

Original Research Article

OESTROGEN AND GASTROESOPHAGEAL REFLUX DISEASE DYNAMICS IN PREMENOPAUSAL AND POSTMENOPAUSAL WOMEN: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Gastroesophageal reflux disease (GERD) is a common gastrointestinal disorder influenced by multiple physiological and hormonal factors. Oestrogen has been implicated in the modulation of lower esophageal sphincter function and esophageal mucosal integrity. However, limited data are available regarding the relationship between menopausal status, serum oestrogen levels, and GERD severity among Indian women. The present study aimed to evaluate the dynamics of oestrogen and GERD among premenopausal and postmenopausal women.

Materials and Methods: This hospital-based cross-sectional study included 163 women with symptoms suggestive of GERD, comprising 81 premenopausal and 82 postmenopausal participants. Detailed clinical evaluation, GERD symptom assessment using the Gastroesophageal Reflux Disease Questionnaire (GERDQ), serum oestrogen estimation, and upper gastrointestinal endoscopy were performed wherever indicated. Endoscopic severity was graded according to the Los Angeles classification. Statistical analysis was carried out using SPSS version 25.0.

Results: Postmenopausal women had significantly higher body mass index, sedentary lifestyle prevalence, hypertension, diabetes mellitus, and longer duration of GERD symptoms compared to premenopausal women. Nocturnal reflux symptoms (52.4% vs 29.6%, $p=0.003$), dysphagia (19.5% vs 7.4%, $p=0.026$), and chronic cough/hoarseness (29.3% vs 13.6%, $p=0.014$) were significantly more common among postmenopausal women. Mean GERDQ scores were significantly higher in postmenopausal women (10.1 ± 2.8 vs 8.4 ± 2.1 , $p<0.001$). Serum oestrogen levels were markedly lower in postmenopausal participants (38.7 ± 16.9 pg/mL vs 142.6 ± 38.5 pg/mL, $p<0.001$). Non-erosive reflux disease predominated among premenopausal women, whereas erosive esophagitis and advanced Los Angeles grades were significantly more frequent in postmenopausal women.

Conclusion: Postmenopausal women demonstrated significantly greater GERD severity, increased erosive esophageal disease, and substantially lower serum oestrogen levels compared to premenopausal women. The findings suggest a protective role of endogenous oestrogen on esophageal mucosal integrity and highlight the importance of menopausal hormonal changes in GERD pathogenesis and progression.

Keywords: Gastroesophageal reflux disease; Premenopausal women; Postmenopausal women; Erosive esophagitis; GERDQ.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common chronic gastrointestinal disorder

characterized by the reflux of gastric contents into the esophagus, leading to symptoms such as heartburn and acid regurgitation.^[1] GERD

significantly affects quality of life and may result in complications including erosive esophagitis, Barrett's esophagus, and esophageal adenocarcinoma if left untreated.^[2] Globally, the prevalence of GERD is estimated to be approximately 13–14%, with increasing incidence reported in both Western and Asian populations.^[3] Several risk factors including obesity, dietary habits, smoking, alcohol consumption, and hiatal hernia have been implicated in the development of GERD.^[4] In recent years, growing attention has been directed toward the influence of sex hormones, particularly oestrogen, on esophageal physiology and reflux disease.^[5] Literature have demonstrated notable gender differences in GERD manifestations, with women more frequently reporting reflux symptoms and non-erosive reflux disease, whereas men are more likely to develop erosive complications.^[6]

Oestrogen is known to affect smooth muscle tone and gastrointestinal motility, including relaxation of the lower esophageal sphincter (LES), which may predispose to reflux episodes.^[7] Conditions associated with elevated oestrogen levels, such as pregnancy and exogenous hormone therapy, have been linked with increased reflux symptoms.^[7] However, oestrogen also exhibits anti-inflammatory and mucosal protective effects on esophageal epithelium, suggesting a complex relationship between hormonal status and GERD severity.^[8]

Menopause is associated with a marked decline in endogenous oestrogen levels along with metabolic and physiological changes that may influence GERD occurrence.^[9] Literature have reported a higher prevalence of GERD symptoms among postmenopausal women compared to premenopausal women. Furthermore, hormone replacement therapy has been associated with an increased risk of reflux symptoms in several observational studies.^[10,11]

Despite increasing evidence regarding hormonal influences on GERD, data comparing reflux disease patterns between premenopausal and postmenopausal women remain limited, particularly in the Indian population. Understanding the role of oestrogen in GERD may provide insights into gender-specific pathophysiology and aid in improving disease management. Therefore, the present study was aimed to evaluate the dynamics of oestrogen and gastroesophageal reflux disease among premenopausal and postmenopausal women in a cross-sectional setting.

MATERIALS AND METHODS

Study Design and Setting: The present study was a hospital-based cross-sectional observational study conducted in the Department of Obstetrics and Gynaecology at a tertiary care teaching hospital. The study was carried out over a period of 12 months from July 2023 to June 2024.

Study Population: The study population comprised adult women attending the outpatient and inpatient departments with symptoms suggestive of gastroesophageal reflux disease. Women aged between 20 and 65 years presenting with complaints of heartburn, acid regurgitation, retrosternal burning sensation, sour belching, epigastric discomfort, dysphagia, or nocturnal reflux symptoms were screened for eligibility. Eligible participants were categorized into premenopausal and postmenopausal groups based on menstrual history. Premenopausal women were defined as women having regular menstrual cycles during the preceding 12 months. Postmenopausal women were defined as women with spontaneous cessation of menstruation for at least 12 consecutive months not attributable to pregnancy, lactation, endocrine disorders, chemotherapy, or surgical menopause. Consecutive sampling technique was used for participant recruitment until the required sample size was achieved. Women aged 20–65 years with symptoms clinically suggestive of GERD were included in the study. Both newly diagnosed and previously symptomatic untreated cases of GERD were considered eligible.

Women with previous upper gastrointestinal surgery, known malignancy of the esophagus or stomach, peptic ulcer disease, chronic liver disease, inflammatory bowel disease, connective tissue disorders, severe cardiopulmonary illness, chronic kidney disease, pregnancy, or lactation were excluded from the study. Patients receiving proton pump inhibitors, H₂ receptor blockers, hormonal replacement therapy, oral contraceptive pills, corticosteroids, prokinetics, calcium channel blockers, nitrates, or drugs known to influence lower esophageal sphincter tone within the previous four weeks were also excluded. Women with active smoking, alcohol dependence, or inability to provide reliable clinical history were not included in the study.

Clinical Evaluation and Data Collection: After obtaining written informed consent, detailed demographic and clinical information was collected using a predesigned structured case record form. Information regarding age, occupation, socioeconomic status, dietary habits, body mass index (BMI), physical activity, comorbidities, menstrual history, menopausal duration, parity, and medication history was recorded. Particular emphasis was placed on identifying risk factors associated with GERD including obesity, spicy food intake, caffeine consumption, late-night meals, and sedentary lifestyle. A detailed history regarding reflux symptoms was obtained, including duration, frequency, severity, aggravating factors, nocturnal symptoms, and associated gastrointestinal complaints. Symptom assessment was performed using the validated Gastroesophageal Reflux Disease Questionnaire (GERDQ). The questionnaire included assessment of heartburn, regurgitation, sleep disturbance due to reflux symptoms, use of

over-the-counter medications, nausea, and epigastric pain. GERD severity was categorized based on GERDQ scores and symptom frequency. Comprehensive physical examination including general examination and systemic examination was carried out in all participants. Height and weight were measured using standardized instruments, and body mass index was calculated using the formula: $BMI = \text{Weight(kg)}/\text{Height}^2(\text{m})$. Waist circumference and blood pressure measurements were also recorded using standard procedures.

Laboratory Assessment: Venous blood samples were collected from all participants under aseptic precautions after overnight fasting of 8–10 hours. In premenopausal women, blood sampling was preferably performed during the follicular phase of the menstrual cycle (days 3–7) to minimize cyclic hormonal variation. Serum samples were separated by centrifugation and processed in the institutional biochemistry laboratory. Serum oestrogen levels were estimated using chemiluminescent immunoassay (CLIA) technique following standard manufacturer protocols. Internal quality control procedures were followed throughout the study period to ensure assay reliability and accuracy. Routine laboratory investigations including complete blood count, fasting blood glucose, liver function tests, renal function tests, and lipid profile were performed wherever clinically indicated.

Endoscopic Evaluation

Upper gastrointestinal endoscopy was advised in patients with persistent or severe symptoms, high GERDQ scores, refractory symptoms, or alarm features such as dysphagia, weight loss, anemia, or gastrointestinal bleeding. Endoscopy was performed using a flexible video endoscope under standard preparation and monitoring protocols. Endoscopic findings including erosive esophagitis, mucosal erythema, ulceration, hiatal hernia, and Barrett's esophagus were documented. Severity of erosive esophagitis was graded according to the Los Angeles (LA) classification system. Patients without visible mucosal breaks on endoscopy but having typical reflux symptoms were categorized as non-erosive reflux disease (NERD).

Outcome Measures: The primary outcome measure of the study was the association between serum oestrogen levels and GERD symptom severity among premenopausal and postmenopausal women. Secondary outcome measures included comparison of GERDQ scores, prevalence of erosive esophagitis, frequency of nocturnal symptoms, and correlation between menopausal duration and reflux severity.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee prior to commencement of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants after explaining the nature and objectives of the study in their local language.

Confidentiality of participant information was strictly maintained throughout the study.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 25.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean $\pm$ standard deviation, whereas qualitative variables were presented as frequencies and percentages. Normality of data distribution was assessed using the Shapiro–Wilk test. Comparison of continuous variables between premenopausal and postmenopausal women was performed using independent Student's t-test for normally distributed variables and Mann–Whitney U test for non-normally distributed data. Categorical variables including clinical symptoms, comorbidities, GERD severity categories, and endoscopic findings were analyzed using chi-square test or Fisher's exact test wherever appropriate. Association between serum oestrogen levels and GERD severity parameters including GERDQ score and Los Angeles grading of erosive esophagitis was assessed using Pearson's or Spearman's correlation analysis depending on data distribution. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 163 women with symptoms suggestive of GERD were included in the study, comprising 81 premenopausal and 82 postmenopausal participants. The mean age was significantly higher among postmenopausal women compared to premenopausal women (56.9 ± 6.4 vs 36.8 ± 7.2 years, $p < 0.001$). Postmenopausal women also had significantly higher body mass index values (27.4 ± 4.2 vs 25.1 ± 3.7 kg/m², $p = 0.001$). Urban–rural distribution was comparable between the groups ($p = 0.568$). A sedentary lifestyle was significantly more common among postmenopausal women (57.3% vs 34.6%, $p = 0.004$). Although spicy food intake and tea/coffee consumption were relatively frequent in both groups, no statistically significant differences were observed ($p = 0.171$ and $p = 0.482$, respectively). The prevalence of hypertension and type 2 diabetes mellitus was significantly greater among postmenopausal women (41.5% vs 11.1% and 35.4% vs 8.6%, respectively; $p < 0.001$ for both). Duration of GERD symptoms was also significantly longer in postmenopausal participants (18.9 ± 9.7 vs 11.6 ± 6.8 months, $p < 0.001$), whereas family history of GERD was comparable between the two groups ($p = 0.492$) [Table 1].

Heartburn and acid regurgitation were the most commonly reported symptoms in both study groups. Although these symptoms were more frequent among postmenopausal women, the differences were not statistically significant ($p = 0.309$ and $p = 0.134$, respectively). Postmenopausal women demonstrated significantly higher prevalence of

nocturnal reflux symptoms (52.4% vs 29.6%, $p=0.003$), dysphagia (19.5% vs 7.4%, $p=0.026$), and chronic cough/hoarseness (29.3% vs 13.6%, $p=0.014$) compared to premenopausal women. Retrosternal chest discomfort and nausea/bloating showed no significant intergroup differences. The mean GERDQ score was significantly higher among postmenopausal women than premenopausal women (10.1 ± 2.8 vs 8.4 ± 2.1 , $p<0.001$), indicating greater

symptom burden. Severity analysis based on GERDQ scores revealed that severe GERD was more prevalent among postmenopausal women (28.0% vs 13.6%), whereas mild GERD was more common among premenopausal women (38.3% vs 19.5%). Overall GERD severity distribution differed significantly between the two groups ($p=0.012$) [Table 2].

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants.

Variable	Premenopausal (n=81)	Postmenopausal (n=82)	p-value
	Frequency (%) / mean $\pm$ SD		
Age (years)	36.8 $\pm$ 7.2	56.9 $\pm$ 6.4	<0.001
BMI (kg/m ²)	25.1 $\pm$ 3.7	27.4 $\pm$ 4.2	0.001
Residence			
Rural	32 (39.5%)	36 (43.9%)	0.568
Urban	49 (60.5%)	46 (56.1%)	
Lifestyle			
Sedentary	28 (34.6%)	47 (57.3%)	0.004
Active	53 (65.4%)	35 (42.7%)	
Spicy food intake			
>4 times/week	52 (64.2%)	44 (53.7%)	0.171
$\leq$ 4 times/week	29 (35.8%)	38 (46.3%)	
Tea/Coffee consumption			
>2 cups/day	43 (53.1%)	39 (47.6%)	0.482
$\leq$ 2 cups/day	38 (46.9%)	43 (52.4%)	
Comorbidities			
Hypertension	9 (11.1%)	34 (41.5%)	<0.001
Type 2 Diabetes Mellitus	7 (8.6%)	29 (35.4%)	<0.001
Duration of GERD symptoms (months)	11.6 $\pm$ 6.8	18.9 $\pm$ 9.7	<0.001
Family history of GERD	14 (17.3%)	11 (13.4%)	0.492

BMI – Body Mass Index; GERD – Gastroesophageal Reflux Disease.

Table 2: Comparison of GERD Symptoms and GERDQ Scores Between Premenopausal and Postmenopausal Women.

Women:			
Variable	Premenopausal (n=81)	Postmenopausal (n=82)	p-value
	Frequency (%) / mean $\pm$ SD		
Heartburn	62 (76.5%)	68 (82.9%)	0.309
Acid regurgitation	57 (70.4%)	66 (80.5%)	0.134
Nocturnal reflux symptoms	24 (29.6%)	43 (52.4%)	0.003
Retrosternal chest discomfort	29 (35.8%)	38 (46.3%)	0.171
Dysphagia	6 (7.4%)	16 (19.5%)	0.026
Chronic cough/hoarseness	11 (13.6%)	24 (29.3%)	0.014
Nausea/bloating	33 (40.7%)	29 (35.4%)	0.484
GERDQ score	8.4 $\pm$ 2.1	10.1 $\pm$ 2.8	<0.001
GERD Severity Based on GERDQ Score			
Mild GERD	31 (38.3%)	16 (19.5%)	0.012
Moderate GERD	39 (48.1%)	43 (52.4%)	
Severe GERD	11 (13.6%)	23 (28.0%)	

GERD – Gastroesophageal Reflux Disease; GERDQ – Gastroesophageal Reflux Disease Questionnaire. Mean serum oestrogen levels were markedly lower among postmenopausal women compared to premenopausal women (38.7 ± 16.9 pg/mL vs 142.6 ± 38.5 pg/mL, $p<0.001$). A significantly greater proportion of postmenopausal women underwent upper gastrointestinal endoscopy due to persistent or severe symptoms (72.0% vs 56.8%, $p=0.041$). Non-erosive reflux disease (NERD) was more frequently observed among premenopausal women (63.0% vs 37.3%, $p=0.009$), whereas erosive esophagitis was significantly more common in postmenopausal

women (52.5% vs 28.3%, $p=0.012$). Hiatal hernia was also observed more frequently among postmenopausal participants (23.7% vs 8.7%, $p=0.039$). Barrett's esophagus was identified only in postmenopausal women; however, the difference was not statistically significant ($p=0.112$). Assessment of erosive esophagitis severity using the Los Angeles classification demonstrated relatively advanced grades among postmenopausal women, with higher proportions of Grade C and Grade D esophagitis. The distribution of LA grades differed significantly between the two groups ($p=0.047$) [Table 3]

Table 3: Serum Oestrogen Levels and Endoscopic Findings Among Study Participants.

Variable	Premenopausal (n=81)	Postmenopausal (n=82)	p-value
	Frequency (%) / mean $\pm$ SD		
Serum oestrogen (pg/mL)	142.6 $\pm$ 38.5	38.7 $\pm$ 16.9	<0.001
Patients undergoing upper GI endoscopy	46 (56.8%)	59 (72.0%)	0.041
Non-erosive reflux disease (NERD)	29 (63.0%)	22 (37.3%)	0.009
Erosive esophagitis overall	13 (28.3%)	31 (52.5%)	0.012
Hiatal hernia	4 (8.7%)	14 (23.7%)	0.039
Barrett's esophagus	0 (0%)	3 (5.1%)	0.112
Los Angeles (LA) Classification of Erosive Esophagitis			
Grade A	8 (61.5%)	10 (32.3%)	0.047
Grade B	4 (30.8%)	12 (38.7%)	
Grade C	1 (7.7%)	7 (22.6%)	
Grade D	0 (0%)	2 (6.4%)	

GI – Gastrointestinal; NERD – Non-Erosive Reflux Disease; LA – Los Angeles classification.

DISCUSSION

The present cross-sectional study evaluated the relationship between oestrogen status and gastroesophageal reflux disease (GERD) dynamics among premenopausal and postmenopausal women. In the present study, postmenopausal women had significantly higher BMI and greater prevalence of sedentary lifestyle, hypertension, and type 2 diabetes mellitus compared to premenopausal women. These findings are clinically relevant because obesity and metabolic disorders are recognized contributors to GERD pathogenesis through increased intra-abdominal pressure, delayed gastric emptying, and impaired lower esophageal sphincter (LES) function.^[5,12] The significantly longer duration of GERD symptoms observed among postmenopausal women further indicates chronicity and progressive disease severity in this population.^[13] Similar observations have been reported by Kim et al., and Sakaguchi et al., who demonstrated increased GERD prevalence among older and postmenopausal women, particularly in the presence of obesity and metabolic syndrome components.^[13,14]

The symptom profile analysis revealed significantly greater nocturnal reflux symptoms, dysphagia, and chronic cough/hoarseness among postmenopausal women, along with significantly higher mean GERDQ scores (10.1 $\pm$ 2.8 vs 8.4 $\pm$ 2.1; $p < 0.001$). Additionally, severe GERD was observed in 28.0% of postmenopausal women compared to 13.6% of premenopausal women. These findings suggest that menopause is associated not only with increased symptom frequency but also with more clinically significant disease manifestations. Comparable findings were reported by Kang et al., and Praveena et al., who observed greater reflux symptom severity among postmenopausal women and attributed this to age-related decline in esophageal motility and hormonal changes affecting LES competence.^[7,15] The higher frequency of nocturnal reflux symptoms in postmenopausal women may also be related to impaired esophageal clearance, delayed gastric emptying, and increased prevalence of hiatal hernia in older individuals.^[15]

One of the most important findings of the present study was the marked reduction in serum oestrogen levels among postmenopausal women (38.7 $\pm$ 16.9 pg/mL) compared to premenopausal women (142.6 $\pm$ 38.5 pg/mL), which was accompanied by significant differences in endoscopic patterns of GERD. Premenopausal women more commonly exhibited non-erosive reflux disease (NERD), whereas erosive esophagitis predominated among postmenopausal women (52.5% vs 28.3%, $p = 0.012$). Furthermore, advanced Los Angeles grades (Grade C/D) were more frequently identified in postmenopausal participants. These findings support the studies by Honda et al., and Manning et al., that endogenous oestrogen may exert protective effects on esophageal mucosal integrity despite its known influence on LES relaxation.^[16,17]

Iijima et al., has demonstrated that oestrogen enhances epithelial barrier function, improves mucosal blood flow, and suppresses inflammatory cytokine-mediated mucosal injury.^[18] Grishina et al. reported that oestrogen increases expression of tight junction proteins such as occludin, thereby protecting against acid-induced mucosal damage.^[19] This may explain why premenopausal women often experience symptomatic reflux without significant erosive injury, whereas postmenopausal women develop more severe mucosal disease after loss of hormonal protection.^[19] Similar observations were reported by Kim et al., who demonstrated higher prevalence of erosive esophagitis in postmenopausal women independent of age and BMI.^[13]

The significantly greater prevalence of hiatal hernia among postmenopausal women in the present study (23.7% vs 8.7%, $p = 0.039$) may also have contributed to increased reflux severity. Age-related weakening of diaphragmatic musculature and connective tissue support can predispose to hiatal hernia formation, thereby promoting reflux by impairing the antireflux barrier.^[20] Barrett's esophagus was identified only among postmenopausal women, although the difference was not statistically significant, likely because of the relatively smaller sample size.^[21] Nevertheless, this finding is clinically important because chronic uncontrolled reflux and erosive disease are recognized precursors for Barrett's metaplasia.^[21]

The findings of the present study collectively suggest that the relationship between oestrogen and GERD is complex and potentially dual in nature. While oestrogen may contribute to reflux symptoms through smooth muscle relaxation and transient LES relaxation, it simultaneously appears to protect the esophageal mucosa against inflammatory and erosive injury.^[22] The decline in endogenous oestrogen after menopause may therefore predispose women to more severe and complicated GERD manifestations.^[23] These observations are supported by previous studies by Santoro et al., and Richter et al., evaluating hormonal influences on reflux disease.^[24,25]

Limitations: The present study had certain limitations. Being a single-center cross-sectional study, causal relationships between serum oestrogen levels and GERD severity could not be definitively established. The relatively modest sample size may have limited the detection of less frequent findings such as Barrett's esophagus. Endoscopy was not performed in all participants, which may have resulted in underestimation of asymptomatic erosive disease. Additionally, lifestyle and dietary factors were partly based on self-reported history and may be subject to recall bias.

CONCLUSION

The present study demonstrated that postmenopausal women had significantly greater GERD symptom burden, higher GERDQ scores, increased prevalence of erosive esophagitis, and markedly lower serum oestrogen levels compared to premenopausal women. Premenopausal women more commonly exhibited non-erosive reflux disease, suggesting a possible protective role of endogenous oestrogen on esophageal mucosal integrity despite its influence on reflux symptoms. The findings indicate that menopausal hormonal changes contribute substantially to GERD severity and endoscopic progression. Recognition of hormonal status and associated metabolic risk factors may help in early identification, risk stratification, and individualized management of GERD among women, particularly in the postmenopausal population.

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