International Journal of Research in Dermatology
Devi B et al. Int J Res Dermatol. 2020 Jan;6(1):95-99
http://www.ijord.com

DOI: http://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20195676

Original Research Article

Rosacea: do microbes have some role in its causation? A cross-sectional study from North-East India

Bijayanti Devi[1], Jantu Kumar Bhaumik[2], Nandita Bhattacharjee[1]*

[1]Department of Dermatology, Venereology and Leprology, Regional Institute of Medical Sciences, Imphal, Manipur, India
[2]Department of Dermatology, Venereology and Leprology, Indira Gandhi Memorial Hospital, Agartala, Tripura (West), India

Received: 30 July 2019
Revised: 07 October 2019
Accepted: 19 October 2019

***Correspondence:**
Dr. Nandita Bhattacharjee,
E-mail: piyubhattacharjee@gmail.com

ABSTRACT

Background: Rosacea is a common inflammatory disease affecting the centrofacial skin. The etiopathogenesis is unknown and the disease follows a chronic course. It causes great social discomfort and reduces quality of life.
Methods: A cross sectional study was conducted from October 2011 to September 2013 in the Department of Dermatology, Venereology and Leprology of Regional Institute of Medical Sciences in Imphal, Manipur and all the patients diagnosed with rosacea were included. A detailed history and clinical examination were done and recorded in a preset proforma. Potassium hydroxide mount of skin scrapings and Gram stain as well as culture from lesion and control were performed.
Results: A total of 72 patients were included with female predominance. The mean age of the patients was 31.64±9.623 years. Sun exposure (70.8%) was the commonest exacerbating factor followed by fried spicy food (69.4%). Persistent erythema was seen in most of the patients (97.2%) and ETR was the commonest subtype (65.3%). Associated ocular manifestations were present in 4.2% of patients. The prevalence of *Demodex* mite was found to be higher in lesional skin as compared to the control. Culture from both lesion and control showed predominant growth of coagulase-negative staphylococcus (87% and 78.3% respectively).
Conclusions: Rosacea is a multifactorial disorder with diverse clinical spectrum. Elimination of the triggering factors may help in controlling the flares and improve the quality of life.

Keywords: Rosacea, Aggravating factors, *Demodex folliculorum*, Coagulase-negative *Staphylococcus*

INTRODUCTION

Rosacea is a common, chronic and recurrent inflammatory cutaneous disorder of unknown etiology. It primarily affects the convex areas of face (cheeks, chin, nose and central forehead) and the eyes. It was first described medically in 14th century by French surgeon, Chauliac as "goutterose" (French meaning for "pink droplet").[1] It's reported prevalence ranges from 0.09% to 22%.[2]

Rosacea is characterised by flushing, erythema, papules, pustules, telangiectasia and occasionally sebaceous hyperplasia.[3] The National Rosacea Society Expert Committee had classified this disease into four subtypes in the year 2002: 'erythematotelangiectatic'(ETR), 'papulopustular' (PPR), 'phymatous' and 'ocular'

rosacea.[4] The etiopathogenesis of rosacea is unknown and multiple triggering factors have been reported, but there is paucity of literature on rosacea from our country. Therefore, this study was undertaken to document the clinic-epidemiological profile and triggering factors of rosacea as well as to isolate the associated microbial agents in the North-East region of India.

METHODS

A cross-sectional study was conducted from October 2011 to September 2013 in the Department of Dermatology, Venereology and Leprology in collaboration with Department of Microbiology in Regional Institute of Medical Sciences at Imphal, Manipur. Seventy two patients clinically diagnosed as rosacea were included in the study. The diagnosis of rosacea was based on the presence of atleast one primary criteria (flushing, permanent erythema, papules, pustules and facial telangiectasia) and one secondary criteria (burning, stinging, elevated red facial plaques with or without scales, dry scaly skin, persistent facial edema, phymatous changes and ocular manifestations) as stated by the Expert National Rosacea Society Committee.[4] Written informed consent was obtained from every patient before enrolment in the study. A detailed history was taken and clinical examination findings were recorded in a present proforma for all the patients. Patients with age less than 20 years, with associated other facial dermatoses (e.g., atopic dermatitis, perioral dermatitis, systemic lupus erythematosus, discoid lupus erythematosus), with history of use of topical or systemic antibiotic in the preceding 2 weeks and patients unwilling to participate were excluded from the study.

Skin samples were taken from both lesional skin and non-lesional facial skin (control-2 cm away from the lesion) by skin scraping method (SSM) and skin pressurization method (SPM) in all the patients and smeared on a clean glass slide. A drop of 20% potassium hydroxide was added and the samples were examined under microscope using low and high power lens for identification of *Demodex* mite. Number of mites were counted in all the fields and recorded in a record sheet. Gram staining and culture of the pus from the pustules and swab from non-lesional facial skin (control-2 cm away from lesion) were done in all PPR patients.

Statistical analysis was done by SPSS software, version 16.0 for Windows. P value was calculated and a value of <0.05 was taken as statistically significant.

Ethical approval for the study was obtained from the institutional ethical committee.

RESULTS

A total of 72 patients (26 males and 46 females) were included in this study. The age of the patients ranged from 20 to 60 years with mean age of 31.64±9.623 years. Maximum number of our patients (n=33; 45.8%) were between 20 to 29 years of age. There was a female predominance in all the age groups except above 49 years of age and the male: female ratio was 1: 1.76. The age and sex distribution of the patients are shown in Table 1. Majority of the patients were from urban area (n=46; 63.9%). Occupation wise, students were the predominant group (n=25; 34.7%) followed by housewives (n=24; 33.3%).

Table 1: Age and sex distribution of patients with rosacea.

Age (in years)	Male N (%)	Female N (%)	Total N (%)
20-29	10 (13.9)	23 (31.9)	33 (45.8)
30-39	6 (8.3)	19 (26.4)	25 (34.7)
40-49	6 (8.3)	4 (5.6)	10 (13.9)
Above 49	4 (5.6)	0 (0)	4 (5.6)
Total	26 (36.1)	46 (63.9)	72 (100)

The duration of disease at the time of presentation varied from 1 month to 7 years with mean duration of 14.85±15.79 months. Majority of our patients presented with less than 1 year duration (n=49; 68.1%). Most of the patients belonged to Fitzpatrick's skin phototype IV (n=51; 70.8%) followed by phototype V (n=20; 27.8%). Sun exposure (n=51; 70.8%) and fried spicy food (n=50; 69.4%) were the prevalent aggravating factors (Table 2). Consumption of alcohol was found as an exacerbating factor in males only (n=16; 22.2%).

Table 2: Aggravating factors in rosacea.

Factors	Exposure N (%)	Aggravation N (%)
Chronic sun exposure	53 (73.6)	51 (70.8)
Fried and spicy foods	72 (100)	50 (69.4)
Hot drinks and beverages	64 (88.9)	33 (45.8)
OTC medication	47 (65.3)	22 (30.6)
Alcohol	18 (25)	16 22.2)
Cosmetics	54 (75)	16 (22.2)
Exertion and anxiety	72 (100)	8 (11.1)

OTC: Over the counter.

Majority of the patients presented with persistent erythema (n=70; 97.2%) followed by burning and flushing (Table 3). On cutaneous examination, telangiectasia was seen in 44 patients (61.1%). The lesions were predominantly present over cheeks (83%) followed by cheeks and forehead (8%), cheeks, forehead and nose (7%) and only nose (1%). ETR (Figure 1) was seen in maximum patients (n=47; 65.3%), whereas 31.9% and 2.8% of our patients belonged to PPR (Figure 2) and phymatous (Figure 3) subtype respectively (Table 4). Concomitant dermatological diseases were present in 50% patients (n=36) with melasma (n=22; 30.6%) being the commonest one followed by dermatophytosis (13.9%)

and seborrhoeic dermatitis (2.8%). Associated ocular diseases (conjunctivitis, blepharitis) were seen in 4.2% of the patients. None of the patients had features of acid peptic disorder.

Table 3: Clinical features in patients with rosacea.

Features	No. of patients	%
Persistent erythema	70	97.2
Burning	67	93.1
Flushing	52	72.2
Stinging	51	70.8
Telangiectasia	44	61.1
Induration	26	36.1
Scaling	5	6.9
Itching	5	6.9

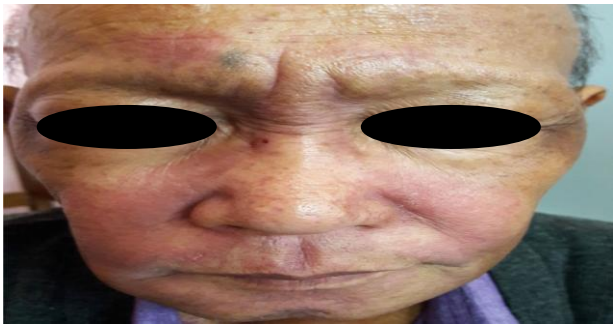

Figure 1: ETR with erythema, scaling and telangiectasia with periorbital sparing.

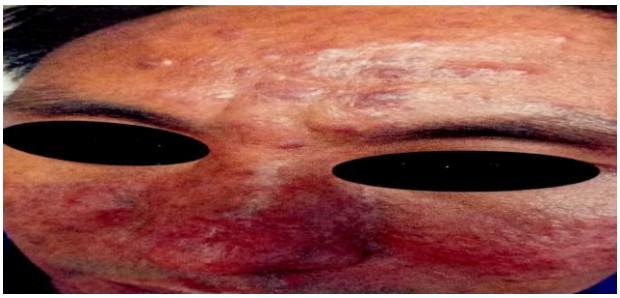

Figure 2: PPR with erythema, papules, pustules and sparing of periorbital region.

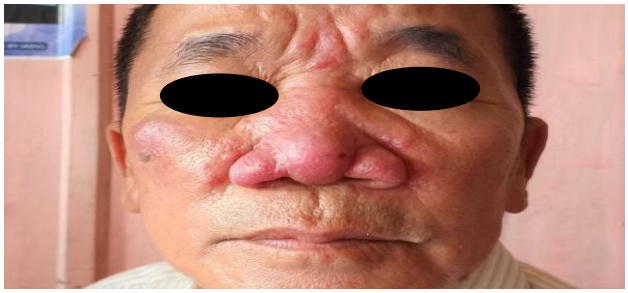

Figure 3: Phymatous rosacea.

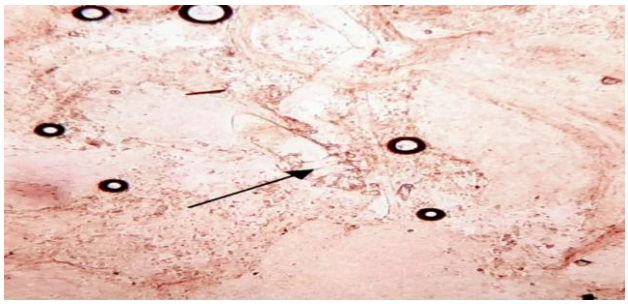

Figure 4: Demodex folliculorum mite in 20% potassium hydroxide mount.

Potassium hydroxide examination for *Demodex* mites was done in all the patients by SSM and SPM from both lesional and non-lesional (control) skin. Among total 72 patients, lesional mite positivity (Figure 4) was seen in 22 (30.6%) and 23 (31.9%) patients and control was positive for mite in 14 (19.4%) and 13 (18.1%) patients by SSM and SPM respectively. P value was significant ($P<0.05$) in both the methods (Table 5). The *Demodex* mite statistics in lesional skin of ETR and PPR patients are shown in Table 6. P value was not significant by both the methods ($p>0.05$). Gram stain examination of the pus and control was done in all PPR patients. Gram positive cocci were found from both pus and control ($p>0.05$). Culture of pus in all PPR patients showed growth of coagulase-negative *Staphylococcus* (n=20; 87%) followed by *Micrococcus* (n=1; 4.3%) and culture of control showed growth of coagulase-negative *Staphylococcus* (n=18; 78.3%) followed by *Micrococcus* (n=3; 13%) and *Staphylococcus aureus* (n=1; 4.3%). P value was not significant ($p=0.705$). Other routine laboratory parameters were within normal limit.

Table 4: Age and sex wise distribution of clinical subtypes of rosacea.

Age (in years)	ETR†		PPR		Phymatous	
	Male	Female	Male	Female	Male	Female
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
20-29	5 (6.9)	13 (18.1)	5 (6.9)	10 (13.9)	0 (0)	0 (0)
30-39	3 (4.2)	14 (19.4)	2 (2.8)	5 (6.9)	1 (1.4)	0 (0)
40-49	5 (6.9)	4 (5.6)	1 (1.4)	0 (0)	0 (0)	0 (0)
Above 49	3 (4.2)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)
Total	16 (22.2)	31 (43.1)	8 (11.1)	15 (20.8)	2 (2.8)	0 (0)

Table 5: Statistics of *Demodex* mite in lesion and control.

Parameter	Method	No. of patients (%)	Range of mite number	Mean mite count	P value
Mite in lesion	SSM	22 (30.6)	1-20	3.77±3.77	SSM=0.001**
	SPM	23 (31.9)	1-7	3.52±1.59	
Mite in control	SSM	14 (19.4)	1-20	3.43±4.87	
	SPM	13 (18.1)	1-8	3.15±1.99	SPM=0.010**

**: Significant.

Table 6: *Demodex* mite statistics in lesions of ETR and PPR.

Mite in lesion	Method	No. of patients (%)	Range of mite numbers	Mean mite count	P value
ETR[†]	SSM	13 (18.06)	1-5	3.00±1.29	SSM=0.203
	SPM	14 (19.4)	1-5	2.79±1.42	
PPR[‡]	SSM	9 (12.5)	2-20	4.89±5.71	SPM=0.121
	SPM	9 (12.5)	3-7	4.44±1.42	

DISCUSSION

Rosacea is a chronic inflammatory disease involving the central facial skin and eyes. It can present with a variety of clinical features. Middle aged adults are usually affected with peak incidence between 30-50 years.[5] In the present study, the mean age was 31.64±9.62 years with majority of the patients (45.8%) belonging to 20 to 29 years of age which is in contrast to most of the studies.[2,6,8-10] The involvement of the younger age group was probably related to genetic predisposition, excessive ultraviolet radiation exposure and greater use of cosmetics. Female predominance is seen in various literatures.[2,6,7,9-11] Males are prone to develop phymatous lesions and follow a severe course of disease.[5] In our study, majority of the patients (63.9%) were female with a male: female ratio of 1: 1.76. However, all of our patients (n=4) above 49 years of age were males which is in concordance to the findings of Lazaridou et al.[10] Majority of our study population were students (34.7%) and housewives (33.3%) probably because of greater chances of exposure to triggering factors in form of outdoor activities and kitchen work respectively. In the present study, most of the patients were from urban areas (63.9%) which is similar to the findings of Bae et al.[9]

Rosacea predominantly affects lighter-skinned populations of Celtic origin.[5] We also found more involvement in type IV skin phototype (70.8%) than type V skin phototype. The pathogenesis of rosacea remains unclear. The possible pathological processes include abnormalities of cutaneous vasculature, immune dysregulation, dermal connective tissue degeneration, dysfunction of pilosebaceous unit, chemical, nutritional and microbial factors.[12] Various precipitating factors have been reported including sunlight, heat, spicy food, hot beverages, drugs, microorganisms, smoking and alcohol.[2,12] Sun exposure was the most common triggering factor (70.8%) in our study which is in concordance with previous studies.[8-11] Bae et al had described the positive correlation of the severity of ETR with degree of sun exposure.[9] We found aggravation by fried, spicy food and alcohol in 69.4% and 22.2% of patients respectively which are close to the findings of Bhattarai et al.[8] Long term use of topical corticosteroids can produce rosacea like cutaneous eruptions.[13] In the present study, use of over the counter medications was reported by 30.6% of patients, the most common medications being clobetasol propionate (0.05%) and betamethasone dipropionate (0.05%).

In our study, persistent erythema was the commonest clinical feature (97.2%) which is in concordance with other studies.[8,11] Most common site of involvement in our patients was cheek (83.3%) which is similar to the findings of Bhattarai et al.[8] This may be due to greater exposure to sunlight and use of cosmetics. ETR was the major clinical subtype in our patients (65.3%) which is comparable to previous studies.[6,7] Associated ocular manifestations were present in 4.2% of our patients in form of conjunctivitis and blepharitis. Higher prevalence of ocular diseases has been reported in other studies.[8,10,11] In our study population, other co-existing cutaneous diseases were present in 50% of patients with melasma being the prevailing one (30.6%). This may be explained by the greater use of over the counter medications as well as cosmetics to get rid of the blemishes. Concurrent systemic diseases were seen in 2.8% patients in form of cholecystitis and hypertension. None of our patients had symptoms suggestive of acid peptic disorder which is in contrast to previous studies.[8,10,11]

Demodex folliculorum mites are normal commensals of human hair follicles. These mites have been reported as an important factor in the pathogenesis of rosacea when these are present in high densities.[12,14] A T-cell mediated immune response to *Demodex* antigens has been suggested in patients with rosacea.[15] In our study, the lesional mite positivity rate was almost similar by both SSM and SPM. We found lesional mite positivity rate of 30.6% and 31.9% by SSM and SPM respectively which was less as compared to other studies.[10,14,16] This may be due to the use of less sensitive techniques like SSM and

SPM in our study as compared to skin surface biopsy which was used in most of the previous studies. The prevalence of *Demodex* mite was found to be higher in lesional skin as compared to the control (2 cm away from lesion) by both SSM and SPM ($p<0.05$). The mean mite counts in ETR patients were 3 and 2.79 as compared to 4.89 and 4.44 in PPR patients by SSM and SPM respectively, but it was not statistically significant ($p>0.05$).

Coagulase-negative staphylococci are one of the predominant normal commensal of human skin surface. Changes in the cutaneous microenvironment in patients with rosacea may result in overgrowth of normal microbial flora.[5] In our study, gram stain of both pus and control showed growth of gram positive cocci in PPR patients ($p>0.05$). Predominant growth of coagulase-negative *Staphylococcus* was found in culture of both pus (87%) as well as control (78.3%). The result was not statistically significant ($p=0.705$). In a study by Whitfeld et al pure growth of *Staphylococcus* epidermidis was found in 60% patients of pustular rosacea in comparison with the normal surrounding skin.[17]

CONCLUSION

Rosacea is a chronic disorder with diverse etiologies. Proper identification and avoidance of triggering factors is necessary for successful management of this disease. This study differs from other studies because we used patient's own skin as control to find out microbial association with the disease. The major limitations of the present study were the small sample size, limited study duration and lack of more sensitive diagnostic technique like skin surface biopsy. Further large scale studies are required to illustrate various factors involved in the pathogenesis of rosacea. We hope that our study will contribute useful data regarding the clinico-epidemiological profile and microbial association of rosacea from the North-East region of India.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Debersaques J. Historical notes on (acne) rosacea. Eur J Dermatol. 1995;5(1):16-22.
2. Spoendlin J, Voegel JJ, Jick SS, Meier CR. A study on the epidemiology of rosacea in the UK. Br J Dermatol. 2012;167:598-605.
3. Hsieh F, Lee JY, Hsu MM. Rosacea: an often overlooked or misdiagnosed disease. Dermatol Sinica. 2004;22:213-20.
4. Wilkin J, Dahl M, Detmar M, Drake L, Feinstein A, Odom R, Powell F. Standard classification of rosacea: report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. J Am Acad Dermatol. 2002;46(4):584-7.
5. Powell FC. Rosacea. In: Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, eds. Rook's Textbook of Dermatology. 9th ed. UK: Wiley-Blackwell; 2016: 91.1-91.19.
6. Berg M, Liden S. An epidemiological study of rosacea. Acta Derm Venereol. 1989;69:419-23.
7. Abram K, Silm H, Oona M. Prevalence of rosacea in an Estonian working population using a standard classification. Acta Derm Venereol. 2010;90:269-73.
8. Bhattarai S, Agrawal S, Rijal A. Clinico-epidemiological profile of rosacea at a tertiary care hospital in eastern Nepal. NJDVL. 2012;10(1):27-32.
9. Bae YI, Yun SJ, Lee JB, Kim SJ, Won YH, Lee SC. Clinical evaluation of 168 Korean patients with rosacea: the sun exposure correlates with the erythematotelangiectatic subtype. Ann Dermatol. 2009;21(3):243-9.
10. Lazaridou E, Apalla Z, Sotiraki S, Ziakas NG, Fotiadou C, Loannides D. Clinical and laboratory study of rosacea in northern Greece. J Eur Acad Dermatol Venereol. 2010;24(4):410-4.
11. Khaled A, Hammami H, Zeglaoui F, Tounsi J, Zermani R, Kamoun MR, et al. Rosacea: 244 Tunisian cases. Tunis Med. 2010;88(8):597-601.
12. Crawford GH, Pelle MT, James WD. Rosacea: I etiology, pathogenesis, and subtype classification. J Am Acad Dermatol. 2004;51:327-41.
13. Litt JZ. Steroid-induced rosacea. Am Fam Physician. 1993;48:67-71.
14. Georgala S, Katoulis AC, Kylafis GD, Koumantaki-Mathioudaki E, Georgala C, Aroni K. Increased density of Demodex folliculorum and evidence of delayed hypersensitivity reaction in subjects with papulopustular rosacea. J Eur Acad Dermatol Venereol. 2001;15:441-4.
15. Rather PA, Hassan I. Human demodex mite: the versatile mite of dermatological importance. Indian J Dermatol. 2014;59:60–6.
16. Forton FM, De Maertelaer V. Papulopustular rosacea and rosacea-like demodicosis: two phenotypes of the same disease? J Eur Acad Dermatol Venereol. 2018;32(6):1011-6.
17. Whitfeld M, Gunasingam N, Leow LJ, Shirato K, Preda V. Staphylococcus epidermidis: a possible role in the pustules of rosacea. J Am Acad Dermatol. 2011;64(1):49-52.

Cite this article as: Devi B, Bhaumik JK, Bhattacharjee N. Rosacea: do microbes have some role in its causation? A cross-sectional study from North-East India. Int J Res Dermatol 2020;6:95-9.