Original Article

GASTROINTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS: CORRELATION WITH IMMUNOLOGICAL ACTIVITY – A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background. Gastrointestinal involvement is a frequent complication of systemic sclerosis, contributing to morbidity and mortality. Standardized approaches for assessment remain limited in low-resource settings**.**

Objective. To describe gastrointestinal involvement in Albanian systemic sclerosis patients, evaluate correlations with immunological markers, and compare findings with international data.

Methods: Retrospective review of 75 systemic sclerosis patients treated at the University Hospital Center "Mother Teresa," Tirana (2018–2022); complete data available for 62 patients. Gastrointestinal symptoms were assessed using the UCLA SCTC GIT 2.0 questionnaire. Clinical, laboratory, and selective endoscopic evaluations were performed. ANA, ENA, and Anti-Scl-70 antibodies were measured. Follow up every six months.

Results. Esophageal involvement was most frequent (90%), followed by intestinal involvement (40–70%). Oral manifestations: xerostomia (32%), microstomia, microcheilia. Dysphagia 25%, reflux 36%, GERD 32%, esophageal inflammation 39%. Gastric: gastroparesis 39%, GAVE 3.2%. Duodenal erosions 21.2%, malabsorption 26%. ANA+ 90%, ENA+ 78%, Anti-Scl-70+ 71%, all significantly correlated with Gastrointestinal involvement ($p<0.05$).

Conclusion. GI involvement in Albanian systemic sclerosis patients mirrors international patterns. ANA, ENA, and Anti-Scl-70 positivity are associated with Gastrointestinal manifestations. Systematic assessment using clinical, immunological, and selective endoscopic evaluation is feasible in low-resource settings. Prospective studies and local validation of symptom scoring tools are recommended.

Keywords. systemic sclerosis, gastrointestinal involvement, ANA, Anti-Scl-70, immunological activity

MANIFESTIMET GASTROINTESTINALE NË SKLEROZËN SISTEMIKE: KORRELACIONI ME AKTIVITETIN IMUNOLOGJIK – STUDIM RETROSPEKTIV

ABSTRAKT

Hyrje. Manifestimet gastrointestinale janë një komplikacion i shpeshtë i sklerozës sistemike, duke kontribuar në morbiditet dhe mortalitet. Qasjet standarde për vlerësim mbeten të kufizuara në vende me burime të pakta diagnostike.

Qëllimi. Të përshkruhen manifestimet gastrointestinale tek pacientët shqiptarë me sklerozë sistemike, të vlerësohen korrelacionet me treguesit imunologjikë dhe të krahasohen me të dhënat ndërkombëtare.

Metoda. U realizua një rishikim retrospektiv i 75 pacientëve me sklerozë sistemike të trajtuar në Qendrën Universitare të Spitalit "Nënë Tereza", Tiranë (2018–2022); të dhëna të plota ishin të disponueshme për 62 pacientë. Simptomat GI u vlerësuan me pyetësorin UCLA SCTC GIT 2.0, ndërsa u kryen ekzaminime klinike, laboratorike dhe endoskopike selektive. U matën antitrupat ANA, ENA dhe Anti-Scl-70. Pacientët ndiqeshin çdo gjashtë muaj.

Rezultate. Përfshirja ezofageale ishte më e shpeshta (90%), e ndjekur nga ajo intestinale (40–70%). Manifestimet orale përfshinin xerostomia (32%), microstomia dhe microcheilia, ndërsa 23% plotësonin kriteret për sindromën e Sjogren-it. Manifestimet ezofageale: dysphagia 25%, odynophagia 18%, reflux 36%, GERD 32%, strictures 28%, inflamacion 39%. Manifestimet gastrike përfshinin gastroparezë 39%, gastritis 30%, erosive gastritis 27%, ulcer gastrik 16%, dhe GAVE 3.2%. Në zorrët e vogla: erozionet duodenale 21.2%, malabsorbim 26%, mungesë e vitaminës B6 28%, mungesë e vitaminës B12 31%, anemi 32%, dysmotility intestinale 13%, dhe SIBO 12%. Koloni/anorektumi përfshinte dysmotility 15%, sindromin e zorrëve irritabile 21%, dhe disfunksion të sfinkterit anal 3%. Antitrupat ANA ishin pozitiv në 90% të pacientëve, ENA në 78%, dhe Anti-Scl-70 në 71%, të gjitha duke treguar korrelacion të ndjeshëm me manifestimet gastrointestinale ($p<0.05$).

Përfundimi. Manifestimet gastrointestinale tek pacientët shqiptarë me sklerozë sistemike pasqyrojnë modelet ndërkombëtare. Pozitiviteti i ANA, ENA dhe Anti-Scl-70 lidhet me shfaqjen e manifestimeve gastrointestinale. Vlerësimi sistematik duke përdorur ekzaminime klinike, imunologjike dhe endoskopike selektive është i realizueshëm edhe në mjedise me burime të kufizuara. Rekomandohen studime prospective dhe validimi lokal i instrumenteve për vlerësimin e simptomave.

Fjalë kyçe. sklerozë sistemike, manifestime gastrointestinale, ANA, Anti-Scl-70, aktivitet imunologjik

INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune connective tissue disease with microvascular injury, fibrosis, and multi-organ involvement [1–4]. Gastrointestinal (GI) complications occur in >90% of patients and impact prognosis and quality of life [5–7]. Esophageal dysmotility, gastroparesis, malabsorption, and colonic dysmotility are most frequent [8–10]. Immunological markers such as ANA, ENA, and Anti-Scl-70 often correlate with disease activity and organ involvement [11-13]. Data from low-resource countries are scarce, where access to endoscopy and imaging may be limited [14]. This study evaluates the prevalence, patterns, and immunological correlations of GI manifestations in Albanian SSc patients.

MATERIALS AND METHODS

This retrospective observational study included 75 patients with systemic sclerosis (SSc) treated between 2018 and 2022 at the Rheumatology Clinic and Consultation Center, University Hospital Center "Mother Teresa," Tirana. Complete data were available for 62 patients and were analyzed for this study.

Gastrointestinal (GI) involvement was assessed using the UCLA SCTC GIT 2.0 questionnaire, in conjunction with a clinical evaluation of the oral cavity, esophagus, stomach, small intestine, and colon/anorectum. Fibrogastroscopy was performed when clinically indicated. Patients were followed every six months according to international guidelines [5, 16], which included clinical assessments, laboratory tests, symptom scoring, and selective endoscopic evaluations [5, 16] evaluations [5, 16]. Small intestinal bacterial overgrowth (SIBO) was assessed based on breath testing, which was systematically performed.

Immunological assessment included testing for antinuclear antibodies (ANA), extractable nuclear antigen (ENA) profile, and anti-Scl-70 antibodies in all patients. Additional tests, such as rheumatoid factor (RF), anti-dsDNA, ANCA, and complement levels, were performed as clinically indicated.

Statistical Analysis

Descriptive statistics were used for demographic and clinical variables. Categorical variables were compared using Chi-square tests, and continuous variables were compared using t-tests. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 62 patients were analyzed, of whom 92% were female. The mean age was 48.2 years (men 56.2, women 49.5), with the most frequent age group being 56–65 years (39%). Male patients exhibited 38% higher gastrointestinal (GI) involvement compared to females.

Oral manifestations were common, with xerostomia and salivary gland fibrosis each present in 32% of patients, and Sjogren's syndrome in 23%. Esophageal involvement was the most frequent, including dysphagia in 25%, odynophagia in 18%, reflux in 36%, GERD in 32%, strictures in 28%, and esophageal inflammation in 39%. Gastric involvement included gastroparesis in 39%, gastritis in 30%, erosive gastritis in 27%, gastric ulcers in 16%, and GAVE in 3.2%. Small intestinal manifestations comprised duodenal erosions in 21.2%, malabsorption in 26%, vitamin B6 deficiency in 28%, vitamin B12 deficiency in 31%, anemia in 32%, intestinal dysmotility in 13%, and small intestinal bacterial overgrowth (SIBO) in 12%. Colonic and anorectal involvement, though less frequent, included dysmotility in 15%, irritable bowel syndrome in 21%, and anal sphincter dysfunction in 3%. Indirect manifestations such as muscle atrophy, altered intestinal reflexes, and dysmotility may contribute to functional GI impairment even in asymptomatic patients. Regarding immunological markers, ANA positivity was observed in 90% of patients, ENA in 78%, and Anti-Scl-70 antibodies in 71%. All three markers showed a significant correlation with GI involvement, with p-values of 0.01, 0.03, and 0.01, respectively.

Figure 1 illustrates the overall prevalence of GI manifestations across different organ systems, highlighting the predominance of esophageal and gastric involvement. These findings emphasize the importance of systematic assessment and monitoring, including both clinical evaluation and selective endoscopic examination, even in low-resource settings.

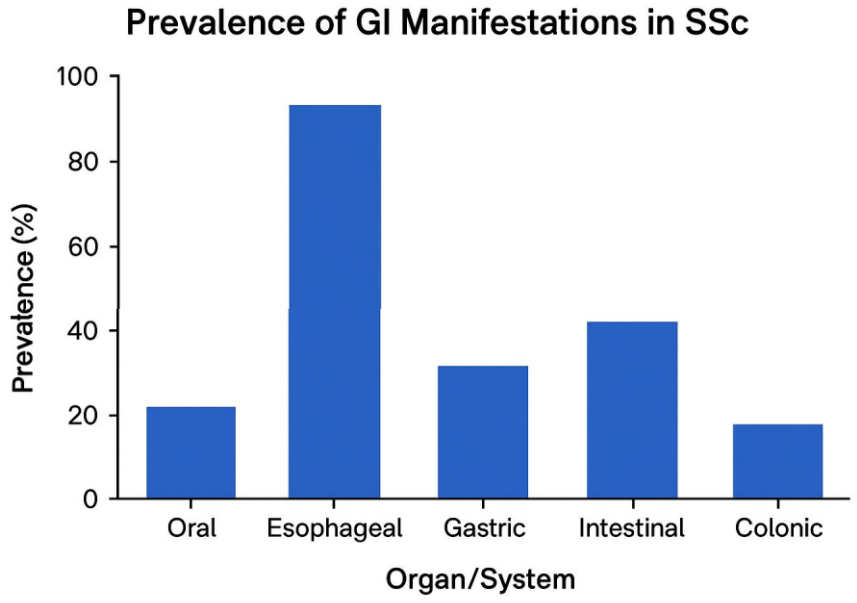

Figure 1. **T**he overall prevalence of GI manifestations across different organ systems.

DISCUSSION

Gastrointestinal (GI) involvement is highly prevalent among Albanian patients with systemic sclerosis (SSc), with esophageal manifestations, particularly dysmotility and gastroesophageal reflux, being the most frequent. This finding is consistent with data from European and US cohorts, which report esophageal involvement in up to 70–90% of patients with SSc [8,9,17]. The predominance of esophageal manifestations underscores the importance of early recognition and monitoring, as delayed diagnosis may lead to complications such as strictures, Barrett's esophagus, and significant nutritional deficiencies. Our study demonstrated significant correlations between autoantibody profiles, namely ANA, ENA, and anti-Scl-70, and the presence of GI manifestations. These results align with prior international literature, indicating that specific immunological patterns may predispose patients to more severe or extensive GI involvement [11,12,18]. In particular, anti-Scl-70 positivity has been previously associated with diffuse cutaneous SSc and increased risk of esophageal dysmotility, suggesting a possible pathogenic link between autoimmunity and gastrointestinal fibrosis. The UCLA SCTC GIT 2.0 questionnaire was used in this cohort to provide a structured evaluation of GI symptoms, including reflux, bloating, diarrhea, and constipation. Although this instrument is widely validated internationally, local cultural and linguistic validation is recommended to ensure accuracy and relevance of patient-reported outcomes in the Albanian population. Such validation would improve symptom assessment, enhance patient monitoring, and allow for better comparability with other cohorts [5,16].

From a clinical management perspective, systematic follow-up is essential. We recommend follow-up visits every six months, supplemented by selective fibrogastroscopy based on symptom severity or progression. Even in low-resource settings, this approach enables timely detection of esophageal complications and allows for earlier intervention, including dietary modifications, prokinetic therapy, and endoscopic management where indicated [5,16].
Although this study provides important insights into GI involvement in Albanian SSc patients, the relatively small sample size (n=62) and female predominance (92%) may limit the generalizability of the findings. Therefore, larger, multicenter studies are needed to confirm these observations and improve representativeness. Future research should also integrate comprehensive biomarker analysis, nutritional assessments, and detailed immunological profiling to elucidate pathogenic mechanisms, identify patients at higher risk for severe GI involvement, and guide individualized therapy.

CONCLUSIONS

Gastrointestinal involvement is common in Albanian SSc patients, particularly esophageal manifestations, and mirrors patterns seen internationally. ANA, ENA, and anti-Scl-70 positivity correlate with GI symptoms. Structured symptom assessment and selective endoscopic evaluation are feasible even in low-resource settings. Future studies should focus on local validation of symptom scores and prospective analyses to improve monitoring and management.

Conflicts of interest: The authors declare that they have no conflicts of interest.

REFERENCES

1. Gu YS, et al. Gastrointestinal manifestations in systemic sclerosis: clinical features and pathophysiology. Seminars in Arthritis and Rheumatism. 2008;38:132–160.
2. Thoua NM, et al.Assessment of gastrointestinal symptoms in systemic sclerosis using the UCLA SCTC GIT 2.0 questionnaire. Rheumatology (Oxford). 2010;49:1770– 1775.
3. Barnes J, Mayes MD. Epidemiology, clinical features, and pathogenesis of systemic sclerosis. Current Opinion in Rheumatology. 2012;24:165–170.
4. Chifflot H, et al. Gastrointestinal involvement in systemic sclerosis: a prospective study. Seminars in Arthritis and Rheumatism. 2008;37:223–235.
5. Jaeger AC, et al. Prevalence and impact of gastrointestinal involvement in systemic sclerosis. Journal of Rheumatology. 2016;43.
6. Ciaula AD, et al. Small intestinal bacterial overgrowth and motility disorders in systemic sclerosis. Digestive Diseases and Sciences. 2008;53:1234–1242.
7. Åkesson A, et al. Gastrointestinal manifestations of systemic sclerosis. British Journal of Rheumatology. 1989;28:81–86.
8. Marie I, et al. Digestive tract involvement in systemic sclerosis. Revue de Médecine Interne. 1999;20:504–513.
9. Lock G, et al. Gastrointestinal manifestations of progressive systemic sclerosis. American Journal of Gastroenterology. 1997;92:763–771. Sjogren RW.
10. Gastrointestinal motility disorders in systemic sclerosis. Arthritis and Rheumatism. 1994;37:1265–1282.
11. Jimenez SA, Derk CT. Following the molecular pathways toward an understanding of the pathogenesis of systemic sclerosis. Annals of Internal Medicine. 2004;140:37–50.
12. Greenblatt MB, Aliprantis AO. The immune pathogenesis of systemic sclerosis. Current Rheumatology Reports. 2013;15:297.
13. Zheng T, et al. Role of immune dysregulation and fibrosis in systemic sclerosis. Journal of Investigative Dermatology. 2009;129:742–751.
14. Savarino E, et al. Gastroesophageal reflux and pulmonary fibrosis in systemic sclerosis. American Journal of Respiratory and Critical Care Medicine. 2009;179:408–413.
15. Khanna D, et al. Development of a patient-reported outcome measure for

gastrointestinal involvement in systemic sclerosis: the UCLA SCTC GIT 2.0. Arthritis and Rheumatism. 2009;61:1257–1263.

16. EUSTAR Group. EULAR/EUSTAR recommendations for the management of systemic sclerosis. Annals of the Rheumatic Diseases. 2020.
17. Jaovisidha K, et al.Gastrointestinal manifestations of systemic sclerosis. Seminars in Arthritis and Rheumatism. 2005;34:689–702.
18. Assassi S, et al. Clinical and genetic factors predictive of organ involvement in systemic sclerosis. Arthritis and Rheumatism. 2009;61:1403–1411.