Prevalence of gastroesophageal reflux disease in patients with rheumatoid arthritis

Mohamed A. Esmail[1], Dalia S. Mustafa[1], Doaa A. Ibrahim[1] and El-Zahraa M. Meghezel[2]

(1) Department of Rheumatology and Rehabilitation, Sohag Faculty of Medicine, Sohag University

(2) Department of Tropical Medicine and Gastroenterology, Sohag Faculty of Medicine, Sohag University

Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune systemic inflammatory multisystem disease of unknown cause marked by symmetric, peripheral polyarthritis. The prevalence of GERD began to increase from the end of the 1990s, and is now very common, especially in the elderly population, ranging from 1.4% to 52.1% in the literature, Furthermore, GERD often accompanies many chronic diseases such as diabetic mellitus (DM), chronic liver disease, obstructive sleep apnea syndrome (OSAS), and bronchial asthma.

Aim of the work: To assess the prevalence of GERD symptoms in patients with Rheumatoid arthritis (RA).

Patients and Methods: Case control study, included 100 adult rheumatoid arthritis patients and 25 age and sex matching control, All recruited from rheumatology outpatient clinics in Sohag university hospital diagnosed according to the European League Against Rheumatism (EULAR) classification criteria 2010 for RA.

Results: the percentage of GERD according to the FSSG score was higher among cases (49%) compared to controls (20%), with significant difference.

although mHAQ is increased among patients with GERD compared to those without, the difference was not significant. GERD was much prevalent among high and moderate disease activity group compared to low disease activity and remission cases but difference was not statically significant.

Conclusion: Rheumatoid arthritis can be considered as an independent risk factor for GERD. Disease activity could not be considered as risk factor for GERD

Keywords: RA, GERD.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune systemic inflammatory multisystem disease of unknown cause marked by symmetric, peripheral polyarthritis. As it is systemic disease, it may result in a variety of extraarticular manifestations, including gastrointestinal manifestations (1).

Gastro-esophageal reflux disease (GERD) is a chronic, relapsing disorder characterized by recurrent symptoms of heartburn and regurgitation whereas atypical symptoms are epigastric fullness or pressure, epigastric pain, nausea, bloating and belching that may overlap with other conditions such as peptic ulcer disease, gastritis, dyspepsia and gastroparesis. Lastly, there are many extra-esophageal complications including cough, wheezing, hoarseness and sore throat (2).

The prevalence of GERD began to increase from the end of the 1990s, and is now very common, especially in the elderly population, ranging from 1.4% to 52.1% in the literature,

Furthermore, GERD often accompanies many chronic diseases such as diabetic mellitus (DM), chronic liver disease, obstructive sleep apnea syndrome (OSAS), and bronchial asthma (3).

Patients with chronic autoimmune conditions such as rheumatic disorders, are associated with increased gastrointestinal (GI) symptoms. Patients with RA are frequently complicated with gastric mucosal injury; however, there are few reports investigating gastroesophageal reflux disease (GERD) among patients with RA (3).

Aim of the work:

1. To assess the prevalence of GERD symptoms in patients with Rheumatoid arthritis (RA).
2. To assess whether GERD symptoms correlate with several clinical factors of RA, including medications, patients' functional status and disease activity or not.

Patients and Methods:

Design: Case control study.

Patients: This study included 100 adult rheumatoid arthritis patients and 25 age and sex matching control, All recruited from rheumatology outpatient clinics in Sohag university hospital diagnosed according to the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria 2010 for RA (4).

Exclusion criteria:

1- Any collagen disease other than RA.
2- Pregnant women.
3- Chronic liver diseased patient.
4-Cardiovasculardiseased patients.
5-Patients who had undergone cholecystectomy or with chronic cholecystitis.
6-Asthmatic patients.

Ethical consideration: All participants (Patients and controls) were given a written consent before participating in the study which approved by the Ethical Committee of Sohag faculty of medicine, and asked during face-to-face interviews.

Methods:

- All of the patients were selected randomly and underwent:

1- Medical and rheumatological history taking with a special focus on symptoms of GERD.

2-Careful general, musculoskeletal examination.

3-All patients were interviewed to respond to the Frequency Scale questionnaire (5) for the Symptoms of GERD (FSSG).

4-Assessment if GERD symptoms correlate with several clinical factors of RA, including medications (Prednisolone, DMARDs, NSAIDs, PPI, histamine 2 receptor-antagonists, gastro mucosal protective agents, and other anti-osteoporosis agents).

5- Patients' functional status was evaluated by the Modified Health Assessment Questionnaire (mHAQ) (6, 7).

6-Assessment of disease activity will be performed using the Disease Activity Score (DAS28) including 28 tender and swollen joint count score, ESR and visual analogue score (8). A DAS28 score of higher than 5.1 is indicative of high disease activity, whereas a DAS28 below 3.2 indicates low disease activity. A patient is considered to be in remission if they have a DAS28 lower than 2.6.

7- Laboratory investigations: complete blood count (CBC), erythrocytic sedimentation rate (ESR), C-reactive protein (CRP), alanine amino-transferase (ALT), fasting and postprandial blood sugar, serum creatinine and urine analysis.

Statistical analysis:

Statistical analysis was carried out using (SPSS Inc., Chicago, USA, version 22), Student's test was done to compare means of quantitative data and Chi-square test was done to compare percentages of qualitative data. Pearson correlation coefficient was done to correlate FSSG score with each of the mHAQ and DAS28. P value was considered significant if < 0.05%.

Results

The mean age of our study population was 47.8±9.2 years for cases and 44.5±12.3 years for controls with no significant difference (P value = 0.134). The majority of the study participants were females (79% among cases and 88% among controls); also with non significant differences (P value = 0.307). Both groups showed non significant differences regarding routine investigations; with the exception of ESR which were significantly higher among cases compared to controls (40.4±22.6 for cases, 21.2±8.3 for control; p value <0.001).

The mean GERD questionnaire was higher in case group than control group with a significant difference. Here, we used Mann Whitney test instead of Student's t test, because the data was non parametric (very high SD compared to mean) (table 1). The percentage of GERD according to the FSSG score was higher among cases (49%) compared to controls (20%), with significant difference (table 2)

The mean mHAQ was higher in case group than control group with high significant difference (p value < 0.001) (table 3).

Although mHAQ is increased among patients with GERD compared to those without, the difference was not significant (table 4).

Also, although GERD was much prevalent among high and moderate disease activity group compared to low disease activity and remission cases, the difference was non significant using chi square test (table 5).

Using Pearson Correlation test, there is weak, positive and significant correlation between FSSG score and DAS score. Also, there is weak, positive and significant correlation between FSSG score and mHAQ (table 6).

Using Univariate logistic regression analysis, we found that RA can be considered as an independent risk factor for GERD. Disease activity could not be considered as risk factor for GERD. There is no need to do multivariate regression analysis, as there is only one item (rheumatoid arthritis) which showed significant result on univariate regression analysis (table 7).

Table 1: Mean FSSG Score (GERD Questionnaire) among 2 groups

	Group	Mean	Std. Deviation	Std. Error Mean
GERD Questionnaire	Case	10.420	8.6832	.8683
	Control	6.640	6.5056	1.3011

Mann Whitney test = 880, p value = 0.022 (S)

Table 2: Number of GERD cases according to the questionnaire in both groups

		Group		Total
		Case	Control	
Group	Not GERD	51(51%)	20(80%)	71(56.8%)
	GERD	49(49%)	5(20%)	54(43.2%)

Chi square = 6.855, p value = 0.009 (S)

Table 3: mHAQ between cases and control

Group		Mean	Std. Deviation	Std. Error Mean
mHAQ	Case	1.1700	.76655	.07666
	Control	.0000	.00000	.00000

T test =7.608, p value < 0.001 (HS)

Table 4: Mean mHAQ of patients according to presence or absence of GERD

Presence of GERD	Mean mHAQ	Std. Deviation
GERD	1.019	0.829
No GERD	0.873	0.832

Mann Whitney test = 1662.5, p value = 0.201

Table 5: Relation between disease activity score and prevalence of GERD among case group

		Group	
		Not GERD	GERD
DAS	RA in Remission	8(50%)	8(50%)
	Low disease activity	14(77.8%)	4(22.2%)
	Moderate disease activity	21(43.8%)	27(56.2%)
	High disease activity	8(44.4%)	10(55.6%)

Chi square = 6.490, p value = 0.090 (NS)

Table 6. Correlation between FSSG score and both of RA disease activity (DAS) and quality of life (mHAQ)

		GERD Questionnaire
DAS Score	Pearson Correlation	0.248
	P value	0.013
mHAQ	Pearson Correlation	0.111
	P value	0.027

Table 7: Univariate regression analysis for the possible risk factors of GERD

Item	Odd's ratio	CI of odd's	P value
RA	3.843	1.337-11.043	**0.012 (S)**
Age	1.017	0.981-1.055	0.347
Male sex	2.114	0.807-5.538	0.128
Hypertension	1.081	0.439-2.663	0.886
DM	1.339	0.537-3.343	0.531
MTX dose	0.963	0.890-1.042	0.352
Steroid	1.297	0.585-2.876	0.522
NSAIDs	1.518	0.686-3.361	0.303
mHAQ	0.851	0.508-1.427	0.542
DAS-28 score	1.258	0.924-1.714	0.145
ESR	0.994	0.977-1.012	0.529
CRP	1.014	0.994-1.034	0.172
RF	3.261	0.327-32.470	0.313
Anti CCP	1.042	0.439-2.472	0.926
Fasting blood sugar	1.015	0.996-1.034	0.119

Discussion

In our study, patients in case group were slightly older than control group and this difference was non significant (P = 0.134). Our study shows that majority of patients in 2 groups were female and only 21 patients were males (from case group) and this difference was non significant and may be related to RA which is common in females than males.

In the present group of RA patients mean of GERD questionnaire was 10.4±8.6. Also the prevalence of GERD according to the FSSG score was higher among cases (49%) compared to controls (20%), with significant difference.

Similar to a study was done in Japan in 2013 by **Nampei et al** (1) the prevalence of GERD symptoms was 29.5% (82/278) also In a review by **Fujiwara and Arakawa** (9), the prevalence of GERD symptoms in Japanese patients with chronic liver disease and OSAS evaluated by the FSSG was 15.3–19.3% and 30.4–31.5%, respectively.

The mechanism of GERD symptoms in RA patients is unclear. A well known histological disorder in GI system in RA should be amyloidosis, in which excessive serum amyloid, an acute phase reactant protein produced by liver in chronic inflammatory diseases, deposit within GI mucosa causing dysfunction of GI tract (10).

In our study, the mean of mHAQ was 1.1±0.7 which is higher in case group than control group with high significant difference (p value < 0.001). Higher HAQ was also significantly associated with occurrence of GERD in RA patients in **Myasoedova's** report (11).

Also, the results of the study done by **Miura et al** (3) showed that mHAQ was significantly higher among RA patients with GERD (diagnosed by FSSG score) compared to RA patients without GERD. The difference between these studies and our study as non significant mHAQ difference (P value= 0.2) between GERD and non GERD cases may be due to lower number of cases included in our study.

As regard the relation between disease activity score and GERD occurrence, we found that, although GERD was much prevalent among high (55,6%) and moderate (56,3%) disease activity group compared to low disease activity (22,2%) and remission cases (50%), the difference was non significant using chi square test. The limited number of remission cases (only 16 cases) and the relatively high GERD prevalence among them (50%) may be the cause of this non significance.

Our results were similar to that seen by **Miura et al** (3) as they found that the prevalence of GERD was positively correlated with disease activity among RA patients. However, they stated that this correlation was statistically significant ($p<0.001$).

When we studied the Correlation between FSSG score and both of RA disease activity (DAS) and quality of life (mHAQ) by using Pearson Correlation test, there was weak, positive and significant correlation between FSSG score and DAS score. Also, there was weak, positive and significant correlation between FSSG score and mHAQ. This was similar to studies done by both of **Nampei et al** (1) and **Miura et al** (3), who stated a positive and significant correlations between FSSG score and each of DAS and mHAQ using Pearson Correlation test.

Our study shows that rheumatoid arthritis can be considered as an independent risk factor for GERD. Disease activity could not be considered as risk factor for GERD using Univariate regression analysis for the possible risk factors of GERD; as p value = 0,012 and Odd's ratio =3,8. There is no need to do multivariate regression analysis, as there is only one item (rheumatoid arthritis) which showed significant result on univariate regression analysis. This was unlike the study done by **Nampei et al** (1) which showed that statistically significant factors for the risk of GERD symptoms were increase in height, 0.960; 95% CI, 0.927–0.995; p = 0.0211), higher mHAQ score (odds ratio for a SD (= 0.67) increase in mHAQ, 3.428; 95% CI, 2.242–5.243; p<0.0001), and prednisolone intake (odds ratio, 2.579; 95% CI, 1.448–4.592; p = 0.0008). It should be noted that **Nampei et al** (1) did not include any controls, and that they included higher number of cases (278 cases), this may explain the difference between our results and their results.

Conclusion:

Rheumatoid arthritis can be considered as an independent risk factor for GERD. Disease activity could not be considered as risk factor for GERD

We believe that clinicians should be aware of GERD symptoms in patients with RA, especially those with relatively low functional status or poor quality of life.

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