

## Prevalence of infectious agents in patients with systemic sclerosis: defining the control group

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### To the Editor,

In a recent interesting monocentre, prospective study published in the *Turkish Journal of Medical Sciences*, Bilgin et al. found a prevalence of *Helicobacter pylori* (*H. pylori*) antibodies (both IgM and IgG) significantly higher among systemic sclerosis (SSc) patients (73.3%) than in controls (46.6%) ( $P < 0.05$ ) (1).

In the latest two decades, several studies have reported potential links between chronic *H. pylori* infection and a variety of extragastric manifestations; these include ischemic heart disease, liver diseases, skin diseases, rheumatic diseases, blood disorders, and others (2).

Although the etiology of SSc remains uncertain, it has been reported that viral or bacterial infections can trigger autoimmune diseases. Some researchers have suggested that the production of specific autoantibodies in SSc patients is the result of an antigen-driven response caused by molecular mimicry (3) and the endothelial cells may be infected by bacteria that may be instrumental in inducing vasculitis, hence the importance of looking for infectious causal mechanisms.

The findings of the study by Bilgin et al. (1) and the conflicting results in the literature (4,5) deserve attention. It is crucial to avoid selection biases. In particular, defining the control group is a key step in planning and conducting a study.

The control group is used to compare the history of exposure in the cases with that in individuals who are free of the study disease. Individuals selected as controls should not only be free of the study disease, but should also be similar to the cases in regards to past potential for exposure. Stated somewhat differently, controls should be comparable to the cases in the sense that both groups would have been at equal risk of exposure if there were no disease-exposure association (6). *H. pylori* infection is associated with low socio-economic conditions and this should be taken into account when the control populations are selected (7). In assessing socio-economic status, its broad nature and the variety of elements that it includes should be recognised. Hence, such studies would require socially homogeneous populations to minimise confounding factors.

This information is not reported in the paper by Bilgin et al. (1); moreover, the authors reported a prevalence of *H. pylori* infection in the controls of only 46.6%, diagnosed by antibodies to *H. pylori* in serum, markers of exposure, and not necessarily of true infection, while in the literature (8) in Turkey *H. pylori* prevalence is very high, with a weighted overall prevalence of 82.5% tested with the urea breath test, able to diagnose the direct presence of the bacterium.

In conclusion, Bilgin et al. should report details about the control groups; this could enrich their findings.

### References

1. Bilgin H, Kocabaş H, Keşli R. The prevalence of infectious agents in patients with systemic sclerosis. *Turk J Med Sci* 2015; 45: 1192-1197.
2. Pellicano R, Franceschi F, Saracco G, Fagoonee S, Roccarina D, Gasbarrini A. Helicobacters and extragastric diseases. *Helicobacter* 2009; 14: 58-68.
3. Tachibana I, Bodorova J, Berditchevski F, Zutter MM, Helmer ME. NAG-2, a novel transmembrane-4 superfamily (TM4SF) protein that complexes with integrins and other TM4SF proteins. *J Biol Chem* 1997; 272: 181-189.
4. Sulli A, Serriolo B, Savarino V, Cutolo M. Lack of correlation between gastric *Helicobacter pylori* infection and primary or secondary Raynaud's phenomenon in patients with systemic sclerosis. *J Rheumatol* 2000; 27: 1820-1821.

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5. Danese S, Zoli A, Cremonini F, Gasbarrini A. High prevalence of *Helicobacter pylori* type I virulent strains in patients with systemic sclerosis. *J Rheumatol* 2000; 27: 1568-1569.
6. Stolley PD, Schlesselman JJ. Palnning and conducting a study. In: Schlesselman JJ editor. *Case-control studies*. New York, NY, USA: Oxford University Press; 1982. pp. 69-104.
7. Adriani A, Fagoonee S, De Angelis C, Altruda F, Pellicano R. *Helicobacter pylori* infection and dementia: can actual data reinforce the hypothesis of a causal association? *Panminerva Med* 2014; 56: 195-199.
8. Ozaydin N, Turkyilmaz SA, Cali S. Prevalence and risk factors of *Helicobacter pylori* in Turkey: a nationally-representative, cross-sectional, screening with the <sup>13</sup>C-Urea breath test. *BMC Public Health* 2013; 13: 1215.

## Reply to Letter to the Editor:

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### To The Editor;

We thank Dr Ribaldone for his interest in our article entitled “The prevalence of infectious agents in patients with systemic sclerosis” regarding the evaluation of the association between past and recent infections and the etiology of systemic sclerosis (1). We agree with his opinion that the control group should be similar to the cases in regards to past potential for exposure. In our study, the control group was similar to the study group in terms of age and sex. We conducted the study in the central parts of Turkey. However, we did not take into account socioeconomic status when both groups were determined.

The prevalence of *H. pylori* infection differs among developing and developed countries. The prevalence of

*H. pylori* infection is not more than 10% in developed countries, whereas it may reach up to 75%–80% in developing countries. In the studies carried out in different areas of Turkey, the rates of *H. pylori* positivity were found by Kesli et al. (2) to be 36.9%, by Us et al. (3) 53%, by Kaklıkaya et al. (4) 58.6%, and by Erzin et al. (5) 86%. In our study, the prevalence of *H. pylori* antibodies was 73.3% in SSc patients and 46.6% in the control group.

The infection prevalence alone should not be expected to provide adequate evidence for or against a pathological role in SSc. Thus, additional factors such as coinfections, and immunological and genetic host factors will have to be further identified and controlled to understand the role of infectious agents in SSc.

### References

1. Bilgin H, Kocabaş H, Keşli R. The prevalence of infectious agents in patients with systemic sclerosis. *Turk J Med Sci* 2015; 45: 1192-1197.
2. Kesli R, Gokturk HS, Erbayrak M, Karabagli P, Terzi Y. Comparison of the diagnostic values of the 3 different stool antigen tests for the noninvasive diagnosis of *Helicobacter pylori* infection. *J Investig Med* 2010; 58: 982-986.
3. Us D, Hascelik G. Seroprevalence of *Helicobacter pylori* infection in an asymptomatic Turkish population. *J Infect* 1998; 37: 148-150.
4. Kaklikkaya N, Akdogan RA, Ozgur O, Uzun DY, Cobanoglu U, Dinc U, Gungor E, Dabanca PA, Arslan M, Aydin F. Evaluation of a new rapid lateral flow chromatography test for the diagnosis of *Helicobacter pylori*. *Saudi Med J* 2006; 27: 799-803.
5. Erzin Y, Altun S, Dobrucali A, Aslan M, Erdamar S, Dirican A, Kocazeybek B. Comparison of two different stool antigen tests for the primary diagnosis of *Helicobacter pylori* infection in Turkish patients with dyspepsia. *Helicobacter* 2004; 9: 657-662.

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