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LETTER TO THE EDITOR

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Post COVID-19 joint pain: Preliminary report of the relationship with antinuclear antibodies and inflammation

1 | INTRODUCTION

Post-COVID syndrome includes a variety of symptoms after a SARS-CoV2 infection.[1] Close to 25% of the post-COVID patients have muscle or joint pain and there are case series reporting a prevalence of up to 50% of antinuclear antibodies (ANAs) in acute critically ill COVID-19 patients.[2] Our aim is to present a preliminary comparison of post-covid patients and their self-reported joint and muscle pain, their inflammatory markers, and ANAs.

2 | METHODS

We conducted a cross-sectional study of the initial patients evaluated at our post-COVID clinic. To be included in the post-COVID clinic patients had to have a positive test for SARS-CoV-2 and have symptoms 3 months after the initial COVID-19 diagnosis.

We collected post-COVID symptoms using the CDC chronic fatigue symptom inventory as self-reported by patients. The CDC inventory collects a battery of 22 symptoms and has been validated in chronic fatigue.[3] We report the presence of joint pain, along with the frequency and severity, as well as the contribution of the symptom to feeling ill.

We report information on C-reactive protein (CRP) and ANAs. ANAs were measured using immunofluorescence and for positive patients, we reported the pattern and the titer. We also collected if patients had a previous positive or negative screen. A positive ANA screen was defined as a positive test regardless of the pattern and titter.

3 | RESULTS

We included the first 15 patients who enrolled in our post-COVID clinic. Table 1 reports the baseline characteristics of the included patients. The majority of patients were female, belonged to a minority group, 20% were hospitalized for COVID-19, 26% were healthcare workers and were seen in the post covid clinic around 7 months after the initial infection. Table 1 shows the entire cohort stratified by having a positive ANA screen. The prevalence of a positive ANA screen was 53% (95% confidence interval [CI]: 28–79). Those who had a positive ANA were more likely to be female, white, and more likely to be hospitalized. Five patients had a speckled ANA pattern and the others had a homogenous pattern. The median ANA titer was 120 (interquartile range [IQR]: 60–240). Three patients had a prior positive ANA and their median titer before COVID was 80 (IQR: 40–120), and in those three patients, the titer increased. None of the patients had a diagnosis of connective tissue disease and two patients had fibromyalgia. Patients with a positive ANA had a higher CRP compared with those with a negative ANA. Those who had a positive ANA screen presented earlier than those who had a negative screen. Figure 1 shows the association between the ANA and joint pain reported on the CDC inventory.

TABLE 1 Baseline characteristics

Characteristic	Entire cohort	ANA positive	ANA negative
Number	15	8	7
Age	52.6 ± 13.4	54.1 ± 7.4	51.2 ± 17.5
Female gender, %	53	63	43
Black race, %	40	25	57
Hispanic ethnicity, %	47	50	43
Healthcare worker, %	27	13	43
Number of days after the SARS-CoV2 infection	200.6 ± 116.5	186.3 ± 80.5	217 ± 153.3
Hospitalized for COVID, %	20	25	14
Mean C-reactive protein (SD)	2.8 (2.1)	3.1 (2.4)	2.5 (1.9)
Body mass index	29 ± 2.9	30 ± 1.6	28.2 ± 3.6
Depression, %	38	43	33
Hypertension, %	31	33	29
Hypothyroidism, %	23	33	14
Obstructive sleep apnea, %	31	67	0

Abbreviation: ANA, antinuclear antibody.

4 | DISCUSSION

Our study shows a high prevalence of ANA positive screen with a high titer of antibodies in post-COVID patients. We also found that patients with a positive ANA screen had more joint pain. Our main limitations are the small sample size and the cross-sectional design.

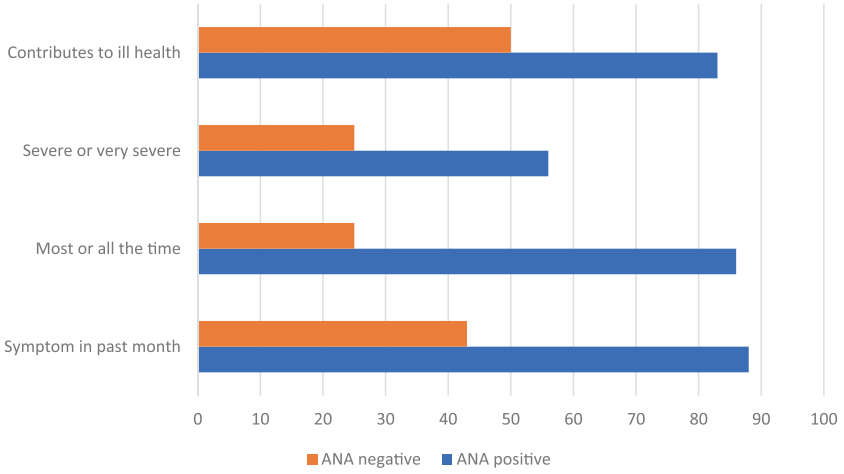

FIGURE 1 Association between joint pain and ANA screen in post COVID syndrome. ANA, antinuclear antibody

Several manuscripts have documented an association between ANA and COVID-19.[2,4–6] Two recent studies have documented the relationship between ANA and post-COVID syndrome. In the first, Seesle et al.[7] included 96 patients after 5 months after an acute COVID-19 infection and found that after 12 months patients who had a positive ANA had more neurocognitive symptoms. The second, Peluso et al.[8] reported 115 patients after 4–6 months of the initial infection and showed that only 3 out of 69 patients at 8 months had a positive ANA. Our study stands out in that we document the presence of ANA positivity in post-COVID rather than acute disease. Furthermore, this high prevalence was documented in patients who had fairly mild COVID-19.

Joint pain is common in post-COVID patients and there are case reports of inflammatory arthritis in this group of patients. Our study contributes to this field as it associates post-COVID syndrome with self-reported joint pain and ANA positivity. There are several explanations for our findings. First, ANAs have been found in 5% of screened healthy adults.[9] Second, ANAs are antibodies that bind to cellular components in the nucleus and autoimmunity has been proposed as a potential underlying etiology of post-COVID.[10–12]

In conclusion, our study documents a high frequency of positive ANA screens in patients with post COVID syndrome and ta association between the positive screen with self-reported joint pain. Future studies should evaluate the prognostic significance of this finding.

AUTHOR CONTRIBUTIONS

Study conception and design: Ana Palacio, Elizabeth Bast, Pat Caralis, Leonardo Tamariz, and Nancy Klimas. *Data collection*: Pat Caralis, Leonardo Tamariz, Maria Abad. *Analysis*: Leonardo Tamariz and Maria Abad. *Interpretation of results*: Elizabeth Bast, Ana Palacio, Leonardo Tamariz, Nancy Klimas, and Pat Caralis. *Draft manuscript preparation*: Maria Abad, Leonardo Tamariz, Ana Palacio, and Elizabeth Bast. *Revision of the final draft*: Nancy Klimas, Ana Palacio, Elizabeth Bast, and Pat Caralis.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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