in another study entitled" Risk factors for sebaceous gland disease and their relationship to gastrointestinal dysfunction in Hanadolescents" studied, the prevalence and risk factors for certain sebaceous gland diseases and their relationship to gastrointestinal dysfunction in adolescents. The study found that factors Such as age; duration of local residency; halitosis; gastric reflux; abdominal bloating; constipation; sweet food; spicy food; family history of acne; late night sleeping on a daily basis; excessive axillary, body and facial hair; excessive periareolar hair; and anxiety are the risk factors for sebaceous gland diseases.

They also found a statistically significant difference in the prevalence of gastrointestinal symptoms (halitosis; gastric reflux; abdominal bloating; constipation) between patients with and without sebaceous gland diseases [10].

In a study Alan C.Logan, Martin kdtzman as "*Acne vulgaris*: Nutritional factors may be influencing psychological sequelae" they found that certain nutrients as Zinc, folic acid, selenium, chromium and x-3 fatty acids and alsoa weakened antioxidant defense system and altered intestinal microflora may interplay to increase the risk of psychological sequelae in *Acne vulgaris* [14].

In another study that A Szlachcic entitled "The link between Helicobacter Pylori infection and rosacea" concluded that rosacea is a disorder with various gastrointestinal symptoms closely related to gastritis, especially involving the antrum mucosa; and the eradication of Hp leads to improvement of symptoms of rosacea and reduction in related gastrointestinal symptoms; the lack of improvement of cutaneous symptoms in rosacea after eradication of Hp from the gastric mucosa could depend on bacteria in the oral cavity; and rosacea could be considered as one of the extragastric symptoms of Hp infection probably mediated by Hp-related cytotoxins and cytokines [15].

Material and Methods

In this cross sectional, case-control study, 221 person including 112 patients with *Acne vulgaris* disease reviewed and approved by a dermatologist and 109 individuals without any skin disorder and *Acne vulgaris* disease from patient's scorts, all randomly recruitedfrom dermatology department of Bu-Ali hospital in the city of Qazvin over a one year period (2014-2015). The two groups were matched for their member's age, sex, education and marital status.

Patients with any skin disorder In addition *Acne vulgaris*, participants who use drugs with gastrointestinal symptoms and acne side effects and pregnant individuals, were excluded.

A questionnaire containing two parts including general information, such as age, sex, education level, marital status, illness and drug use in the first part and gastrointestinal symptoms, including "gastric dysfunction", "GI inflammation", "Small intestine and pancreas disorder" and "colon disorder" in the second part, were handed to each participant. In the second part, the severity of GI symptoms was investigated. The asked GI symptoms are defined as follows:

Gastric Dysfunction

Indigestion, excessive burping and belching or bloating following meals, Stomach spasms and cramping during or after eating, belching, filling up immediately with small amounts of food, having no appetite, bad taste in mouth.

GI Inflammation

Heartburn, stomach pain, nausea, pain when swallowing or drinking.

Small Intestine and Pancreas Disorder

Discomfort or fullness or tension with delay in the abdomen, abdominal discomfort relieving by gas passing, frequent changes in stool consistency or form, undigested food in the stool, three or more large bowel movements per day or shortly after eating food.

Colon Disorder

Discomfort or pain or cramps lower abdominal area, incomplete evacuation, Abdominal cramps or bloating after eating food containing fiber, frequent constipation, alternating constipation and diarrhea, no urge to have a defecation.

Method of scoring to the questionnaire are summarized in Table-1.

The frequency of the severity of gastrointestinal disorders in patients was compared with controls. The relationship between the severity of acne in patients with severity of gastrointestinal disorders, and factors such as gender, age, education and marital status were examined.

Table-1 Method of scoring to the questionnaire

Gastrointestinal symptoms	Low severity	Moderate severity	High severity
Gastric dysfunction score	0-4	5-8	9-56
GI inflammation score	0-4	5-8	9-72
Small intestine and pancreas disorder score	0-8	9-16	17-80
Colon disorder score	0-8	9-16	17-72

Statistical Analysis

Data were shown as frequency and relative percentage of frequency. The SPSS software version 19 was used. Chi-square tests, T-tests, ANOVA were performed for analyzing and P <0.05 was considered statistically significant.

Results
Demographic

In the group with acne there were 93(83%) participant less than 25 years and 19 (17%) participant 25 years and more. In the control group, there were 87 (79.8%) participant less than 25 years and and 22 (20.2%) participant 25 years and more.

In the group with acne there were 30 (26.8%) male and 82 (73.2%) female. In the control group, there were 34(31.2%) male and 75(68.8%) female.

In the group with acne there were 17 (15.2%) participant less than high school diploma, 13 (11.6%) participant with high school diploma and 82 (73.2%) participant higher than diploma. In the control group, there were 9 (8.3%) participant less than high school diploma, 6 (5.5%) participant with diploma and 94 (86.2%) participant higher than diploma.

In the group with acne,there were 90 (80.4%) single and 22 (19.6%) married. In the control group, there were 77 (70.6%) single and 32 (29.4%) married.

The group with acne and the control group were comparable in terms of age, sex, education and marital status (p-value amounts are respectively 0.60, 0.55, 0.055 and 0.11) Table-2.

Table-2 Demographics of studied population including patients and controls.

		Patient(%)	Control(%)	P-value
Age	less than 25 years	83	79.8	0.60
	25 years and more	17	20.2	
Sex	Male	26.8	31.2	0.55
	Female	73.2	68.8	
Education	less than high school diploma	15.2	8.3	0.055
	High school diploma	11.6	5.5	
	Higher than high school diploma	73.2	86.2	
Marital status	Single	80.4	70.6	0.11
	Married	19.6	29.4	

Data are presented as relative frequency(%), p-value = 0.05 is statistically significant.

Gestational Symptoms

Gastric dysfunction severity frequency was 56(50%) low, 31(27.7%) moderate and 25(22.3%) sever in group with acne and 73(67%) low, 20(18.3%) moderate and 16(14.7%) sever in control group.

GI inflammation severity frequency was 57(50.9%) low, 19 (17.7%) moderate and 36 (32.1%) sever in group with acne and 73 (67%) low, 17 (15.6%) moderate and 19 (17.4%) sever in control group.

Small intestine and pancreas disorder severity frequency was 67 (59.8%) low, 35 (31.3%) moderate and 10 (8.9%) sever in group with acne and 81 (74.3%) low, 16 (14.7%) moderate and 12 (11%) sever in control group.
Colon disorder severity frequency was 65 (58%) low, 29 (25.9%) moderate and 18 (16.1%) sever in group with acne and 80 (73.4%) low, 16 (14.7%) moderate and 13 (11.9%) sever in control group.

Therefore in acne group, severity of the gastrointestinal tract disorders is higher compared to control group (p value amounts are respectively 0.03, 0.02, 0.01 and 0.04) Table-3.

Patients with Acne

In acne group, acne severity was significantly related to sex but not to age, education or marital status (p value amounts are respectively 0.03, 1.00, 0.31 and 0.30).

Gastric dysfunction severity was not related to sex, age, education or marital status (p value amounts are respectively 0.06, 0.80, 0.11 and 0.52).

GI inflammation severity was significantly related to sex but not to age, education or marital status (p value amounts are respectively 0.007, 0.14, 0.91 and 0.56).

Small intestine and pancreas disorder severity was significantly related to age but not to sex, education or marital status (p value amounts are respectively 0.009, 0.31, 0.12, and 0.81).

Colon disorder severity was significantly related to sex but not to age, education or marital status (p value amounts are respectively 0.001, 0.78, 0.11 and 0.34).

Therefore in acne group acne severity and also "GI inflammation" and "colon disorder" severity were significantly related to sex and "Small intestine and pancreas disorders" severity was significantly related to age Table-4.

Gastrointestinal disorders severity except "Small intestine and pancreas disorder" severity was significantly related to acne severity in patients with acne Table-5.

Table-3 Frequency distribution of gastrointestinal symptoms in patients and controls

GI symptom's		Patient(%)	Control(%)	P-value	
Gastric dysfunction	Low severity	56(50)	73(67)	0.03	
	Moderate severity	31(27.7)	20(18.3)		
	High severity	25(22.3)	16(14.7)		
GI inflammation	Low severity	57(50.9%)	73(67%)	0.02	
	Moderate severity	19(17.7%)	17(15.6%)		
	High severity	36(32.1%)	19(17.4%)		
Small intestine and pancreas disorder	Low severity	67(59.8%)	81(74.3%)	0.01	
	Moderate severity	35(31.3%)	16(14.7%)		
	High severity	10(8.9%)	12(11%)		
Colon disorder	Low severity	65(58%)	80(73.4%)	0.04	
	Moderate severity	29(25.9%)	16(14.7%)		
	High severity	18(16.1%)	13(11.9%)		

Data are presented as frequency and relative frequency(%), p-value = 0.05 is statistically significant.

Table-4 Chi-square test's p-values of The frequency of gastrointestinal symptoms and acne severity, according to demographics.

	Age	Sex	Education	Marital status
Acne severity	1.00	0.03	0.31	0.30
Gastric dysfunction severity	0.80	0.06	0.11	0.52
GI inflammation severity	0.14	0.007	0.91	0.56
Small intestine and pancreas disorders severity	0.009	0.31	0.12	0.81
Colon disorder severity	0.78	0.001	0.11	0.34

P-value = 0.05 is statistically significant.

Table-5 p value amounts of Chi-square test of GI disorders severity with acne severity.

GI disorders	Gastric dysfunction	GI inflammation	Small intestine and pancreas disorder	Colon disorder
P value	0.02	0.01	0.08	0.03

Discussion

In people with acne, severity of the gastrointestinal tract disorders, including "gastric dysfunction", "GI inflammation", " Small intestine and pancreas disorder " and "colon disorder" is higher compared to healthy controls (p value amounts are respectively 0.03, 0.02, 0.01 and 0.04).

Many years ago, two dermatologist named H. Stokes and Donald M. Pillsbury proposed a gastrointestinal mechanism for the overlap between depression, anxiety and skin conditions.

They conclude that *Acne vulgaris* is a symptom of GI disorders [13]. They hypothesized that emotional states might alter the normal intestinal microflora, increase intestinal permeability and contribute to systemic inflammation fallowed by GI disorder and acne symptoms. In a same result, this study presented a relationship between GI disorder and acne symptoms too. Gut- Brain- Skin provide a mechanism that makes gastrointestinal system and skin health together through probiotics [16]. gastrointestinal tract that has the largest number of bacteria, is the largest barrier for body immune defense; Probiotics with creating immunomodulatory and anti-inflammatory conditions are the strengthening of the defense [17, 18]. This ability of probiotics is effective to improve chronic inflammatory diseases such as inflammatory bowel diseases, Reactant air ways diseases, acne, rosacea and atopic dermatitis [19]. In addition, factors such as follicular hyperkeratinization , increased production of sebum and propionibacterium acnes colonization are effective in the pathogenesis of acne; probiotics improves acne by producing proteins against propionibacterium acnes, reducing systemic inflammation and influence on skin permeability [17, 20]. Also consumption of Some foods such as low fiber carbohydrates and dairy increases IGF-1 and improve acne; While probiotics by adjusting the concentration of IGF-1 stop the process [21, 22, 23]. affection of certain foods on the health of skin is another conjunctive factor between gastrointestinal system and skin. Several studies show that improving insulin sensitivity and acne after receiving a low glycemic diet indicates the role of nutrition in the pathogenesis of acne [24]. Researchers have shown that interactions between insulin sensitivity, hormonal mediators and acne represents effective role of low-glycemic foods to improve acne lesions. milk consumption because of its hormones is associated with an increased risk of acne and its severity. High- glycemic foods are associated with elevated levels of serum insulin, which causes sebaceous cell proliferation and increased production of sebum and decrease concentration of androgens and sex hormone binding globulin; all the factors involved in the pathogenesis of acne [25]. Obviously, the role of unhealthy nutrition including High- glycemic and low-fiber foods is also undeniable to creat variety of gastrointestinal disorders.

In another study A Szlachcic concluded that rosacea is a disorder with various gastrointestinal symptoms closely related to gastritis, especially involving the antrum mucosa; and the eradication of Hp leads to improvement of symptoms of rosacea and reduction in related gastrointestinal symptoms and also rosacea could be considered as one of the extragastric symptoms of Hp infection probably mediated by Hp-related cytotoxins and cytokines [15]. Consequences of this event are alterations in gastric secretion [15] and therefore less than adequate stomach acid would set the stage for migration of bacteria from the colon towards the distal portions of the small intestine, as well as an alteration of normal intestinal microflora, as a basic cause of acne symptoms [13]. we also concluded that there could be a connection between Hp-related gastritis and acne vulgaris as a sebaceous gland diseases such as rosacea.

Hong Zhang and colleagues in another study considered, the prevalence and risk factors for certain sebaceous gland diseases and their relationship to gastrointestinal dysfunction in adolescents. They also found a statistically significant difference in the prevalence of gastrointestinal symptoms (halitosis; gastric reflux; abdominal bloating; constipation) between patients with and without sebaceous gland diseases [10]. In this study we proposed a significant correlation between GI disorders symptoms and acne disease as a sebaceous gland diseases. They found that factors such as halitosis; gastric reflux; abdominal bloating; constipation are the risk factors for sebaceous gland diseases [10]. according to this result, existing of more than one of these symptoms can increase acne severity, like what we acquired as a significant correlation between GI disorders severity and acne disease severity.

In a study by Daniel D Bike entitled "Vitamin D deficiency in digestive disorders" in 2007 in United States of America, it is mentioned to a lack of vitamin D in many gastrointestinal diseases. Liver, small intestine and pancreas Diseases lead to a deficiency in vitamin D and its absorption in the body. Also discontinuity of entrohepatic cycle cause excessive excretion of vitamin D metabolites in the urine and feces [26]. Increased fatty acids reduce vitamin D [27].

In another study Wedad Z.Mostafa and Rehab A.Hegazy as "complex relationship between vitamin D and skin" in 2014, in Egypt, vitamin D deficiency is referred as the cause of many skin diseases including acne vulgaris. Propionibacterium acnes causes inflammatory response of the skin immune system that causes acne. Propionibacterium acnes is the stimulating factor for Th17 cells and 1,25 (OH) D inhibits Th17 cells change in response to Propionibacterium acnes and inhibits inflammation. As a result vitamin D deficiency exacerbates acne symptoms [28]. Therefore, it is possible that gastrointestinal disorders through the impaired absorption of vitamin D may lead to a worsening of inflammation in acne lesions and exacerbation of acne severity.

Clement A Adebamowo and colleagues in a study called "milk consumption and acne in young girls" in 2015 in California, the role of vitamin D in preventing keratinocytes proliferation and its impact on acne is mentioned [29]. Gastrointestinal symptoms association with acne disease can be concluded from the above studies. In fact, vitamin D deficiency causes gastrointestinal disorders associated with acne and aggravate it. This is in line with the findings of this study.

In a study Alan C.Logan, Martin kdtzman found that certain nutrients and a weakened antioxidant defense system and altered intestinal microflora may interplay to increase the risk of psychological sequelae in *Acne vulgaris*. They also presented that people with *Acne vulgaris* disease use more carbohydrate, fast food and sweets [14]. Absolutely this regimen leads to GI disorders symptoms and could be followed by acne disease, as we concluded in this study. Certain psychological conditions such as anxiety and depression in some studies been introduced as a factor in the pathogenesis of acne and also in theory Gut- Brian- Skin.

Stress induces changes in the normal microbial flora and thus change the permeability of the small intestine lining and form systemic inflammation, which is one of the causes of acne [30].In another study it was shown that acne patients compared with healthy people react strongly to the lipopolysaccharide of intestinal Escherichia coli; The situation occurs in many acne patients affected by changes in intestinal permeability and it is similarly seen in patients with irritable bowel syndrome with stress [31, 32]. Empirical studies show that stress by reduction draining bowel movements causes excessive growth of bacteria in the gut and impairs the permeability of the small intestine. These conditions are more associated with anxiety and depressive disorders and bacterial overgrowth treatment will also improve these diseases [33, 34, 35].The role of anxiety has been found in a variety of gastrointestinal diseases, including gastrointestinal dysfunction, inflammatory bowel disease, irritable bowel syndrome, gastroesophageal reflux and peptic ulcer disease [36]. Given the above, it seems obvious that anxiety and stress are another common factor in association between acne diseases and gastrointestinal disorders.

H. Ismaili and his colleagues proposed a strong correlation between GI symptoms frequency and *Acne vulgaris* severity as "Gastrointestinal dysfunction symptoms and lipid profile in patients with various severities of *Acne vulgaris*" in 2014 in Tabriz. They found that the prevalence of gastrointestinal dysfunction symptoms includes bloating and constipation in patients with medium and high severity acne is significantly higher than in healthy individuals [37].

The study also investigated the relationship between the acne severity and the severity of gastrointestinal disorders in patients with acne, and concluded that the severity of acne significantly related to frequency and severity of gastrointestinal disorders including gastric dysfunction, GI inflammation and colon dysfunction in them. In fact, the severity of these disorders except "small intestine and pancreas disorder" is directly related to acne severity; These findings are in line with H.Ismaili's study.

Among the studies on the subject of our study, Hong Zhang's study and H.Ismaili's study have more similarity with ours, but in both study only a few specific gastrointestinal symptoms such as constipation, bloating, gastric reflux and halitosis are investigated; While in this study we have inquired all four of gastrointestinal disorders, including gastric dysfunction, GI inflammation, small intestine and pancreas disorder and colon dysfunction.

Also unlike other studies we have discussed the severity of these disorders and the role of factors such as gender, age, education and marital status on the severity of acne and GI symptoms in patients with acne.

In this study, unlike Hong Zhang study the severity of acne was evaluated and it is concluded that acne severity has a significant coherence with "gender" (p = 0.03). Moderate and severe acne, was more frequent in females than in males, but acne severity was not significantly correlated with age, education and marital status (p = 0.30, 0.31 and 1.00 respectively).

As a result the "age" was not known as an effective factor in the severity of acne disease versus it has been introduced as a risk factor for acne by Hong Zhang [10].

Acne is a common disease that is more common in women than men [38].In Asian race Acne affects women 1.1 to 1.25 times more than men [39, 40]. This indicate the accuracy of the findings of this study. In general, compared to men, women are more at risk for depression, anxiety and neurological disorders that reduce the overall quality of their lives [41]. In adults with acne increased risk of depressive symptoms is seen [42, 43, 44].Acne is associated with the development of major depression and suicide. Given that depression and suicide involve women and people with acne more than other and acne is more common in women than men, so acne affect mental health of life , especially in women. Female and Acne desease independently associated with increased risk of major depression and suicide [38].Given the role of anxiety and stress in the pathogenesis of acne, acne can be more severe in women than in men because of higher prevalence of depression and anxiety disorders in women. The more severity of gastrointestinal disorders in women can be justified from relationship between anxiety and this disorders. The study showed that the prevalence of "GI inflammation" and "colon dysfunction" among gastrointestinal symptoms, has a significant relation with "gender" (p = 0.007 and 0.001 respectively). Whereas there is no significant relationship between "GI inflammation" or "colon dysfunction" and "gender" in healthy individuals (p = 0.27 and 0.90 respectively).

In patients with acne, "GI inflammation" with high severity is almost 4 times more in women than men (40.2 vs. 10) and moderate and severe "colon dysfunction" in women is significantly more than men (percentage of relative frequency 29.3 to 16.7 and 22 to 0 respectively); so it can be said "GI inflammation" and "colon dysfunction" is more sever in women with acne than men.

From all mentioned above it is concluded that gender plays an important role in acne severity and the severity of GI symptoms including "GI inflammation" and "colon dysfunction".

Among GI symptoms, "small intestine and pancreas disorders" is associated with age in patients with acne. In other words, "small intestine and pancreas disorders" is more sever in 25 years or older patients than less than 25 years patients (p = 0.009). However, in healthy subjects we didn't find a significant association between severity of "small intestine and pancreas disorders" and age (p = 0.38).

Conclusion

In this study we have concluded that the severity of gastrointestinal disorders is more in patients with acne compared to healthy individuals. Also there is a direct relationship between acne severity with severity of gastrointestinal disorders including "gastric dysfunction", "GI inflammation", "Small intestine and pancreas disorders " and "colon disorder". However, acne disease is more severe in women than men, and in women with acne "GI inflammation" and "colon disorder" is more severe than men. Also severity of "Small intestine and pancreas disorders" increases with age.

References

1. Habif TP (2011) Skin Disease Diagnosis and treatment. Third Edition, Edinburgh: ELSEVIER, 108-109.

2. Yeung CK, Teo LH, Xiang LH, Chan HH (2002) A communitybased epidemiological study of Acne vulgaris in Hong Kong adolescents. Acta Derm Venereol 82: 104-107.

3. Pearl A, Arroll B, Lello J, Birchall NM (1998) The impact of acne: A study of adolescents' attitudes, perception and knowledge. N Z Med J 111: 269-271.

4. Mascaro JM (2000) Pathogenesis of acne. J Dermatol Treat 11: 1-4.

5. Zhang H, Yu L, Yi M, Li K (1999) Quantitative studies on normal flora of seborrhoeic dermatitis. Chin J Dermatol 32: 299-340.

6. Zhang H, Chao H, Wu C, Zeng H (2006) Risk factors of some sebaceous gland diseases and their relation to gastrointestinal dysfunction in adolescents: an epidemiological study. Chin J Dermatol 39: 102-104.

7. Sandström Falk MH, Tengvall Linder M, Johansson C, Bartosik J, Bäck O, et al. (2005) The prevalence of Malassezia yeasts in patients with atopic dermatitis, seborrhoeic and healthy controls. Acta Derm Venereol 85: 17-23.

8. Freyre EA, Rebaza RM, Sami DA, Lozada CP (1998) The prevalence of facial acne in Peruvian adolescents and its relation to their ethnicity. J Adolesc Health 22: 480-484.

9. Rebora AE (2000) Helicobacter pylori and rosacae. J Eur Acad Dermatol Venereol 14: 344-348.

10. Zhang H, Liao W, Chao W, Chen Q, Zeng H, et al. (2006) Risk factors of some sebaceous gland diseases and their relation to gastrointestinal dysfunction in adolescents: an epidemiological study. Chin J Dermatol 39: 102-104.

11. White GM (1998) Recent findings in the epidemiologic evidence, classification, and subtypes of *Acne vulgaris*. J AM Acad Dermatol 39: s34-s37.

12. Wikins JW, Voorhees JJ (1970) Prevalence of nodulocystic acne in white and Negro male. Arch Dermatol 102: 631-634.

13. Bowe WP, Logan AC (2011) Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future? Gut Pathog 3: 1.

14. Katzman M, Logan AC (2007) *Acne vulgaris*: Nutritional factors may be influencing psychological sequelae. Med Hypotheses 69: 1080-1084.

15. Szlachcic A (2002) The link between Helicobacter Pylori infection and rosacea. J Eur Acad Dermatol Venereol 16: 328-333.

16. Benyacoub J, Bosco N, Blanchard C, Demont A, Phillippe D, et al. (2014) Immune modulation property of Lactobacillus paracasei NCC2461 (ST11) strain and im-pact on skin defenses. Benef Microbes 5: 129-136.

17. Savage DC (1977) Microbial ecology of the gastrointestinal tract. Ann Rev Microbiol 31: 107-133.

18. Bowe WP (2013) Probiotics in acne and rosacea. Cutis 92: 6-7.

19. Bowe WP, Filip JC, DiRienzo JM, Volgina A, Margolis DJ (2006) Inhibition of Propionibacterium acnes by bacteriocin-like inhibitory substances (BLIS) produced by Streptococcus salivarius. J Drugs Dermatol 9: 868-870.

20. Adebamowo CA, Spiegelman D, Berkey CS, Bandy FW, Rockett HH, et al. (2006) Milk consumption and acne in adolescent girls. Dermatol Online J 12: 1.

21. Adebamowo CA, Speigelman D, Berkey CS, Bandy FW, Rockett HH, et al. (2008) Milk consumption and acne in teenage boys. J Am Acad Dermatol 58: 787-793.

22. Bowe WP, Joshi S, Shalita AR (2010) Diet and acne. J Am Acad Dermatol 63: 124-141.

23. Smith RN, Mann NJ, Braue A, Makelainen H, Varigos GA (2007) A low-glycemic-load diet improves symptoms in Acne vulgaris patients: a randomized controlled trial. Am J Clin Nutr 86: 107-115.

24. Cunningham BB (2010) Acne Controversies: An update based on recent findings. Pract Dermatol Pediat.

25. Bikle DD (2007) Vitamin D insufficiency/deficiency in gastrointestinal disorders. J Bone Miner Res 22: Suppl 2:V50-54.

26. Hollander D, Muralidhara KS, Zimmerman A (1978) Vitamin D3 intestinal absorption in vivo: Influence of fatty acids, bile salts, and perfusate pH on absorption. Gut 19: 267-272.

27. Mostafa WZ, Hegazy RA (2014) Vitamin D and the skin: Focus on a complex relationship: A review. J Adv Res 6: 793-804.

28. Adebamowo CA, Spiegelman D, Berkey CS, Danby FW, Rockett HH, et al. (2006) Milk consumption and acne in adolescent girls. Dermatol Online J 12: 1.

29. Stokes JH, Pillsbury DH (1930) The effect on the skin of emotional and nervous states: theoretical and practical consideration of a gastrointestinal mechanism. Arch Dermatol Syphilol 22: 962-993.

30. Viana AF, Maciel IS, Dornelles FN, Figueiredo CP, Siqueira JM, et al. (2010) KininB1 receptors mediate depression-like behavior response in stressed mice treated with systemic E. coli lipopolysaccharide. J Neuroinflammation 7: 98.

31. Liebregts T, Adam B, Bredack C, Röth A, Heinzel S, et al (2007) Immune activation in patients with irritable bowel syndrome. Gastroenterology 132: 913-920.

32. Wang SX, Wu WC (2005) Effects of psychological stress on small intestinal motility and bacteria and mucosa in mice. World J Gastroenerol 11: 2016-2021.

33. Addolorato G, Mirijello A, D'Angelo C, Leggio L, Ferrulli A, et al. (2008) State and trait anxiety and depression in patients affected by gastrointestinal diseases: psychometric evaluation of 1641 patients referred to an internal medicine outpatient setting. Int J Clin Pract 62: 1063-1069.

34. Pimentel M, Hallegua D, Chow EJ, Wallace D, Bonorris G, et al. (2000) Eradication of small intestinal bacterial overgrowth decreases symptoms in chronic fatigue syndrome: a double blind, randomized study. Gastroenterol 118: A414.

35. Mayer EA (2000) The neurobiology of stress and gastrointestinal disease. Gut 47: 861-869.

36. Esmaeili H, Halimi M, Hagigi A (2014) Gastrointestinal dysfunction symptoms and lipid profile in patients with various severities of *Acne vulgaris*. J Med Sci 14: 130-136.

37. Yang YC, Tu HP, Hong CH, Chang WC, Fu HC,et al. (2014) Female Gender and acne disease are jointly and independently associated with the risk of major depression and suicide: a national population-based study. Biomed Res Int 2014: 504279.

38. Fung WK, Lo KK (2000) Prevalence of skin disease among school children and adolescents in a student health service center in Hong Kong. Pediatric Dermatol 17: 440-446.

39. Kubota Y, Shirahige Y, Nakai K, Katsuura J, Moriue T, et al. (2010) Community-based epidemiological study of psychosocial efects of acne in Japanese adolescents. J Dermatol 37: 617-622.

40. Chien IC, Chou YJ, Lin CH, Bih SH, Chou P (2004) Prevalence of psychiatric disorders among National Health Insurance enrollees in Taiwan. Psychiatr Serv 55: 691-697.

41. Uhlenhake E, Yentzer BA, Feldman SR (2010) Acne vulgaris and depression: a retrospective examination. J Cosmet Dermatol 9: 59-63.

42. Kilkenny M, Stathakis V, Hibbert ME, Patton G, Caust J, et al. (1997) Acne in Victorian adolescents: associations with age, gender, puberty and psychiatric symptoms. J Paediatr Child Health 33: 430-433.

43. Purvis D, Robinson E, Merry S, Watson P (2006) Acne, anxiety, depression and suicide in teenagers: a cross-sectional survey of New Zealand secondary school students. J Paediatr Child Health 42: 793-796.