Prevalence of gastroesophageal reflux disease in patients with rheumatoid arthritis

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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 patients recruited from rheumatology out patient clinics in Sohag university hospital diagnosed according to the European League Against Rheumatism (EULAR) classification criteria 2010 for RA.

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

Conclusion: Our results showed that in the present group of RA patients mean of GERD questionnaire was 10.4 which is higher in case group than control group with significant difference

Keywords: RA, GERD.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune systemic inflammatory multisystem disease of unknown cause marked by symmetric, peripheral polyarthritis. It is the most common form of inflammatory arthritis and often results in joint damage and physical disability. As it is systemic disease, it may result in a variety of extraarticular manifestations, including fatigue, subcutaneous nodules lung involvement, pericarditis, peripheral neuropathy, vasculitis and hematologic abnormalities, also including gastrointestinal manifestations, with high prevalence (1).

Although the cause of RA is unknown, autoimmunity plays a pivotal role in both its chronicity and its progression through the high level of cytokines, especially the tumor necrosis factor alpha. 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 a variety of 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. This may be due to medications used for treatment of these rheumatic disorders, such as the non-steroidal anti-inflammatory drugs (NSAIDs), steroids and disease modifying drugs, have been associated with significant GI adverse events. Patients with rheumatoid arthritis (RA) are frequently complicated with gastric mucosal injury; however, there are few reports investigating gastroesophageal reflux disease (GERD) among patients with RA (3). The effect of GERD on Quality Of Life was also investigated in a Swedish study of a representative sample of a predominantly rural population. Evidence from a random sample showed that subjects reporting GERD symptoms had significantly lower. Health-related quality of life (HRQL) scores than people without such symptoms, whether or not esophagitis was present (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 patients recruited from rheumatology out patient clinics in Sohag university hospital diagnosed according to the European League Against Rheumatism (EULAR) classification criteria 2010 for RA.

Methods:
All of the patients will be selected randomly and will undergo:
1- Medical and rheumatological history taking with a special focus on symptoms of GERD .
2- Careful general , musculoskeletal examination.
3- All patients will be interviewed to respond to the the Frequency Scale questionnaire for the Symptoms of GERD (FSSG) . The questionnaire is a self-report instrument, written in simple and easy-to understand language, containing 12 questions.

(1) Do you get heartburn?
(2) Does your stomach feel bloated?
(3) Does your stomach ever feel heavy after meals?
(4) Do you sometimes subconsciously rub your chest with your hand?
(5) Do you ever feel sick after meals?
(6) Do you get heartburn after meals?
(7) Do you have an unusual sensation in your throat?
(8) Do you feel full while eating meals?
(9) Do some things get stuck when you swallow?
(10) Do you get bitter liquid coming up into your throat?
(11) Do you get heartburn if you bend over?
(12) Do you burp a lot?

Symptom frequency will be measured on the following scale:
Never = 0; occasionally = 1; sometimes = 2;often = 3; and always = 4. If points ≥8., GERD is considered to be present .

We also asked about:
1. The presence of nocturnal asthma like symptoms, cough, hoarseness of voice.
2. Do you ever seek medical advice for any of the above mentioned problems?
3. If yes; what type of medication and
4. Special habits as drinking alcohol, cigarette or goza smoking.

**Inclusion criteria:**
Patients previously diagnosed as Rheumatoid arthritic according to the European League Against Rheumatism (EULAR) classification criteria 2010 for RA.

**Exclusion criteria:**
1- Any collagen disease other than RA.
2- Pregnant women.
3- Chronic liver diseased patient
4- Cardiovascular diseased patients
5- Patients who had undergone cholecystectomy or with chronic cholecystitis.
6- Asthmatic patients.
7- Esophageal cancer.

**Results**
Patients in case group were slightly older than control group and this difference was non significant. Mean of GERD questionnaire was higher in case group than control group with a significant difference. Here, we used Mann Whitney test in stead of Student's t test, because the data was non parametric (very high SD compared to mean). The percentage of GERD according to the FSSG score was higher among cases (49%) compared to controls (20%), with significant difference. Mean of MHAQ was higher in case group than control group. Half of our cases fell in the moderate disease activity group. Remission was seen in only 16% of our cases. 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.

FSSG score was much higher among high and moderate disease activity group compared to low disease activity and remission cases, the difference was non significant using ANOVA test. Rheumatoid arthritis 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 1** show comparison between patients with or without GERD symptoms regarding RF and anti CCP

<table>
<thead>
<tr>
<th></th>
<th>RA with GERD (N=49)</th>
<th>RA without GERD (N=51)</th>
<th>Total</th>
<th>Chi square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RF</strong></td>
<td>47</td>
<td>49</td>
<td>96</td>
<td>0.002</td>
<td>0.964</td>
</tr>
<tr>
<td><strong>Anti CCP</strong></td>
<td>34</td>
<td>37</td>
<td>71</td>
<td>0.121</td>
<td>0.728</td>
</tr>
</tbody>
</table>

**Table 2** show correlation between FSSG score and both of RA disease activity (DAS) and quality of life (MHAQ)

<table>
<thead>
<tr>
<th></th>
<th>GERD Questionnaire</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>DAS Score</td>
<td>Pearson Correlation</td>
<td>0.248</td>
<td>P value</td>
</tr>
<tr>
<td>MHAQ</td>
<td>Pearson Correlation</td>
<td>0.111</td>
<td>P value</td>
</tr>
</tbody>
</table>

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Discussion

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 order to explain this difference. In other cohort of patients from Europe, that showed resemblances with ours, with a large proportion of Caucasians, the percentage of female population varies from 64.3% (Irland) to 88% (Serbia) (4). In other countries (Hungry, Serbia, Poland, Rusia), women with RA represent more than 80% of the analyzed study groups, percentage in accordance to our data. Women with RA report decreased joint symptoms during the postovulatory phase of the menstrual cycle and during pregnancy, when estradiol and progesterone levels are high. In contrast, RA symptoms often flare in the postpartum period, when estrogen and progesterone levels fall. Women are at a decreased risk of developing RA during pregnancy, but the first few months of the postpartum period are a time of increased risk (5).

In this study, we evaluated GERD symptoms using the FSSG questionnaire. It is important which rating system is used in an evaluation of clinical symptoms, and the FSSG questionnaire can be regarded as a reasonable tool, because its sensitivity, specificity and accuracy have been proven equal to those of another structured questionnaire for GERD symptoms, QUEST (questionnaire in the assessment of symptomatic gastroesophageal reflux disease). Furthermore, the FSSG comprises 12 questions about the most commonly experienced symptoms in GERD, concerning not only reflux symptoms (7 questions) but also acid-related dyspepsia (5 questions). Our results shows that mean of GERD questionnaire was higher in case group than control group with a significant difference. Here, we used Mann Whitney test in stead of Student's t test, because the data was non parametric (very high SD compared to mean).

In the present group of RA patients mean of GERD questionnaire was 10.4 and of standard deviation 8.6, also the prevalence of GERD according to the FSSG score was higher among cases (49%) compared to controls (20%), with significant difference. 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. This condition is rather well known in lower GI tract, which often manifests severe diarrhea, but can also be observed in upper GI tract in RA, and significantly associated with reflux esophagitis in chronic renal failure patients, GI amyloidosis in RA, including upper GI lesion, has recently been reported to be improved by treatment with such biologics as infliximab and tocilizumab (6).

Since the prevalence of GI amyloidosis was reported around 10% by histological evaluation of stomach and duodenum biopsy (6), patients with upper GI amyloidosis could have been included in our study. Unfortunately, however, we did not perform endoscopy and biopsy in this study, and it is unclear whether such histological disorders as amyloidosis were included and whether they associated with GERD symptoms.

In our study mean of MHAQ was was 1.1 and SD .7 which is higher in case group than control group with high
significant difference (p value < 0.001).

Several studies Dhir et al. (7), and Deo et al. (8) provided data compiled from administering the Stanford Health Assessment Questionnaire (HAQ) disability index. The scores for a completed HAQ can range from 0 (no disability) to 3 (completely disabled), with 0 to 1 representing mild to moderate difficulty, 1 to 2 representing moderate to severe disability, and 2 to 3 representing severe to very severe disability. Average scores previously reported from a population based study are 0.49 for the general population and 1.2 for RA patients. In those studies providing mean HAQ scores, the mean ranged from 0.7 to 1.2 among RA patients, indicating moderate disability.

Also, in RA and OA patients, QOL evaluated by HAQ was reported to be a significant risk factor for hospitalization because of GI events, with one unit increase (worsening) in HAQ (1).

In our study Mean MHAQ of patients is increased among patients with GERD (1.0) compared to those without(0.8), the difference was statistically not significant p value = 0.2, also when we studied the relation between disease activity and prevalence of GERD 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 (6.4) and p value=0.090. 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).

Our results show that heart burn, bloating, rub chest with hands, liquid bitter and burb a lot are the 5 items which showed significant higher prevalence among RA cases compared to controls.

Also show that majority of patients in both groups no smoke but take spicy food and tea with non significant difference. Majority of patients in both groups not take coffee (p value=0.001) or fatty meals (p value=0.006) with significant difference.

In our study routine investigations were similar in majority of patients in the two groups with non significant differences. Also shows that there is non significant relation between the presence of GERD among RA patients and the positivity of either RF (p value=0.964) or anti-CCP (p value=0.728).

Our study shows that patients with GERD used anti-osteooporosis (49%), NSAIDs (26%) and MTX (46%) drugs more frequently than patients without GERD. As 49% of patients with GERD take antisteooporotic drugs, These differences were statistically significant this is similar to Miyakoshi et al. (9) which studied patients with osteoporosis and reported that GERD symptoms were significantly associated with increases in the angle of lumbar kyphosis and the number of vertebral fractures.

Our study shows that around 44% of cases take NSAIDs and only 28% of the control take NSAIDs, This different was non significant,while different was significant between RA cases with GERD (53%) and RAcases without GERD(35%), this was similar to a study done by Nampei et al. (4) that showed a strong association of NSAIDs with GI lesions, including GERD, has long been
reported in non-arthritic patients. Cryer et al. (10) studied the persistence of NSAID prescription in OA and RA patients with concomitant GERD, comparing non-selective NSAID and celecoxib, a selective COX-2 inhibitor, and reported that significantly more patients treated with celecoxib were persistent than non-selective NSAIDs. From the results of our study along with Cryer’s report, COX-2 inhibitors could be prescribed more safely than non-selective NSAID with regard to GI lesions including GERD.

Conclusion

Our results showed that in the present group of RA patients mean of GERD questionnaire was 10.4 which is higher in case group than control group with significant difference (p value equal 0.02).

In conclusion, prevalence of GERD symptoms was considerably high in RA patients with GERD (49%) to Non GERD patients (20%) with significant difference (p value =0.009), and there was an association with higher MHAQ score , rheumatoid arthritis can be considered as an independent risk factor for GERD.

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

References


10. Cryer B. Luo X, Assaf AR, Sands G, Mardekian J. Persistence with non-