The Study of Prevalence of Helicobacter Pylori in Patients with Acne Rosacea

Bhattarai S,[1] Agrawal S,[1] Rijal A,[1] Majhi S,[2] Pradhan B,[3] Dhakal SS [3]

[1]Department of Dermatology and Venereology

[2]Department of Biochemistry

[3]Department of Internal Medicine

B.P.Koirala Institute of Health Sciences

Dharan, Nepal

Corresponding Author

Sabina Bhattarai

Department of Dermatology and Venereology

B.P.Koirala Institute of Health Sciences.

Dharan, Nepal

E-mail: sabeenab@gmail.com

ABSTRACT

Background

Acne rosacea is an inflammatory disease affecting the central part of the face characterized by erythema, papules, papulo pustules and telangiectasias of unknown etiology. More recently numerous studies have described an association with Helicobacter pylori (Hp) and the extra gastric symptoms of cutaneous origin.

Objectives

To establish the prevalence of Helicobacter pylori (Hp) infection in the stomach in patients with rosacea based on standard Hp serological test.

Methods

All patients with the clinical staging of 2, 3 and 4 rosacea attending the Dermatology Out Patient Department from May 2009 – April 2010 were included in the study. Quantitative serological test using the SERION ELISA classic Helicobacter pylori IgG was done.

Result

A total of 26 patients were enrolled in the study with the age ranging from 26-82 years. There were 14 males and 12 females and the male: female ratio was 1.6:1. Three (11.53%) patients presented with Grade IV rosacea, a severe clinical presentation and symptoms suggestive of acid peptic diseases were found in 14/26 (53.8%) patients. A positive serology to H. pylori was found in 17/26 (65.4%) of patients. A statistically significant correlation was found when association of H.pylori positivity in patients of rosacea compared with the seropositivity in controls. However correlation in the seropositivity was not found amongst the patients having gastritis and rosacea.

Conclusion

There still proves to find a correlation of Hp infection with patients with rosacea but it can still be hypothesised as a cutaneous manifestation of an internal peptic ulcer disease .

KEY WORDS

H.pylori, rosacea

INTRODUCTION

Acne rosacea is an inflammatory disease affecting the central part of the face characterized by erythema, papules, papulo pustules and telangiectasias of unknown etiology.[1] Various reports have linked rosacea with different gastro intestinal disturbances including peptic ulcer disease. More recently numerous studies have described an association with Helicobacter pylori (Hp) and the extra gastric symptoms of cutaneous origin.[2-4] This study is undertaken to find out the association of the prevalence of Hp if any in patients with rosacea which is the first of its kind in Nepal.

METHODS

Twenty six patients attending the Dermatology Out Patient Department with a diagnosis of rosacea was based on the clinical criteria stated by the Expert National Rosacea Society Committee (presence of one or more of the following primary features concentrated on the convex areas of the face: flushing, permanent erythema, papules and pustules and telangiectasia) were included in the study.[5]

Patients with the clinical staging of 2-4 were included in the study. Patients were also diagnosed by histopathology as

and when needed.

All patients with the clinical and supportive diagnosis of rosacea underwent a serological examination using the Quantitative serological test using the SERION ELISA classic Helicobacter pylori IgG test kit. The kit had a sensitivity of 99.4% and specificity of 93.8%. Anti *H. pylori* IgG antibodies were estimated in sera. The results were read as

positive if it was more than 30 U/ml, borderline as 20-30 U/ml and negative if less than 20 U/ml. All ELISAs were read by the same operator who was blinded to patients enrolled.

Patients with history of any application of steroids and other topical medications prior to the study period, any intake of any systemic antibiotics prior to enrollment, history of any chronic gynaecological and other systemic diseases and pregnant and lactating patients were excluded from the study.

Twenty six patients with apparent no clinical findings of rosacea but with various subjective gastrointestinal symptoms suggestive of non ulcer dyspepsia were included in the control group.

A second control group of fifty two patients were also selected from healthy individuals with no cutaneous signs and symptoms of rosacea or history suggestive of any dyspeptic ulcer diseases. Serological test for H. pylori were performed on the two control groups as well.

Consent was taken from the institutional ethics committee and review board. Data were tabulated and interpreted in terms of percentage, mean and standard deviation. To test the significance of association between the variables, Chi square tests were applied using the SPSS software (Version 17). The linear trend of the mean values of anti H pylori IgG antibodies in the different grades of Rosacea was examined by using the ANOVA. The probability of significance was set at 5% level.

RESULTS

The baseline characteristics of patients enrolled in each group in shown in Table 1. The duation of rosacea in patients ranged from 1-240 months with the mean duration of 47.42 ± 12.19 months and symptoms suggestive of Acid
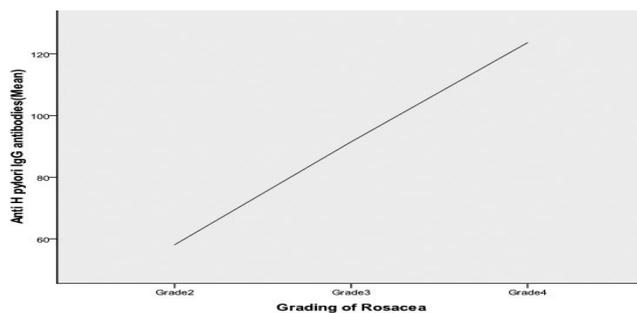

Figure 1. Association graph between anti H pylori antibodies and severity of Rosacea.

Table 1. Baseline characteristics of patients enrolled in each group.

Characteristics		Rosacea (n=26)	Gastritis (n=26)	Control(n=52)
Sex	Female	12	16	19
	Male	14	9	33
	F:M	1:6.1	1.7: 1	1:1.73
Median Age	Range (years)	26-82	21-64	19-65
	(Years± SD)	49.96±2.77	37.4±9.5	33.96±12.09

Table 2. Results of analysis of association between symptoms of APD positivity among Rosacea patients and H.pylori seropositivity.

H.pylori	APD symptoms Present	APD symptoms absent	Total	Pearson Chi- Square test	P Value
Present	11 (78.6%)	6(50.0%)	17	2.33	0.127
Absent	3(21.4%)	6(50.0%)	9		
	14	12	26		

Table 3: Results of analysis of association between Rosacea and H.pylori bioassay results.

H.pylori	Case	Control	Total	OR(CI)	X2 value	P value
Present	17(65.4%)	6(11.5%)	23	14.48 (3.94-56.75)	24.17	<0.0001
Absent	9 (34.6%)	46(88.5%)	55			
	26	52	88			

Table 4. Results of analysis of association between H.pylori bioassay results with rosacea and gastritis only patients.

	H.pylori (Present)	H.pylori(Absent)	Total	OR(CI)	X2 value	P value
Rosacea	17(65.4%)	9(34.6%)	26	2.2 (0.63-7.89)	1.95	0.163
Gastritis	12(46.1%)	14(53.9%)	26			
Total	29(55.8%)	23(44.2%)	52			

Peptic Diseases (APD) was observed in 14/26 (53.8%) patients. Rosacea Severity Grading of 2, 3 and 4 were seen in 15(57.69%), 8(30.76%) and 3(11.53%) patients respectively. The measures of association was estimated with multiple correlation (R=0.447) showing a positive linear trend. (Figure 1)

The association of positive serology of H.pylori among cases having history of APD was also sought however it was not found to be statistically significant. (Table 2)

When the association of seropositivity of H.pylori among cases and and controls were evaluated it was found to be statistically significant.(Table 3) while no association was seen when evaluated amongst rosacea patients and patients who presented with history of gastritis only (Table 4).

DISCUSSION

Acne rosacea is an inflammatory skin disease that commonly affects the central part of the face and usually appears at any time from the third or fourth decade onwards.1The classic type of rosacea is characterized by erythema, papules, papulo pustules and telangiectasias usually appearing symmetrically along with flushing episodes. The disease lasts for years with episodes of improvement or exacerbations.[2-4]

The aetiology of rosacea is still unknown and it is assumed that skin changes are caused by many unrelated factors. It is believed that the abnormal vascular response to heat, stress and other stimuli dependent on excessive vessel sensitivity to endogenous opiates or its excessive secretion may play a marked role.[6-7]

Rosacea has been linked with different gastro intestinal disturbances including peptic ulcer disease.[2-4] At present it is known that Helicobacter pylori (Hp) plays the key role in the development of gastritis, peptic ulcer, MALT lymphoma and even gastric cancer strongly suggesting involvement of the bacterium also in the mechanism of certain skin changes.[8-10] H.pylori increases the synthesis of oxygen metabolites such as superoxide and proinflammatory cytokines. These cytokines have been shown to stimulate the synthesis of the inflammatory species nitric oxide contributing to the inflammation of the gastric mucosa and the skin changes.[11-12]

The relationship between rosacea and Helicobacter pylori infection has previously been investigated by a number of researches. Our study found a seroprevalence of (65.4%) and the association was found to be statistically significant CI= 14.48(3.94-56.75), p value: <0.0001 which supported the authors who believe that H. pylori probably constitutes a risk factor and was found to be associated in 27-90% of patients or at least in certain groups of individuals.[13-20] Others comment on the beneficial effect of H. pylori eradication in rosacea.[15,17,21–24] Some other

investigators contradict any associations between rosacea and H. pylori infection.[25–28] Based on the different studies to date Lazaridou et al later concluded that due to the high prevalence of anti-Hp antibodies in humans in conjunction with the fact that the antibiotics are effective for both disease entities, it would be very difficult to stratify the population studied against all factors that influence both rosacea and H. pylori infection.[29]

Similarly the trend for an increasing prevalence of H. pylori with severity of rosacea is suggested by the study reported by Diaz et al.[30] Though the study did not achieve statistical significance a suggestion of a potential positive association between the severity of rosacea and both concurrent H. pylori infection and magnitude of anti-H. pylori CagA antigen humoral immune response was observed .Our study also shows that the mean values of anti H pylori IgG antibodies follow the linear trend. The measures of association was estimated with multiple correlation (R=0.447) showing a positive linear trend and the values increases with the clinical severity of rosacea has been supported statistically (F=5.74, df=1, P=0.025).

The concurrent symptoms of gastritis in patients with rosacea was found in 12/26 (46.1%) patients slightly lower than reported by Sclachic et al where he had found 65% of patients having a positive serology to H.pylori and a statistical significance was found.[18] However an association amongst the study group comprising of patients having symptoms of gastritis and H.pylori seropositivity with rosacea patients yielded no statistically significant findings. CI = 2.2 (0.63- 7.89) p value: 0.163 in our study.

CONCLUSION

We would thus conclude that there still proves to find a correlation of Hp infection with patients with rosacea and whether it can be hypothesised that rosacea could act as a cutaneous manifestation of an internal peptic ulcer disease need to be thought of and large scale study is needed to confirm the findings.

REFERENCES

1. Chu T. Treatment of Rosacea. *Practioneer Practitioner* 1993; 237 (1533):941-5.

2. Jabloska S, Chorzelski T. Choroby skory. PZWL. Warszawa, 1994; 386-87.

3. Gwiezdzinski Z. Rosacea- pathogenesis and treatment. *Medipress Dermatologica* 1998; 3:1-3

4. Braun-Falco O, Plewig G, Wolff HH, Winklemann RK. Dermatology. Springer Verlag, Berlin,Heidelberg,1991.

5. Wilkin J, Dahl M, Detmar M, Drake L, Liang M, Odom R et.al. Standard grading system for rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. *J Am Acad Dermatol* 2004; 50: 907–12.

6. Wilken JK. Rosacea. Pathophysiol treatment. *Arch Dermatol* 1994; 130:359-62.

7. Zegarska B. Pathological processes in the upper digestive tract in patients with rosacea and role of foods allergens in etiopathogenesis of this disease. Doctor's thesis, Medical academy, Bydgoszcz, 1993.

8. Danesh J. Helicobacter pylori imfection and gastric carcinoma, systemic review of the epidemiologic studies. *Aliment Pharmacol ther* 1999;13:851-56.

9. Issacson PG. Mucosa associated lymphoid tissue lymphoma. *Semin Haematol* 1999;36:139-47.

10. Nedrod JG,Czinn SJ. Helicobacter pylori. *Curr opin Gastroenterol* 1997;13:71-2

11. Franco L, Talamani G, Carra G, Doria D. Expression of COX-1 , COX -2 and nitric oxide synthetase protein in human gastric antrum with helicobacter pylori infection. *Prostraglandins Other Lipid Med* 1999;58:9-17

12. Tsuji S, Kawano SD, Tsujii M, Takei Y, Tanaka M, Sawaoka H et al. Helicobacter pylori extract stimulates inflammatory nitric acid production. *Cancer Lett* 1996;108:195-200.

13. Mini R, Figura N, D'Ambrosio C, Braconi D, Bernadini G, Di Simplicio F et al. Helicobacter pylori immunoproteomes in case reports of rosacea and chronic urticaria. *Proteomics* 2005; 5: 777–87.

14. Bonamigo RR, Leite CS, Wagner M ,Bakos L. Rosacea and Helicobacter pylori: interference of systemic antibiotic in the study of possible association. *J Eur Acad Dermatol Venereol* 2000; 14: 424– 25.

15. Rebora A, Drago F, Parodi A. May Helicobacter pylori be important for dermatologists? *Dermatology* 1995; 191: 6–8.

16. Jones MP, Knable AL, White MJ, Durning SJ. Helicobacter pylori in rosacea: lack of an association. *Arch Dermatol* 1998; 134: 511.

17. Herr H, You CH. Relationship between Helicobacter pylori and rosacea: It may be a myth. *J Korean Med Sci* 2000; 15: 551 – 54.

18. Szlachcic A. The link between Helicobacter pylori infection and rosacea. *J Eur Acad Dermatol Venereol* 2002; 16: 328–33.

19. Zandi S, Shamsadini S, Zahedi MJ, Hyatbaksh M. Helicobacter pylori and rosacea. *East Mediterr Health J* 2003; 9: 167–71.

20. Diaz C, O'Callaghan CJ, Khan A,Ilchyshshyn A. Rosacea: a cutaneous marker of Helicobacter pylori infection? Results of a pilot study. *Acta Derm Venereol* 2003; 83: 282–86.

21. Szlachcic A. The link between Helicobacter pylori infection and rosacea. *J Eur Acad Dermatol Venereol* 2002; 16: 328–33.

22. Boixeda de Miquel D, Va´zquez Romero M, Va´zquez Sequeiros E, Foruny Olcina JR, Boixeda de Miquel P, López San Román A. Effect of Helicobacter pylori eradication therapy in rosacea patients. R*ev Esp Enferm Dig* 2006; 98: 501-9.

23. Mayr-Kanhaeuser S, Kraenke B, Kaddu S, Muellegger RR . Resolution of granulomatous rosacea after eradication of Helicobacter pylori with clarithromycin, metronidazole and pantoprazole. *Eur J Gastroenterol Hepatol* 2001; 13: 1379–83.

24. Son SW, Kim IH, Oh CH, Kim JG . The response of rosacea to eradication of Helicobacter pylori. *Br J Dermatol* 1999; 140: 984–85.

25. Utas¸ S, Ozbakir O, Turasan A, Utas C. Helicobacter pylori eradication treatment reduces the severity of rosacea. *J Am Acad Dermatol* 1999 40: 433-35.

26. Bamford JT, Tilden RL, Blankush JL, Gangeness DE. Effect of treatment of Helicobacter pylori infection on rosacea. *Arch Dermatol* 1999; 135: 659–63.

27. Gedik GK, Karaduman A, Sivri B, Caner B . Has Helicobacter pylori eradication therapy any effect on severity of rosacea symptoms? *J Eur Acad Dermatol Venereol* 2005; 19: 398–99.

28. Sharma VK, Lynn A, Kaminski M ,Vasudeva R,Howden CW. A study of the prevalence of Helicobacter pylori infection and other markers of upper gastrointestinal tract disease in patients with rosacea. *Am J Gastroenterol* 1998; 93: 220–22.

29. Abram K, Silm H, Maaroos H-I, Oona.M . Risk factors associated with rosacea. *J Eur Acad Dermatol Venereol* 2010;24:565-71.

30. Lazaridou E, Giannopoulou C, Fotiadou C, Vakirlis E,Trigoni A, Ioannides D. The potential role of microorganisms in the development of rosacea. *J Dtsch Dermatol Ges* 2011 Jan; 9(1):21-5.