Objective: To study the relationship of the presence of secondary SS with disease activity, duration in RA.

Methods: Eighty two patients with RA were submitted to Schirmer test, minor salivary gland biopsy, questionnaire on sicca symptoms, DAS-28 4v determination.

Results: In this population, 20 (24.3%) patients fulfilled the American-European classification criteria for secondary SS. No relation could be found between the presence of secondary SS and disease activity (p = 0.31) and RA duration (p = 0.95).

Conclusion: Appearance of Secondary SS in RA patients is independent of RA duration or activity.

Keywords: Arthritis, rheumatoid; dry eye syndromes; inflammation.
INTRODUCTION
Sjögren’s syndrome (SS) is a chronic autoimmune inflammatory disease that affects lachrymal and salivary glands causing mucous dryness that affects mainly middle aged women\(^1\). SS can be a primary or a secondary disease when it is associated with other autoimmune disorders such as scleroderma and rheumatoid arthritis (RA)\(^2\). Superimposed SS in RA is an interesting finding. B cells and type I interferon are an important role of B cells and type I interferon in primary SS\(^2,3\) in contrast to the predominance of 17 cytokines in RA\(^4\). As the physiopathology of these two diseases is distinct, it is possible to suggest that patients with RA and secondary SS have two different diseases or that RA secondary SS has a different physiopathology than the primary form. In this context we aimed to study if RA disease activity or severity have any association with occurrence of secondary Sjögren’s syndrome.

METHODS
is study was approved by the Committee for Ethics in Research of our institution and all participants signed consent. To participate in the study patients had to present at least four criteria of the American College of Rheumatic Diseases for RA\(^7\). Included patients were selected from a single Rheumatology Clinic (Evangelic University Hospital) chosen according to appointment order and willingness to participate in the study. We excluded patients with ophthalmologic complications such as scleritis, episcleritis, scleromalacia, those with prior eye surgery and contact lenses users or those taking medications such as antidepressants, anticholinergics, antihistamine, diuretics, etc, those with hepatitis C or HIV infection or prior irradiation of the neck.

All included patients had Schirmer test done according to standard recommendations and we considered a patient to be with definitive dry eye when values were equal or under 5 mm in at least one eye\(^8\). Biopsy of minor salivary gland was done in all included patients and sections were stained by hematoxylin-eosin and considered positive when a focus of 50 lymphocytes/4 mm\(^2\) was found\(^9\). Salivary gland biopsy was read by a blinded pathologist. Simultaneously with eye tests and minor salivary gland biopsy, patients had DAS-28 \(^{4v10,11}\) and also answered a questionnaire on sicca symptoms (oral and ocular). DAS 28 is a measurement of RA disease activity that takes into account number of swollen and tender joints, a measurement of general health by the patients and values of sedimentation rate. Patients with DAS28 values under 2.6 are considered under remission, with values between 2.6 and 3.1 as having mild disease activity; with values between 3.2 and 5.1 as having moderate activity and over 5.1 with high disease activity.

Patient’s joint count was done by just one rheumatologist. Charts were reviewed for demographic data, HAQ\(^2\) and autoantibody profile (latex, anti CCP, anti Ro, Anti La).

To consider a RA patient as having secondary SS it was necessary to fulfill the American European Criteria for secondary SS\(^13,14\).

Data were grouped in contingency and frequency table. For association studies we used the chi-squared test for nominal data and unpaired t and Mann-Whitney tests for numeric data. The significance adopted was 5%.

RESULTS
Eighty two patients were included: 72 women and 10 men with mean age of 51.8 ± 10.0 years and mean disease duration of 10.2 ± 7.0 years. In this sample 50/82 (75%) had rheumatoid factor; 25/35 (71.4%) had a positive anti- CCP; 25/82 (30.4%) were ANA positive; 6/82 (7.3%) had anti-Ro and 1/82 (1.2%) had anti-La. RA treatment was done with prednisone in 62/82 (75.6%); antimalarials in 63/82 (76.8%); methotrexate in 71/82 (86.5%), lefunomide in 33/82 (40.2%), sulphasalazine in 11/82 (13.4%), anti TNF- α in 8/82 (9.7%) and rituximab in 2/82 (2.4%). Dry eye complaints were found in 47/82 (57.3%) and dry mouth in 29/82 (35.3%); antimalarials in 63/82 (76.8%); methotrexate in 71/82 (86.5%), lefunomide in 33/82 (40.2%), sulphasalazine in 11/82 (13.4%), anti TNF- α in 8/82 (9.7%) and rituximab in 2/82 (2.4%).

DAS 28 varied from 0.6 to 6.99 (mean 3.22 ± 1.41). Twenty patients (24.39%) fulfilled the American-European criteria for Secondary SS. Studying DAS-28 according to the presence of secondary SS, we found a mean value of 2.81 ± 1.14 in those with SS and 3.35 ± 1.47 in those without it (p = 0.13). The mean value of DAS-28 in patients with Schirmer test under 5 mm was 3.1 ± 1.3 and in those with values higher than 5 mm it was 3.3 ± 1.4 (p = 0.50). Presence of Secondary SS according to DAS-28 is shown in Figure 1.

Figure 1 – Presence of secondary Sjögren’s syndrome according to DAS-28 in 82 patients with rheumatoid arthritis (p = 0.61).
Table 1 shows data in RA patients with and without Secondary SS Syndrome.

**DISCUSSION**

The presence of sicca symptoms was high in the studied population although only 24% of patients fulfilled criteria for secondary SS. However, the present study could find no relationship with secondary SS when compared to those without it in their study of 72 RA patients. In Japan, 10% of patients without fulfilling the diagnostic criteria for secondary SS had secondary SS, whereas in the Spanish RA population, 10% of patients had secondary SS. The high prevalence of dry eyes in RA patients was noticed by Fujita *et al.*, who found it in 90% of non-SS RA patients. In a study done in Spain, a higher RA activity measured by DAS-28 was found in patients with secondary SS. Although we could not find any relation to disease duration, we could not find a higher RA activity had no significant correlation with the presence of sicca findings, we could not find a higher RA activity measured by DAS-28 in patients with secondary SS when compared to those without it in the present study. Therefore, it could also be established with functional index. Wolfe *et al.* found that sicca symptoms are more common in patients with RA with increased HAQ scores, pain and global severity as well as total joint replacement and work disability.

According to the present findings, rheumatologists and ophthalmologists should be aware of high indices of sicca symptoms in RA and seek for secondary SS independently of the activity or duration of rheumatoid arthritis.

**REFERENCES**