Original article

Clinical evaluation of Libyan patients with rosacea and its correlation with seropositivity to *Helicobacter pylori*

Nadia Abdalhafid El-Sherif [a,*], Salwa Abdalsalam El-Dibany [b]

[a] *Dermatology Department, Faculty of Medicine, Benghazi University, Benghazi, Libya*
[b] *Dermatology Department, Faculty of Medicine, Omer El-muktar University, Elbida, Libya*

Abstract

Introduction: Rosacea is a chronic inflammatory cutaneous disorder. Its pathogenesis was unclear and controversial; *Helicobacter pylori* (*H. pylori*) infection, genetic predisposition and climatic factors are implicated as triggers of rosacea.

Aim of the study: To examine the epidemiological characteristics of rosacea patients, the triggered factors, and to assess the prevalence of *H. pylori* among the patients, and its relation to the subtypes and severity of rosacea.

Patients and methods: Thirty-six Libyan patients with rosacea were assessed with a complete history and subjected to clinical examinations. Blood samples for the detection of IgG antibodies against *H. pylori* were collected.

Results: Females were more frequently affected. The papulopustular subtype was seen in 61% of the patients. The precipitating factors were sun exposure seen in 63.9% and thermal stimuli in 41.7% of the patients. Serum IgG to *H. pylori* was positive in 58.3% of the patients, moreover, it was significantly higher in severe rosacea ($P < 0.05$) regardless of the type of the disease.

Conclusions: The papulopustular subtype of rosacea was the most common, moreover, many patients also had other subtypes of rosacea simultaneously. Sun exposure plays a critical role in its etiology. *H. pylori* represents a significant cofactor that may contribute to the severity of the disease.

1. Introduction

Rosacea is a chronically relapsing inflammatory skin disease that affects mostly middle aged adults. Females are affected more frequently than males (Lazaridou et al., 2010). According to the NRSEC standard classification rosacea is divided into four subtypes and one variant: 1/ erythematotelangiectatic rosacea (ET), 2/papulopustular rosacea (PPR), 3/phymatous rosacea (PR), 4/ocular rosacea, and a granulomatous variant (Wilkin et al., 2002, 2004).

Although the etiology of rosacea remains unknown, various factors that initiate flushing may contribute to this condition (Abram et al., 2010; Bae et al., 2009). It is well known that *Helicobacter pylori* (*H. pylori*) plays the key role in the development of gastritis, peptic ulcer, and even gastric cancer (Szlachcic, 2002). In recent years, a possible correlation was suggested between *H. pylori* infection and dermatological diseases such as rosacea, chronic urticaria and alopecia areata (Leontiadis et al., 1999).

* Corresponding author. Tel.: +218 913760697.
  E-mail address: elsherifnadia@yahoo.com (N.A. El-Sherif).
Peer review under responsibility of King Saud University.

1.1. Aim of the study

- To assess the clinical subtypes of rosacea among Libya patients and the associated risk factors.
- To evaluate the prevalence of *H. pylori* in subjects with rosacea and its correlation with rosacea subtypes and severity.

2. Patients and methods

Thirty-six Libyan patients with rosacea were included in the study. Each patient was assessed with a detailed medical history and subjected to clinical examinations. The staging and grading of rosacea were made according to the standard classification and grading systems of rosacea reported by the NRSEC (Wilkin et al., 2002, 2004). Blood samples for the detection of serum immunoglobulin G (IgG) antibodies against *H. pylori* were obtained from all the patients. Data were analyzed using a statistical package for social science (SPSS) version 10.0. A *p*-value of <0.05 was considered statistically significant.

3. Results

Thirty-six rosacea patients were included in the study, 77.8% were females and 22.2% were males, with female to male ratio of 3.5:1. Their mean age $\pm$ SD was 37.8 ± 6.6 years.

According to the NRSEC standard classification of rosacea, 61.1% of the patients presented with the PPR (Fig. 1), whereas 30.6% and 8.3% of the patients were classified into the ET and phymatous rosacea subtypes, respectively (Figs. 2 and 3). Phymatous changes seen in our patients were in the nose (rhinophyma), only one patient had nodularity in the forehead (metophyma) (Fig. 3). Ocular rosacea was noted in 44.4% of the patients (Fig. 4). All patients with ocular rosacea have overlapped with other rosacea subtypes, mostly with ET rosacea ($P < 0.05$). However, there was no statistically significant correlation
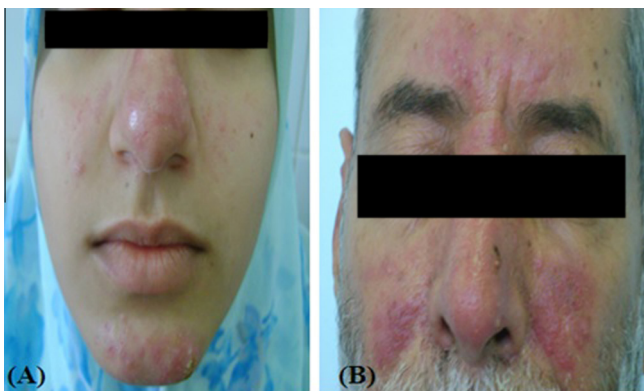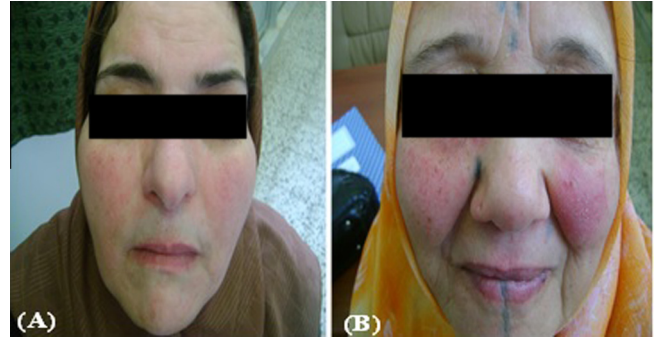

Fig. 2. ETR with mild (A) and (B) moderate presentation.

Fig. 3. Phymatous rosacea with rhinophyma and metophyma.

Fig. 4. Blepharitis in patient with ocular rosacea and ETR.

between the ocular presentations and the severity of the rosacea.

Moreover, ET rosacea presented mostly in the younger age group while phymatous rosacea has been seen only in patients aged >50 years ($P = 0.00$). There was a statistically significant difference in ET and phymatous rosacea subtypes between both genders (Fig. 5). Furthermore, about 50% of the female patients had mild disease presentation.

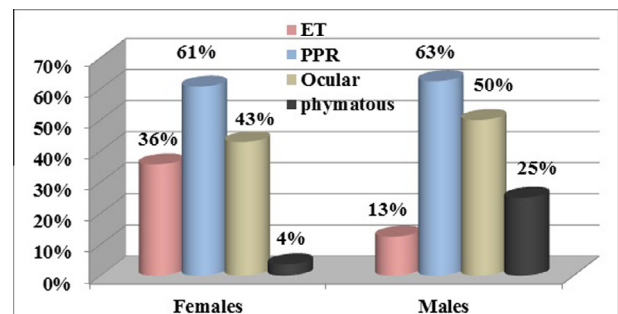Fig. 1. PPR with mild (A), and moderate (B) severity.

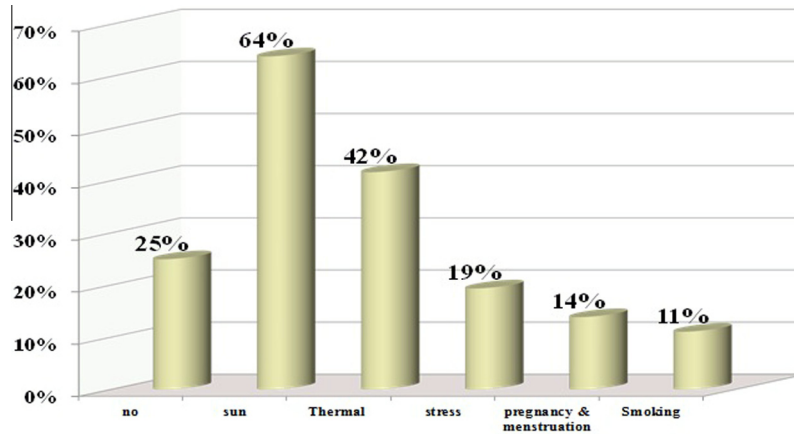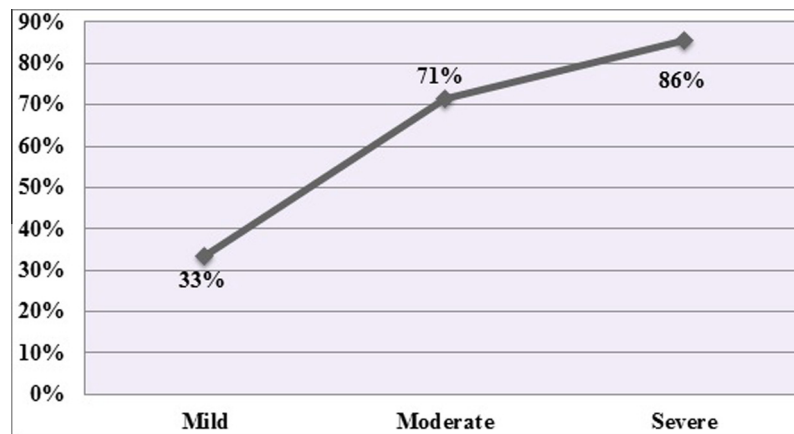Fig. 5. Distribution of rosacea patients according to gender.

Fig. 6. Exacerbating factors of rosacea.

Fig. 7. *H. pylori* IgG seropositivity and rosacea severity.

Sun exposure and thermal stimuli were the most common precipitating factors reported in 63.9% and 41.7% of the patients, respectively (Fig. 6). Photosensitivity has been seen in all ET rosacea patients ($P = 0.000$) and in 93.8% of patients with ocular rosacea ($P = 0.00$).

Serum IgG antibodies to *H. pylori* were found positive in 58.3% of patients under the study. No statistically significant difference was observed between the age or gender of the patients and the serum *H. pylori* antibodies' seropositivity. The prevalence of positive serological test for *H. pylori* was statistically significantly higher in severe rosacea ($P < 0.05$) (Fig. 7), regardless of the subtype of the disease ($P > 0.05$).

4. Discussion

In the present study, a female preponderance is noted, in agreement with previous reports (Lazaridou et al., 2010; Khaled et al., 2010). It is well known that rosacea is more common in women, which may be related to the greater medical request from women, furthermore, hormonal role

has been also suggested in its pathogenesis (Abram et al., 2010; Feldman et al., 2001). Most of our patients were classified in the PPR subtype which is in agreement with previous studies (Lazaridou et al., 2010; Khaled et al., 2010). Furthermore, males had shown to present with phymatous subtype and severe disease more than females who presented mostly with ET subtype and mild disease presentation as has been reported in other studies (Lazaridou et al., 2010; Khaled et al., 2010). It is well known that women seldom suffer the gross tissue and sebaceous gland hyperplasia of rhinophyma (Lazaridou et al., 2010).

Our patients showed a higher prevalence of ocular rosacea in agreement with a previous study (Lazaridou et al., 2011), although a lower prevalence has been reported (Bae et al., 2009; Khaled et al., 2010). This variability of the incidence of ocular rosacea may be due to the lack of definite diagnostic criteria (Lazaridou et al., 2011).

All patients with ocular rosacea have overlapped with other rosacea subtypes irrespective of its severity in agreement with the previous study (Bae et al., 2009). Ocular rosacea has been considered as an extension of ET rosacea,

moreover, the ophthalmic complications are independent of the severity of the facial rosacea (Keshtcar-Jafari et al., 2009).

The role of sun exposure in the pathogenesis of rosacea is controversial (Jaworek et al., 2008; Berg, 1989). Although, actinic elastosis seen in skin biopsy and the predominant facial distribution confirm its important role in rosacea (Bae et al., 2009). Moreover, sun exposure produces reactive oxygen species (ROS), which causes vascular and dermal matrix damage (Yamasaki and Gallo, 2009).

H. pylori is a Gram-negative bacterium that colonizes the gastric mucosa, moreover, *H. pylori* plays the key role in the development of gastritis, peptic ulcer, and even gastric cancer (Szlachcic, 2002).

The role of *H. pylori* as an eliciting factor for rosacea is still controversial (Lazaridou et al., 2010; Szlachcic, 2002; Yamasaki and Gallo, 2009; Jones et al., 1998). About 58% of our patients had positive anti *H. pylori* antibodies, a higher prevalence of *H. pylori* infection has been reported (Szlachcic, 2002; Yamasaki and Gallo, 2009). Furthermore, in infected patients there was improvement in rosacea when *H. pylori* eradication therapy was given (Utas et al., 1999).

Rosacea may be related to a deficient function of the antioxidant system, as *H. pylori* produces reactive oxygen species (ROS) (Yamasaki and Gallo, 2009), and those individuals showed higher ROS including nitric oxide in their plasma than controls (Szlachcic, 2002).

Furthermore, *H. pylori* induces cytokine release through a Toll like receptors TLR2 and TLR4 in gastric epithelial cells (Yamasaki and Gallo, 2009). Thus ROS and cytokines released by TLRs' stimuli in organs other than skin may be mediators that worsen rosacea by *H. pylori* infection (Yamasaki and Gallo, 2009). Moreover, during the immune response to *H. pylori* it is possible that other inflammatory mediators, such as IL-1, TNF-α, IFN-γ, leukotrienes and platelet-activating factors, could play a role in the pathogenesis of rosacea (Szlachcic, 2002).

5. Conclusions and recommendations

- Rosacea affected females more than males, moreover, females usually presented with mild disease.
- Rosacea has a multifactorial genesis, and sun exposure plays a critical role in its etiology.
- *H. pylori* may trigger the disease activity.

- Ophthalmological consultation is mandatory in all rosacea subtype patients.

References

Abram, K., Silm, H., Maaroos, H.I., Oona, M., 2010. Risk factors associated with rosacea. JEADV 24, 565–571.

Bae, Y.I., Yun, S.J., Lee, J.B., Kim, S.J., Won, Y.H., Lee, S.C., 2009. Clinical evaluation of 168 Korean patients with rosacea: the sun exposure correlates with the erythematotelangiectatic subtype. Ann. Dermatol. 21 (3), 243–249.

Berg, M., 1989. Epidemiological studies of the influence of sunlight on the skin. Photodermatol 6, 80–84.

Feldman, S.R., Hollar, C.B., Gupta, A.K., Fleischer Jr., A.B., 2001. Women commonly seek care for rosacea: dermatologists frequently provide the care. Cutis 68, 156–160.

Jaworek, A.K., Wojas-Pelc, A., Pastuszczak, M., 2008. Aggravating factors of rosacea. Przegl Lek 65, 180–183.

Jones, M.P., Knable Jr., A.L., White, M.J., Durning, S.J., 1998. *Helicobacter pylori* in rosacea: lack of an association. Arch. Dermatol. 134, 511.

Keshtcar-Jafari, A., Akhyani, M., Ehsani, A.H., Ghiasi, M., Lajevardi, V., Baradran, O., Toosi, S., 2009. Correlation of the severity of cutaneous rosacea with ocular rosacea. IJDVL 75, 405–406.

Khaled, A., Hammami, H., Zéglaoui, F., Tounsi, J., Zermani, R., Kamoun, M.R., Fazaa, B., 2010. Rosacea: 244 Tunisian cases. Tunis Med. 88 (8), 597–601.

Lazaridou, E., Apalla, Z., Sotiraki, S., Ziakas, N.G., Fotiadou, C., Ioannides, D., 2010. Clinical and laboratory study of rosacea in northern Greece. JEADV 24 (4), 410–414.

Lazaridou, E., Fotiadou, C., Ziakas, N.G., Giannopoulou, C., Apalla, Z., Ioannides, D., 2011. Clinical and laboratory study of ocular rosacea in northern Greece. JEADV 25, 1428–1431.

Leontiadis, G.I., Sharma, W.K., Howden, C.W., 1999. Non-gastrointestinal tract associations of *Helicobacter pylori* infection. Arch. Intern. Med. 159, 925–940.

Szlachcic, A., 2002. The link between *Helicobacter pylori* infection and rosacea. JEADV 16, 328–333.

Utas, S., Ozbakir, O., Turasan, A., Utas, C., 1999. *Helicobacter pylori* eradication treatment reduces the severity of rosacea. J. Am. Acad. Dermatol. 40, 433–435.

Wilkin, J., Dahl, M., Detmar, M., Drake, L., Feinstein, A., Odom, R., Powell, F., 2002. Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. J. Am. Acad. Dermatol. 46, 584–587.

Wilkin, J., Dahl, M., Detmar, M., Drake, L., Liang, M.H., Odom, R., Powell, F., 2004. Standard grading system for rosacea: report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. J. Am. Acad. Dermatol. 50, 907–912.

Yamasaki, K., Gallo, R.L., 2009. The molecular pathology of rosacea. J. Dermatol. Sci. 55 (2), 77–81.