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## Letter to the editor



## Prevalence of anxiety symptoms among COVID-19 patients during the acute versus post symptomatic window

To the Editor:

The coronavirus disease 2019 (COVID-19) pandemic has been associated with increased worry, anxiety, depression, and stress [1]. Such symptoms have been observed across the population during the pandemic, potentially because of fear and uncertainty surrounding the illness. While several studies have assessed the increased psychological distress brought on by COVID-19 among those infected as well as front-line caregivers, few studies have examined the prevalence of anxiety among those who receive a positive COVID-19 test. The primary aim of this cross-sectional study was to assess the prevalence of anxiety symptoms following a positive COVID-19 test during the symptomatic and post-symptomatic period. The secondary aim was to evaluate demographic predictors that may increase the odds of screening positive for anxiety after a positive COVID-19 test.

Data were obtained from the Cleveland Clinic COVID-19 registry. The methods of the registry have been described previously [2]. The registry consists of all patients (approximately 28,000) who were tested for COVID-19 between March 212,020 and November 122,020. Of this population, a subset of positive COVID-19 adult patients (both inpatient and outpatients) completed the Generalized Anxiety Disorder 2-item (GAD-2) scale via Epic's web-based patient portal, MyChart. Patients with an incomplete GAD-2 assessment were excluded from the study. Finally, twelve patients in this study overlap with a previously published paper examining prevalence of anxiety among discharged COVID-19 inpatients [3]. This study was approved by the Cleveland Clinic IRB and requirements for written informed consent were waived (IRB #20–813).

Anxiety was screened using the GAD-2 scale, with a score of  $\geq$ 3 as the cut-off for identifying possible cases of anxiety [4]. The symptomatic period was defined as 14 days following a positive test for COVID-19 [5].

Categorical variables are reported as counts (percentages) and continuous variables as means (standard-deviation). Significance between categorical variables was assessed using the Pearson chi-squared test at an  $\alpha$  of 0.05. Logistic regression was conducted to explore the relationship of anxiety with timing from positive COVID-19 test, accounting for age, sex, and race.

Analysis included 206 individuals who completed the GAD-2 after testing positive for COVID 19. Overall, individuals reported significantly higher levels of anxiety within 14 days of testing positive from COVID-19 (56.8%) compared to the period following resolution of symptoms (36%, p = 0.02). After adjusting for age, gender, and race, we found no difference in the prevalence of anxiety between the acute and post-symptomatic period. However, younger (OR: 1.04, 95% CI: 1.02, 1.06) age and female patients (OR: 3.00, 95% CI: 1.41,6.79) were more likely to screen positive for anxiety after a positive COVID-19 test. (Table 1).

Although patients in the symptomatic phase exhibited higher rates of anxiety than those in the recovery phase, this finding was better explained by differences in age and gender. It is possible that the baseline level of anxiety around COVID 19 in the general population is already so elevated that contracting the disease may not cause an appreciable increase in an individual's anxiety [6].

**Table 1**Patient characteristics and Predictors of positive GAD-2 screening in COVID-19 patients.

	OVERALL	Odds Ratio (95% CI)	Chi-Square Test Statistic (df)	P Value
Sample size	206			
Age (SD) <sup>b</sup>	$43.55 \pm 15.64$	0.96 (0.94, 0.98)	11.94 (1)	0.0005
Gender <sup>a</sup>				
Female	151 (73.3)	2.94 (1.40, 6.67)	7.41 (1)	0.0065
Male	51 (26.7)	1 (referent)		
Race (%) <sup>a</sup>				
Black	59 (29.4)	0.90 (0.45, 1.79)	0.08 (1)	0.77
Other	12 (6.0)	1.30 (0.36, 4.65)	0.71 (1)	0.68
White	130 (64.7)	1 (referent)		
GAD-2 score After Symptom Window (%) <sup>a</sup>	160 (78)	0.59 (0.28, 1.22)	1.99 (1)	0.16
Patients with baseline positive GAD-2 screen (%) <sup>a</sup>	28 (59.6)			
Positive GAD-2 screen after positive COVID test (%) <sup>a</sup>	84 (40.8)			
Mean duration between positive COVID-19 test and GAD-2 score (days) <sup>b</sup>	$61.54 \pm 52.83$			

<sup>&</sup>lt;sup>a</sup> All categorical values reported as N (%).

<sup>&</sup>lt;sup>b</sup> Continuous variables reported as mean  $\pm$  SD.

Females were found to have a higher odds of screening positive for anxiety after a COVID-19 diagnosis, which is consistent with well-established data suggesting a higher baseline prevalence of anxiety among females than males in a 3:1 ratio [7]. This gender discrepancy has also been noted during the COVID-19 pandemic [8]. Additionally, our results suggest that being older decreases the odds of screening positive for anxiety. While this may be due to the economic impact on younger people, it has also been reported outside the context of the COVID-19 pandemic [9].

A strength of this study was the utilization of the Cleveland Clinic COVID-19 registry which included a large sample of COVID-19 positive patients with GAD-2 scores. Additionally, this study utilized the GAD-2, a well validated screening tool for anxiety. However, a limitation of this study was its cross-sectional design which cannot discern temporal relations between variables. The anxiety may have preceded COVID infection rather than a consequence of the infection. Furthermore, such a design is susceptible to non-response bias and misclassification due to recall bias. In addition, patients in the Cleveland Clinic COVID-19 registry who had a GAD-2 score on file were only a small fraction of all those with a positive COVID-19 test at the time of data collection, suggesting that patients may have been more interested in completing the GAD-2 scale if they were experiencing psychiatric distress, leading to selection bias.

In conclusion, our findings indicate a high prevalence of anxiety symptoms among COVID-19 positive patients (56.8%) versus the general population according to the CDC (32%) [10]. Female and younger patients had the greatest odds of anxiety symptoms after a positive COVID-19 test.

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