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ORIGINAL ARTICLE

The Association between Gastrooesophageal Reflux Disease and Subsequent Rheumatoid Arthritis Occurrence

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ABSTRACT

Background and Aims: Rheumatologic disorders (RDs) can manifest as gastrointestinal (GI) symptoms. Patients with systemic sclerosis (SSc) frequently experience upper GI symptoms due to a lack of esophageal contractility (AC). GORD (gastro oesophageal reflux disease) is a common comorbidity in rheumatoid arthritis patients (RA).The aim of the present study was to evaluate the correlation between manifestation of rheumatoid arthritis and gastrooesophageal reflux disease.

Materials and Methods: This cross-sectional study was carried out on 845 gastro-oesophageal reflux disease patients who presented to department of medicine, Qazi Hussain Ahmad Medical Complex Nowshera and Lady Reading Hospital (LRH), Peshawar for period of six months i.e from January 2020 to June 2020. Consecutive patients with were premeditated subsequently taking written informed consent. Patients with prior history of Oesophageal surgery were excluded. The demographics characteristics such as age, BMI, gender, previous history, gastrointestinal symptoms severity, analgesics, and medication usage were recorded on a pre-designed questionnaire. Inflammatory marker's results were taken in the forms of C - reactive protein (CRP), and Erythrocyte Sedimentation Rate (ESR). Ethical approval was taken from the respective institutional review board. SPSS version 20 was used for data analysis.

Results: Out of 845 GORD patients, 110 (13%) had Rheumatologic disorders (mean age 49.5± 2.6 years, 71% females). The prevalence of rheumatoid arthritis (RA), systemic lupus erythematous (SLE), and the most common systemic sclerosis (SSc) were 39 (36%), 24 (21.8%), and 47 (42.2%) respectively. Regurgitation, dysphagia, heartburn, and nausea were the most severe symptoms of gastrointestinal patients having rheumatoid disorder. The GI symptoms had no significant association with SLE, RA, and SSc severity. Upper GI symptom severity did not differentiate between RDs.

Conclusion: Our study concluded that subsequent rheumatoid arthritis has a significant association with gastro-oesophageal reflux disease.

Keywords: Gastro-oesophagealReflux Disease, Rheumatoid arthritis, Systemic sclerosis

INTRODUCTION

Rheumatoid arthritisis generally considered a systemic extra-articular manifestation condition. Its one of the most widely occurring chronic inflammatory diseases [1]. The prevalenceof the adult population affected by rheumatoid arthritis varies from 0.5% to 1% [2].RA is generally referred to as joints worsening progression which leads to morbidity and mortality [3, 4]. Physical function deterioration, declined lifequality, burdens of socioeconomics and medical substantial, and cumulative comorbidity risks experiences are the rheumatoid arthritis symptoms and causes due to musculoskeletal deficits among patients [5]. GORD is a prominent contributor for rheumatoid arthritis patients as major comorbidity associated with rheumatoid arthritis [6]. It is the gastrointestinal tract most prevalent disorder [7]. The major GI symptoms are acid regurgitation and heartburn due to stomach content reflux into oesophagus[8]. A Japan-based study reported a higher prevalence of 24.5% among patients of gastro-oesophageal reflux disease with rheumatoid arthritis compared to the general population 11.5% [9].

Another study found the most prevalent age for gastro-oesophageal reflux disease was <60 years [10]. NSAIDs (non-steroidal anti-inflammatory drugs) as an anti-rheumatoid medication has been attributed as the amplified liability for gastrointestinal disease patients with rheumatoid arthritis [11]. The rheumatoid arthritis clinical pathogenesis and spectrum might cause the GI disorder as proposed as an alternate hypothesis [12].The environmental and genetic parameters such as lower socioeconomic status, smoking, education, family history, and heritability were the pathogenesis to be involved in the association of rheumatoid arthritis and gastro-oesophageal reflux disease. The micro biome plays a vital role in the progression and risks of rheumatoid arthritis as reported in arecent study [13].

The presence of gut microbe peptides in peripheral blood and synovial tissues strengthened the immunological relevance as evidence in newly diagnosed rheumatoid arthritis [14]. It is possible that chronic inflammation caused by acid reflux in GORD may cause mucosal damage and micro biome translocation from the gut into the circulation [15]. Therefore, gastro-oseophageal reflux

disease facilitates the pathogenesis of rheumatoid arthritis. The present study was conducted in order to assess the association between rheumatoid arthritis and gastro-oesophageal reflux disease.

METHODS

This cross-sectional study was carried out on 845 gastro-oesophageal reflux disease patients who presented to department of medicine, Qazi Hussain Ahmad Medical Complex Nowshera and Lady Reading Hospital (LRH), Peshawar for period of six months i.e from January 2020 to June 2020. Consecutive patients with were premeditated subsequently taking written informed consent. Patients with prior history of Oesophageal surgery were excluded. The demographics characteristics such as age, BMI, gender, previous history, gastrointestinal symptoms severity, analgesics, and medication usage were recorded on a pre-designed questionnaire. Inflammatory marker's results were taken in the forms of C - reactive protein (CRP), and Erythrocyte Sedimentation Rate (ESR). Ethical approval was taken from the respective institutional review board.GI symptoms with modified patient'sassessment recorded the severity and duration of GI on the pre-designed questionnairewith scale varies from 0 to 4 presenting very severe 4, severe 3, moderate 2, mild1, and none 0. Vomiting, belching,nausea, chest pain, heartburn, coughing, dysphagia, hoarseness, and regurgitation were the symptoms of GI.

Endoscopy was performed on individuals who attend the unit after eight hours fast in the morning. SPSS version 20 was used for data analysis. Quantitative data and symptoms records on the ordinal scale were utilized using student t-test and Mann Whitney test. P-values <0.05 were considered statistically significant.

RESULTS

Out of 845 GORD patients, 110 (13%) had Rheumatologic disorders (mean age 49.5± 2.6 years, 71% females). The prevalence of rheumatoid arthritis (RA), systemic lupus erythematous (SLE), and the most common systemic sclerosis (SSc) were 39 (36%), 24 (21.8%), and 47 (42.2%) respectively. Regurgitation, dysphagia, heartburn, and nausea were the most severe symptoms of gastrointestinal patients having rheumatoid disorder. The GI symptoms had no significant association with SLE, RA, and SSc severity. Upper GI symptom severity did not differentiate between RDs. Figure-1 demonstrate the gender distribution of 110 RDs patients. The prevalence of different rheumatoid arthritis was shown in Table-3/ Figure-2.

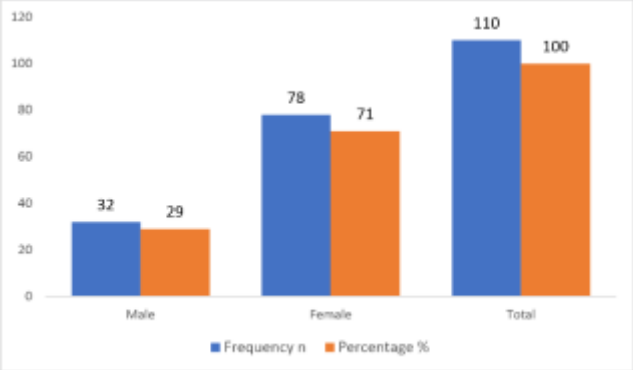

Figure-1. Gender distribution of 110 patients

Inflammatory markers, medical history, demographic details, and symptoms characteristics were shown in Table 1. The mean age of 110 RD patients was 49.5± 2.6 years. The prevalence of females was 78 (71%). SLE, SSc, and RA had no significant association with gender or age. The mean value of 110 patients' BMI was 26.5 ±1.2 kg/m2. The rheumatoid arthritis patients had a higher BMI (28.9 ± 2.3 kg/m2) than SLE (22.9 ± 1.1 kg/m2), and SSc (25.7±1.2 kg/m2). Minor or no abnormalities patients had lower BMI (26.9 ± 0.8 kg/m2) compared to EGJ obstructive disorders (29.1 ± 2.2 kg/m2). Although chronic analogies and PPI (34.7%) were used in 41.5% of RDs patients. But, SSc, SLE, and RA had no significant association with PPI and analgesic prevalence.

Table-1 the inflammatory markers, demographic details, and symptoms characteristics of all rheumatoid disorders patients.

	RD (110)	**RA (21)**	**SSc (12)**	**SLE (29)**	**P-value**
Demographic Parameters					
Age (years)	49.5± 2.6	51.3±1.5	48.3±2.6	49.01±3.7	0.149
Gender (Female %)	78 (71%)	17 (80.9%)	9 (75%)	21 (72.4%)	0.290
BMI (kg/m2)	26.5 ±1.2	28.9 ± 2.3	25.7±1.2	22.9 ± 1.1	0.015
Medications					
NSAIDs	9/53 (16.9%)	0% (0/15)	3/11 (27.3%)	2/8 (25%)	0.167
PPI	41/110 (37.3%)	11/21 (52.4%)	763.6%	38.5%	0.787
Inflammatory Markers					
ESR (mm/hours)	29.6±3.9	33.9±7.1	38.9±4.6	28.9±6.5	0.708
CRP (mg/L)	7.9±1.9	9.8±2.9	11.4±2.5	7.8±4.8	0.098
Duration of GI Symptoms (years)					
	6.9±1.3	4.3±1.4	7.9±1.6	3.9±1.7	0.281

On a 0–4 scale, the patient reported the severity of upper GI symptoms in the previous two weeks (0=none, 1=mild, 2=moderate, 3=severe, or 4=very severe) as shown in Table 2. .

Table-2 GI symptoms with severity on scale 0-4

Symptoms	RDs 110	RA	SSc	SLE	P-value
Dysphagia	1.1±0.2	0.9±0.1	1.1±0.2	1.3±0.3	0.561
Heartburn	1.2±0.1	1.2±0.1	1.1±0.3	1.6±0.3	0.566
Coughing	1.3±0.2	1.4±0.2	1.8±0.2	1.0±0.1	0.312
Regurgitation	1.2±0.1	1.2±0.3	1.2±.2	1.3±0.3	0.765
Nausea	1.2±0.1	1.3±0.4	1.0±0.2	1.7±0.3	0.237
Belching	0.8±0.2	0.6±0.1	1.1±0.1	1.1±0.5	0.873
Vomiting	0.6±0.2	1.1±0.2	0.8±0.3	0.9±0.3	0.874
Hoarseness	0.6±0.2	0.6±0.3	0.6±0.3	0.9±0.2	0.913
Chest Pain	1.1±0.9	0.7±0.4	0.8±0.1	1.5±0.5	0.102

Table 3.The prevalence of rheumatoid disorders among 110 patients

RDs Symptoms	Frequency n	Percentage %
Rheumatoid Arthritis (RA)	39	36
Systemic Lupus Erythematous (SLE)	24	21.8
Systemic Sclerosis (SSc)	47	42.2

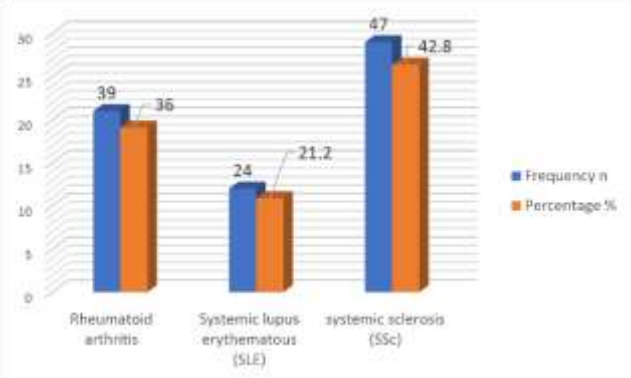

Figure-2 the prevalence of rheumatoiddisorders among 110 patients

DISCUSSION

Gastrointestinal disease is one of the major contributors to increase risks for the quality of life and mortality with rheumatoid disorders such as rheumatoid arthritis [16]. A study conducted on the association between gastro-oesophageal reflux disease and rheumatoid arthritis found a higher prevalence of GORD or GI symptoms in rheumatoid patients compared to the control group [17]. Rheumatoid arthritis treatment especiallyNSAIDs adverse effect was considered as a risk factor for GI disease [18-20]. Inlight of recent research on the role of environmental factors in thepathogenesis of RA, it has been suggested that GORD may be involved at a muchearlier stage in shaping disease risk (eg, microbiome effects) [21]. The presentstudy also reported increased gastro-oesophageal reflux disease caused by succeeding rheumatoid arthritis. The additional analysis reported increased risks of rheumatoid arthritis for females compared to the male population (females OR 3.36, 95% CI 2.30 to 4.91, males OR 2.00, 95% CI 1.18 to 3.37) [22]. The prevalence of rheumatoid arthritis was found at 70% among women patients. Age was found statistically insignificant when stratification was done by age.

It is unclear how the RA risk is increased in patients with GORD. Though preliminary evidence focuses primarily on the lower GI, it suggests that the microbiome may play a role in many autoimmune diseases, including RA [23].Rheumatoid arthritis pathogenesis different parameters were investigated by laboratory and clinical research. These parameters of factors included inflammatory pathways, environmental factors, and genetic factors. The prevailing hypothesis is the mucosal and immune responses affected by gut microbiota or mouth specific organism leads to rheumatoid arthritis joints pain [24]. The comparison was made between recent-onset rheumatoid arthritis and chronic rheumatoid arthritis stool samples revealed over magnified Prevotellacopri in the microbiota of the guts [25]. In human beings, autoantibodies and C - reactive protein was associated with GI, oral, and salivary microbial population with modified citrullinatedpeptides status [26].

Despite the advanced technology such as HREMI, the GI disease and findings of esophageal monomeric were not clearly addressed in rheumatoid arthritis patients. In our study, about 13%patients had rheumatoid disorders such as rheumatoid arthritis, SSc, and SLE among845 patients. The differentiation between different rheumatoid disorders has not been carried out in gastrointestinal disease patients. Rheumatoid disorders patients had higher mean peak pressure and UES residual pressure, frequent HH, lower bolus clearance,and weaker DCI. The most common motility disorders are IEM and AC.

Rheumatoid arthritis 19.1%, SLE 10.9% and SSc 26.4% were the common rheumatoid arthritis patients who underwent high-resolution esophageal manometry impedance. Compared to the general population, rheumatoid disorders were more prevalent in rheumatoid disorders patients. The rheumatoid disorders increase the incidence of GI symptoms on HREMI evaluation. In our study, the BMI and obesity of the SLE, RA, and SSc patients were significantly high while BMI in EGJ obstructive disorder patients were higher than most of the other disorders, minor disorders, and normal population. The chronic inflammatory low-grade state is relevant to obesity which plays a key role in rheumatoid disorders pathogenesis [27]. Some studies reported higher esophageal motility disorders among obese patients due to distal esophagus intra-abdominal pressure leads to compensatory hyper-contractility, sphincter obstruction, and LES function [28]. In contrast, another study reported esophageal motility disorders were lower in obese patients [29].

Esophageal peristalsis reduced by esophageal smooth muscles replacement with fibrous tissue in SSc patients.The abnormal esophageal motility etiology is still uncertain in SLE but inflammation of esophageal muscular to vasculitis might be responsible [30]. Motility disorders of the esophagus were found in 1/3 patients of rheumatoid arthritis, while distal smooth muscles and proximal striated decreased with secondary peristalsis [31]. The prevalent symptoms of gastrointestinal disease in patients who underwent HREMI with rheumatoid patients were dysphagia, vomiting, chest pain, heartburn, nausea, and regurgitation. The GI symptoms severity could not

differentiate the rheumatoid disorders, signifying GI symptoms as deprived prognosticators for primary esophageal motor abnormalities. Previous studies proposed that GI symptoms with RDs are frequently associated with manometric abnormalities in inappropriate ways [32]. The GI symptoms severity has no significant association with RA, SLE, and SSc. While other patients noticed lesser severity of GI symptoms when medicated with PPI and chronic opioids in esophageal abnormalities.

CONCLUSION

Our study concluded that subsequent rheumatoid arthritis has a significant association with gastro-oesophageal reflux disease. About 13% of GORD patients presenting to our OPD had rheumatologic disorders. All rheumatologic disorders patients should be screened for GI diseases and put on prophylactic medication to prevent GI complications in these patients.

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