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Correlation of Hyperglycemia with Rosacea

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Original Article

ABSTRACT

***Background**: The roscaea is a common chronic facial skin disease that affects predominantly Iraqi women. Although the pathogenesis of roscaea is unclear, many systemic co-morbidities are thought to play a major role in development of rosacea. **Objective**: To assess the correlation between hyperglycemia and rosacea. **Patients & Methods**: A cross sectional study carried out in Sulaimani Teaching center for Dermatological diseases in Sulaimani city-Kurdistan region/Iraq during the period, August 2019 to February, 2020 included 40 patients with proved diagnosed roscaea and 40 healthy controls. Diagnosis of roscaea was according to the National Roscaea Society Expert Committee. Laboratory parameters , fasting blood glucose, HbA1c and glucose intolerance test performed at private laboratory center. **Results**: The mean age of roscaea patients was (50.2 years) and female to male ratio was 2.3:1. Common type of roscaea observed was Erythemotelengectatic type (52.2%). A highly significant association between positive history of diabetes mellitus and roscaea ($p<0.001$). Mean fasting blood sugar of roscaea patients was significantly higher than that in controls ($p=0.001$).**Conclusions**: High fasting blood sugar level increases susceptibility to roscaea development that may suggests the link between roscaea and diabetes mellitus in addition to an obvious relationship between positive family history of diabetes mellitus and roscaea incidence..*

Keywords: *Rosacea, Blood sugar, Diabetes mellitus*

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1. INTRODUCTION

The rosacea is a common chronic inflammatory skin disorder that affecting predominantly the skin of central face and its pathogenesis is fully understood [1, 2]. The rosacea is mainly an adulthood skin disease with prevalent female gender [3]. Prevalence of rosacea is reaching to 10% among population with fair skin. However, the rosacea could be seen in any population regardless of skin colour [4]. Disease course of rosacea is variable which remitting or exacerbating according to different factors [5]. Patients with rosacea is clinically presented with transient or persistent facial erythema, oedema, telangectasia, papule and pustule. Sometimes, the patients could be asymptomatic or presented by pain, burning sensation, or pruritus [2]. Rosacea is classified into four major groups; subtype one (Erythematotelengiectasia), subtype two (Papulopustular), subtype three (phymatous) and subtype four (ocular). The granulomatous rosacea is regarded as a variant of rosacea [3]. These subtypes may be presented separately. In Iraq, the major clinical variant of rosacea recorded among patients was Erythematotelengectetic (subtype 1) [6]. In recent classification, the phenotypes are implemented for diagnosis of rosacea (one diagnostic phenotype or two major phenotypes for confirming diagnosis) [4]. These phenotypes are classified into diagnostic (central face persistent erythema affected by risk factors and rhynophyma), major phenotypes (transient erythema, flushing, telangectasia, papules or pustules and ocular changes) and minor phenotypes (burning sensation, stinging, oedema and dryness) [4, 5].

Exact pathogenesis of rosacea is completely explored. However, it was shown that genetic, immune, infective, environmental and neurovascular factors play a major role in pathogenesis of rosacea. Additionally, the exposure to ultraviolet light is considered as etiological and triggering factor for rosacea [7]. Genetic role was detected through strong relation of disease incidence with positive family history with discovered effect of specific human leucocyte antigen loci in development of rosacea [8]. Regarding infective factors, some microorganisms like demodex mites may have an essential role in etiology of rosacea [9]. Also, the helicobacter pylori are highly associated with higher incidence of rosacea [10]. The pathophysiological abnormalities reported for patients with rosacea included neurovascular dysregulation, immune system activations and detection of microorganisms. The blood and lymph vessels are dilated as a result to triggering factors such as temperature changes, alcohols and spicy food. The mechanism of erythema or flushing in rosacea is thought to be

related to effect of higher levels of non-specific cation channels on sensory neurons and keratinocytes that lead to production of vasoactive peptides [11].

Insulin resistance in diabetes mellitus lead to pathophysiologic abnormalitiesn like elevated levels of proinfammatory cytokines, prothrombotic factors, homocysteine, leptin and resistin, in addition to increase in serum viscousity and lower levels of adiponectin, which all play role in development of skin diseases [12-14]. Insulin resistance in metabolic syndrome is considered as risk factor for abnormal skin physiology which also predispose to etiology of metabolic syndrome [15]. The hyperglycemi specifically in type2 diabetes mellitus is accompanied with abnormal metabolic control, abnormal lipid profile and cardiovascular changes which causing many hormonal and inflammatory changes that play significant role in developing and triggering many dermatological diseases [16, 17]. The diabetes mellitus is characterized by impairment of vasodilation accompanying diabetic endothelial dysfunction. Physiologically, the insulin is regulating the vascular function and in diabetes mellitus, the insulin resistance lead to vasoconstriction in addition to nervous system abnormalities which may work as precursors for developing rosacea in diabetic patients [18-20].

The management of patients with rosacea is dependable on subtype or phenotype of rosacea in addition to presenting symptoms [21]. The management includes skin care, avoidance of triggers and specific treatment. The specific treatment is also indicated according to dominant features [22]. Topical therapy must be used in duration of six months and the topical steroids should be avoided [21, 23]. The common topical treatments for subtype 1 are metronidazole, azelaic acid and brimonidine; for subtype 2 are metronidazole, azelaic acid, ivermectin and dapsone; for subtype 3 is mainly oral isotretinoin and lid care and artificial tears for subtype 3 rosacea [24]. The oral zinc sulfate is found to play a significant role in management of rosacea among Iraqi patients [25]. Literatures discussing relationship between hyperglycemia and rosacra among Iraqi population is scarce. For that, this study aimed to investigate whether the hyperglycemia is correlated with rosacea.

2. PATIENTS and METHODS

The current study design was a cross sectional study that carried out in Sulaimani Teaching center for Dermatological diseases in Sulaimani city-Kurdistan region/Iraq through duration period of seven months from first of August, 2019 to 29th of February, 2020. The study population was all patients with a diagnosis of rosacea presented to center during study duration. Adult patients from both genders diagnosed with rosacea were the inclusion criteria. Exclusion criteria were age less than 18 years, steroids induced rosacea, other skin disorders the face (herpes infection, impetigo, perioral dermatitis, seborrhoeic dermatitis, lupus erythematous), pregnancy, lactation, cancer, chronic liver diseases, renal disease, radiotherapy, chemotherapy, topical acaricidal and use of recent oral or topical antibiotics. The ethical considerations were implemented according Helsinki Declaration regarding ethical approval of Health authorities; an ethical approval was taken from Kurdistan Board Ethical Committee, informed consent of patients, management of patients accordingly and confidentiality of data. Forty patients with rosacea were selected after eligibility to inclusion and exclusion criteria. A sample of healthy controls was selected from relatives of patients presented to Sulaimani Teaching center for Dermatological diseases. Data collected by the researchers from study participants directly and fulfilled in a prepared questionnaire. The questionnaire was designed by the researchers. The questionnaire included the following information: general characteristics of rosacea patients (age, gender, occupation, body mass index, smoking and alcohol consumption) clinical history of rosacea patients (history of hyperstension, diabetes mellitus and ischemic heart diseases and family history of diabetes mellitus), clinical types of rosacea and glycemic profile of rosacea patients (fasting blood glucose, HbA1c and glucose tolerance test). The diagnosis of rosacea was done by the Dermatologist in Sulaimani Teaching center for Dermatological diseases according to the National Rosacea Society Expert Committee 3. Also the rosacea was classified into four types (Erythemotelengectatic, inflammatory, Erythemotelengectatic and phymatous and Erythemotelengectatic and ocular type by Dermatologist according to National Rosacea Society Expert Committee classification[3]. Age of rosacea patients was categorized into four groups (<40 years, 40-49 years, 50-59 years and ≥60 years) and ranged from 33 years to 70 years. The gender of rosacea patients was distributed into male or female. Occupation of patients was classified into (housewife, public servant, self employed and retired). The BMI

was regarded normal (if BMI <25 Kg/m2), overweight (if BMI 25-29.9 Kg/m2) and obese (if BMI ≥30 Kg/m2). History of medical illness and family history of diabetes was assessed from patients. Laboratory parameters (fasting blood glucose, HbA1c and glucose intolerance test) were done at private laboratory center in Sulaimani. The data collected were analyzed statistically by Statistical Package of Social Sciences software version 22. Chi square test and Fishers exact test were applied accordingly for analyzing categorical variables. The independent sample t-test was applied for analyzing continuous variables. Level of significance (p value) was regarded statistically significant if it was 0.05 or less.

3. RESULTS

This study included 40 rosacea patients with mean age of (50.2 years); 15% of them were less than 40 years age. Female to male ratio was 2.3:1. Self employed occupation represented (37.5%) of patients, while housewife represented (35%) of them. Mean BMI of rosacea patients was (27.3Kg/m^2), 20% of patients were obese. The smoking and alcohol consumption were found in 40% and 20% of patients, respectively. The history of comorbidities (hypertension, diabetes mellitus and ischemic heart diseases) was observed among 22.5% of rosacea patients. The family history of diabetes mellitus was detected among half of studied rosacea patients. (**Table 1**). The common type of rosacea observed was Erythemotelengectatic type (52.2%), followed by inflammatory type (32.5%), Erythemotelengectatic and phymatous type (7.5%) and Erythemotelengectatic and ocular type (7.5%), (**Figure1**). Mean fasting blood sugar of rosacea patients was (105.7 mg/dl), 25% of patients had high fasting blood sugar. Mean HbA1c of rosacea patients was (5.5%), 22.5% of patients had HbA1c of 6.5% and more. Mean glucose tolerance test of rosacea patients was (152.5 mg/dl), 5% of patients were pre-diabetics and 30% of them were diabetics (**Table 2**). No significant differences were observed between rosacea patients and healthy controls regarding age (p=0.10) and gender (p=0.16). There was a highly significant association between positive family history of diabetes mellitus and rosacea (p<0.001), (**Table 3**). Mean fasting blood sugar of rosacea patients was significantly higher than that of controls (p=0.001). No significant differences were observed between rosacea patients and healthy controls regarding HbA1c (p=0.31) and glucose tolerance test (P=0.44), (**Table 4**).

Table 1: Demographic characteristics of rosacea patients.

Variable		**No.**	**%**
Age (year)	<40 years	6	15.0
	40-49 years	14	35.0.
	50-59 years	12	30.0
	≥60 years	8	20.0
mean Age (SD) : 50.2 (9.6) year		-	-
Gender	Male	12	30.0
	Female	28	70.0
Occupation	Housewife	14	35.0
	Public servant	9	22.5
	Self employed	15	37.5
	Retired	2	5.0
BMI	Normal	10	25.0
	Overweight	22	55.0
	Obese	8	20.0
mean BMI (SD) : 27.3 (3.2 kg/m^2)			
Smoker		16	40.0
Alcohol consumption		6	15.0
Comorbidities*		9	22.5
Family history of DM		20	50.0
* Hypertension, diabetes mellitus and ischemic heart diseases			

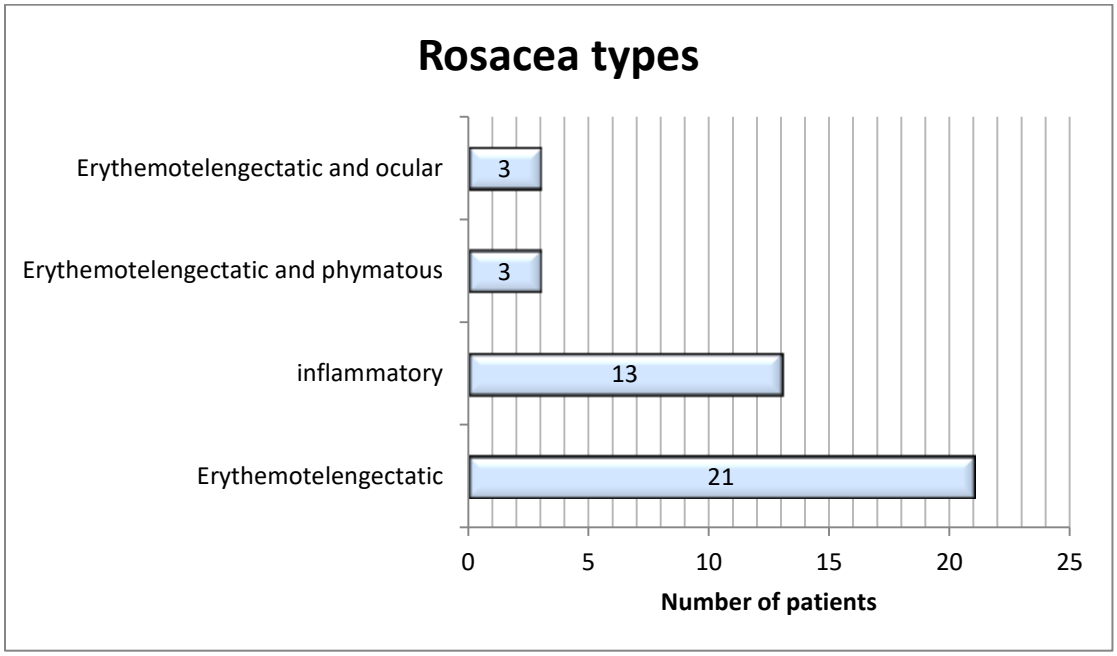

Figure 1: Types of Rosacea.

Table 2. Glycemic profile of rosacea patients.

Variable		**No.**	**%**
Fasting blood glucose (FBG)	Normal	30	75.0
	High	10	25.0
mean FBG (SD) : 105.7 (17.6) mg/dl		-	-
HbA1c	<6.5%	31	77.5
	≥6.5%	9	22.3
mean HbA1c (SD) : 5.5 (0.9)%		-	-
Glucose tolerance test (GTT)	Normal	26	65.0
	Pre-diabetes	2	5.0
	Diabetes	12	30.0
mean GTT(SD) : 152.5 (47.4) mg/dl		-	-

Table 3. Comparison of general characteristics of the studied groups

Variable	Rosacea cases		Controls		P. value
	No.	%	No.	%	
Age					0.100 NS
<40 years	6	15	4	10	
40-49 years	14	35	12	30	
50-59 years	12	30	13	32.5	
≥60 years	8	20	11	27.5	
Gender					0.160 NS
Male	12	30	18	45	
Female	28	70	22	55	
Family history of diabetes mellitus					**<0.001**^{S}
Yes	20	50	0	-	
No	20	50	40	100	

NS: not significant, S: significant

Table 4. Comparison of glycemic profile of the studied groups

Variable	Rosacea	Controls	P. value
	Mean ±SD	Mean ±SD	
Fasting blood sugar (mg/dl)	105.7±17.6	93.2±13.6	**0.001**^{S}
HbA1c (%)	5.5±0.9	5.2±0.8	0.31^{NS}
Glucose tolerance test (mg/dl)	152.5±47.4	144.1±48.8	0.44^{NS}

SD: standard deviation

4. DISCUSSION

The rosacea is the most common clinically facial skin disorder presented to dermatology outpatient clinics affecting all races [26]. The rosacea is regarded as a disease confined to the skin; however, many authors found many evidences linked the rosacea to many systemic abnormalities such as hypelipidemia, hypertension, metabolic abnormalities and diabetes mellitus [27-29]. The present study showed that mean age of patients with rosacea was (50.2 years) with predominance of female gender. These findings are close to results of recent Iraqi study conducted in Basrah city (Southern Iraq) which revealed that mean age of rosacea patients as (46.7 years) and 96.3% of them were females [30]. Our study findings are similar to results of Tan et al [31] population based study which revealed that rosacea is prevalent among Germany and Russian population with predominance of female gender (75% females vs. 25% males). The employed rosacea patients (public servant and self employed) were prevalent in current study. The occupation and environmental exposure are considered as common factors responsible for development and triggering rosacea [4]. Our study found that more than two thirds of studied rosacea patients were overweight and obese. This finding is consistent with results of Li et al [32] study in USA which reported that all measures of obesity were significantly related to higher incidence of rosacea among American women. In present study, 40% of rosacea patients were smokers. In Turkey, a prospective cross sectional study was carried out by Kucukunal et al [33] on sample of 200 rosacea patients found an increase in risk of rosacea among smokers. Our study also found that 15% of rosacea patients were alcohol drinkers. It was found that heavy alcohol intake leads to small intestinal bacterial overgrowth and intestinal dysbiosis which in turn considered as risk factor for rosacea development [34]. Current study revealed that history of medial illness (HT, DM and IHDs) was observed among 22.5% of rosacea patients. Chen et al [35] meta-analysis study which included previous 13 studies found that hypertension and dyslipidemia are correlated with rosacea, but the rosacea was not related to cardiovascular diseases and diabetes mellitus. However, another Chinese case control study conducted by Hua et al [36] reported that coronary artery disease, dyslipidemia and diabetes mellitus were significantly associated with rosacea development after adjusting the hypertension. Our study found that 50% of rosacea patients had positive family history of diabetes mellitus. Also, our study showed a highly significant association between positive history of diabetes mellitus and rosacea

patients (p<0.001). This finding coincides with results of Chang et al [37] study in USA which found a shared genetic locus between patients with rosacea and type1 diabetes mellitus.

In current study, the types of rosacea were Erythemotelengectatic type (52.2%), inflammatory type (32.5%), Erythemotelengectatic and phymatous type (7.5%) and Erythemotelengectatic and ocular type (7.5%). These findings are close to results of Kawen and Al-Sultany study in Iraq [6] which reported that more than half of rosacea cases were Erythemotelengectatic type. Alexis et al study [38] documented that erythemotelengectatic type of is highly predominant clinical presentation of rosacea.

The present study found that mean fasting blood sugar of rosacea patients was significantly higher than mean fasting blood sugar of controls (p=0.001). This finding is similar to results of Akin Belli et al [39] case control study in Turkey on 47 rosacea patients and 50 healthy controls which found a significantly higher level of fasting blood glucose mean among rosacea patients as compared to controls. This association between high blood sugar and rosacea is confirmed by Egeberg et al [40] population based case control study in Denmark which found a significant association between rosacea and autoimmune diseases specifically typ1 diabetes mellitus. In Turkey, a study carried out by Gökçe et al [41] on 69 type2 diabetic patients, revealed poor blood glucose control increase risk of Demodex folliculorum infestation. Elevated intolerance to glucose with hypertension and dyslipedemia which represented main clinical characteristics of metabolic syndrome is associated with rosacea and this relationship might be attributed to role of cathelicidin, oxidative stress and endoplasmic reticulum stress, that play role in etiology of both metabolic syndrome and rosacea [39]. Inconsistently, Spoendlin et al [42] study in Switzerland stated that longer duration of diabetes mellitus or higher HbA1c level of diabetic patients is associated with reduced risk of rosacea. For that, the relationship between rosacea and diabetes mellitus remain unclear precisely.

5. CONCLUSIONS

High blood sugar level increases susceptibility to roscaea development that suggests the link between roscaea and diabetes mellitus. Our study also concluded an obvious relationship between positive family history of diabetes mellitus and roscaea incidence. The current study recommended more awareness of physician toward the etiology and associated disorders of

rosacea. Further researches exploring the pathogenesis of rosacea must be supported.

Ethical Clearance

Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical issues of researches involving humans, informed consent obtained from all patients. Data and privacy of patients were kept confidentially. .

Conflict of interest: Authors declared none

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