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Observational Study

Transdiagnostic considerations of mental health for the post-COVID era: Lessons from the first surge of the pandemic

Sari Goldstein Ferber, Gal Shoval, Rodolfo Rossi, Viviana Trezza, Giorgio Di Lorenzo, Gil Zalsman, Aron Weller, J John Mann

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Abstract

BACKGROUND

The Coronavirus disease 19 (COVID-19)-related psychiatric burden partly results from prolonged social stress world-wide. Studies have examined the psychiatric impact of COVID-19 on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) and International Classification of Diseases 11th Revision (ICD-11) categories, implicating multiple diagnoses, complicating clinical management.

AIM

To verify whether COVID-19-related psychopathology spans multiple DSM-5 and ICD-11 diagnoses, but not in a random pattern. Consequently, empirical analysis of the multiple associated symptoms will better describe COVID-19-related psychopathology.

METHODS

We conducted a bi-national study during the first surge of the pandemic: an Italian sample ($n = 21217$, studied March-April 2020); and three representative longitudinal samples from Israel ($n = 1276$, 1189, and 1432 respectively, studied May-July 2020). Data in Italy were collected by a national internet-based survey with an initially approached sample of about one million persons and in Israel by the Israeli Central Bureau of Statistics using probability-based national representative sampling. Data analysis focused on the frequency and patterns of reported multiple mental health symptoms.

RESULTS

Combinations with all symptoms were more prevalent than combinations with fewer symptoms, with no majorities-minorities differences in both countries, demonstrating the generalizability of the transdiagnostic pattern of mental health issues in both nations. A history of previous mental disorder (Italian study) and an increase in symptom prevalence over time (Israel study) were associated with an increased number of symptoms. Conclusions: Based on finding correlated symptom diversity spanning conventional diagnostic categories, we suggest that the pattern of mental health issues associated with the COVID-19 pandemic is transdiagnostic.

CONCLUSION

The findings have implications for improving prevention and treatment of COVID-19 related psychopathology and for post-pandemic times in conditions resulting from multiplicity of stressors with mixed symptomatology in the clinical picture.

Key Words: Post-COVID-19; Diagnosis; Stress; Mental disorders; Transdiagnosis; Reactive psychiatric disorders

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Core Tip: The unique clinical picture that characterizes the reaction to the pandemic as shown in our findings may raise broader thoughts on diagnostic considerations regarding a new category beyond pandemic mental health symptomatology. This suggested category as outlined in our recently published review in the World Journal of Psychiatry may involve transdiagnostic criteria resulting from multiplicity of stressors. This type of condition may be apparent in the post-coronavirus disease (COVID) era although not recognized to date. Our findings showing this type of complex transdiagnostic symptomatology in two countries indicate a need for a new understanding of the COVID-19 pandemic's psychopathological consequences in the post-COVID era.

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INTRODUCTION

Prolonged stressful situations erode coping capacity[1,2]. The pervasive and persistent stress of the Coronavirus disease 19 (COVID-19) pandemic resulted in psychopathology afflicting millions worldwide. The unique impact of the pandemic on mental health is still pervasive and a significant burden on society[3], including the difficulties in diagnosis[4], which span diagnostic boundaries in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and International Classification of Diseases 11th Revision (ICD-11) defined disorders[5,6]. Past pandemics have raised similar concerns regarding mental health[7,8]. This highlights the concern regarding multiple diagnoses being given to a single patient and excessive use of the term “comorbidity”, with confusing implications for prevention and treatment[9].

A debate about diagnosis has commenced[10-13] and a transdiagnostic approach has been suggested by previous studies[12,14,15]. To examine the transdiagnostic hypothesis, we conducted two independent studies of psychiatric data collected during the first surge of the COVID-19 pandemic, one in Italy and one in Israel. We further hypothesized that the resultant pattern of symptom complexity will be robust enough to be detected in two different countries with different survey methodologies.

MATERIALS AND METHODS

Study 1: A Representative Sample of the Israeli Population - Three Surveys.

Methods: The Israeli Central Bureau of Statistics (CBS) collected data on mental health at three different time points during the early months of the COVID-19 pandemic: 1st survey: 26/4/-1/5/2020; and 2nd survey: 11-14/5/2020; 3rd survey: 12-16/7/2020. Informed consent was obtained verbally, and this was a prerequisite for continuing with the survey questions. The survey was conducted under the Ethical Code, a section on the CBS ethical requirements and commitments, which is part of the Israeli Law of Statistics 1972 regulating the CBS functions. This study complies with the Declaration of Helsinki.

The sampling sought to represent all the Israeli population age 21 years and above except for dispersed rural Bedouins in the South and institutionalized individuals.

The 1st survey sample included 2,279 people, of whom 56% responded by phone. The 2nd survey sample included 2,271 people of whom 52% responded by phone. The 3rd survey sample included 2,291 people of whom 62.5% responded by phone. The Arab minority participants were 15.1% of the sample in the 1st survey, 15.3% in the 2nd, and 17.7% in the 3rd survey.

Sample characteristics: Gender and age distributions (see [Table 1](#)).

To correct for potential non-responder biases, respondent distributions were weighted by the CBS according to their known gender, age, and geographical distributions in the Israeli general population. CBS also tested for data reliability in their standard methods.

Mental health outcome measures: In the 1st survey, 3 mental health symptoms were assessed: Perceived depression, perceived anxiety and perceived loneliness. In the 2nd and 3rd surveys, an additional symptom was added: COVID-19-related phobia.

Data analysis: From these reports, we calculated the proportion of people that reported suffering from a combination of 2, 3, or 4 symptoms. We compared these proportions over the three surveys to assess progression over the ongoing pandemic. To test statistically whether there was a change in the proportion of people that suffer from a combination of symptoms, we used a 2-sample equality of proportions test. We compared the estimated proportion of people suffering from at least 2, 3, or 4 symptoms to that observed in previous surveys (i.e., Survey 2 *vs* Survey 1, and Survey 3 *vs* Survey 1 and 2).

In addition, we identified the most common combination of 3 symptoms (in the 2nd and 3rd surveys).

The major ethnic minority group in Israel is Israeli Arab and the majority group is Israeli Jew. We compared the two groups on the relative proportions of 3- and 4-combined symptoms.

To understand the associations between the four mental health symptoms studied, we performed a Pearson product-moment correlation matrix for them in each survey, separately.

Bonferroni corrections for multiple comparisons were conducted.

Study 2: A survey in Italy during the peak of the COVID-19 pandemic

Study Design: This cross-sectional web-based observational study is a part of a long-term project monitoring mental health outcomes in the general population. The survey was anonymous, and confidentiality was assured. Three weeks after the beginning of the lockdown in Italy, the survey was conducted using convenient sampling. Every person living in Italy ≥ 18 years was eligible. The study was approved by the local Institutional Review Board (IRB) at the University of L'Aquila. Online written consent was obtained from all participants. Participants could terminate the survey at any time as approved by the IRB. This study complies with the Declaration of Helsinki.

Sampling strategy and online questionnaire dissemination: An online questionnaire was presented to the Italian population between March 25th and April 7th. The investigated timeframe corresponded to Italy's first contagion peak (<https://who.sprinklr.com/>). This general population questionnaire was disseminated using sponsored adverts on Facebook®. The questionnaire asked participants to re-share the questionnaire link. Using the Facebook Ads app, it was estimated that the number of link clicks was about 100,000, and the advertisement reached one million people.

Sample characteristics: The demographic characteristics of the sample are presented in [Table 2](#). Briefly, about 80% were women, 48% were 40 years old or older, 2.5% were foreigners and 28% reported previous psychiatric history.

Outcome Measures: The following psychometric scales were used and covered the previous two weeks: The Global Psychotrauma Screen (GPS) post-traumatic stress symptoms (PTSS) subscale (GPS-PTSS)[16, 17]: The validated version of PTSS was used. PTSS were considered of clinical relevance if more than 3 out of five 5 symptoms were reported as present.

The 9-item Patient Health Questionnaire (PHQ-9)[18], using the cut-off for severe depression symptoms at ≥ 15 . The validated version of this questionnaire was used.

The 7-item Generalized Anxiety Disorder scale (GAD-7)[19], using the cut-off for severe anxiety symptoms at ≥ 15 . The validated version of this scale was used.

Table 1 Gender and age distributions of the Israeli samples

Gender distribution		
Survey 1		
Gender	Count	Frequency
Men	541	47.10%
Women	607	52.90%
Survey 2		
Gender	Count	Frequency
Men	528	46.70%
Women	602	53.30%
Survey 3		
Gender	Count	Frequency
Men	684	48.75%
Women	719	51.25%
Age-group distribution		
Survey 1		
Age	Count	Frequency
21-44	509	44.30%
45-64	351	30.60%
65 +	288	25.10%
Survey 2		
Age	Count	Frequency
21-44	507	44.90%
45-64	345	30.50%
65 +	278	24.20%
Survey 3		
Age	Count	Frequency
21-44	664	47.30%
45-64	419	29.90%
65 +	320	22.80%

GPS- Post-Traumatic Stress Disorder-Negative Affect (PTSD-NA): 11 items, including symptoms related to disturbances in self-organization, anxiety, depression, self-harm, substance abuse, and other physical, emotional, or social problems. This cluster of symptoms is related to the Disturbance in Self Organization dimension of Complex PTSD.

The 10-item Perceived Stress Scale (PSS)[20], using quartiles such that the upper quartile was separated from the rest.

Data analysis: We analyzed the frequency of all combinations of symptoms, to determine the most frequent combinations of 3, 4, and 5 symptoms. We also identified the pattern of the most prevalent combination of symptoms. In addition, we used proportion tests to compare Italians and foreigners, and separately people with and without previous psychiatric history, on the frequency of reporting a combination of 3, 4, and 5 symptoms. Bonferroni corrections for multiple comparisons were conducted.

RESULTS

Study 1 The Israeli surveys

The Pearson correlations between pairs of symptoms were significant in all 3 surveys; see Table 3.

Table 2 Gender, age, nationality, and previous psychiatric history distributions of the Italian sample

Gender	Frequency	Percentage
Men	4122	19.40%
Women	17095	80.60%
Age	Frequency	Percentage
20-39	10894	51.30%
40-64	10118	47.70%
65-74	180	0.85%
75 +	25	0.10%
Foreign	Frequency	Percentage
Foreigner	516	2.40%
Italian	20701	97.60%
Psychiatric history	Frequency	Percentage
No	15160	71.40%
Yes	6075	25.88%

Table 3 The association between the three symptoms in the Israeli sample

	Loneliness	Depression	Anxiety
Survey 1			
Loneliness	1		
Depression	0.6364 ¹	1	
Anxiety	0.5027 ¹	0.581 ¹	1
Survey 2			
Loneliness	1		
Depression	0.6364 ¹	1	
Anxiety	0.5027 ¹	0.577 ¹	1
Phobia	0.1638 ¹	0.1684 ¹	0.3145 ¹
Survey 3			
Loneliness	1		
Depression	0.7172192 ¹	1	
Anxiety	0.4570808 ¹	0.5448582 ¹	1
Phobia	0.1467067 ¹	0.1770808 ¹	0.3177728 ¹

¹P < 0.0001.

Analysis of symptom patterns: Table 4 shows that in the 1st survey, 22.1% (95%CI: 19.7-24.5) reported all three symptoms, Depression, Loneliness, and Anxiety, significantly more than those reporting the most frequent 2-symptom pattern (Depression and Anxiety; 6.4%, 95%CI: 4.9-7.8; $P < 0.001$).

In the 2nd survey, 13.3% reported three symptoms and an additional 20.1% reported all four symptoms, totaling about one-third of the population. The prevalence of the four-symptom combination (95%CI: 17.8-22.4) was greater than the most prevalent 3-symptom combination (Phobia, Anxiety and Depression, 5.58%, 95%CI: 4.2-6.9, $P < 0.001$).

In the 3rd survey, 12.8% reported three symptoms, and an additional 24.3%, reported all four symptoms. The prevalence of the four-symptom combination (95%CI: 21.8-26.3) was greater than the most prevalent 3-symptom combination (Phobia, Anxiety and Depression, 7.32%, 95%CI: 6.0-8.7, $P < 0.001$).

Table 4 Frequency of reported symptoms in all three Israeli surveys

Number of symptoms	Count	Frequency
Survey 1		
0	512	44.6%
1	239	20.8%
2	143	12.5%
3	254	22.1%
Survey 2		
0	175	15.5%
1	359	31.8%
2	219	19.4%
3	150	13.3%
4	227	20.1%
Survey 3		
0	159	11.3%
1	396	28.2%
2	328	23.4%
3	179	12.8%
4	341	24.3%

Analysis of quantitative progression of symptom complexity over time: Survey 2 produced a significantly greater prevalence of 2 or 3 combined symptoms, compared to Survey 1 ($P < 0.0001$ and $P < 0.001$, respectively).

Survey 3 produced a greater prevalence of 4 combined symptoms, compared to Survey 2 ($P < 0.01$), attesting to the increase in the prevalence of a complex of symptoms over time.

The frequency of 3 and 4 combined complaints in the Arab compared with the Jewish sub-populations did not differ in any of the 3 surveys (data not shown).

Study 2 Italian general population

All Pearson correlations between pairs of symptoms were significant ($P < 0.001$; Table 5).

Analysis of symptom patterns: Table 6 presents all combinations of symptoms reported in the Italian sample. The most frequent 3-symptom combination was PTSS, Depression, and PTSD-NA (3.3%), compared to the other 3-symptom combinations. The most frequent 4-symptom combination was Anxiety, PTSS, Depression, and PTSD-NA (3.2%), compared to the other 4-symptom combinations. The prevalence of the 5-symptom combination, Anxiety, Perceived stress, PTSS, Depression, and PTSD-NA (9.0%, 95%CI: 8.5-9.3) was greater than of the most prevalent 3- (95%CI: 3.0-3.5) and 4-symptom combinations (95%CI: 2.9-3.4, $P < 0.001$).

This combination of prevalence was comparable in Italians and foreigners. In addition, there were no differences detected between Italians and foreigners in the most frequent symptom combinations.

A proportion test was performed to compare Italians and foreigners that suffered from a combination of three symptoms: 11.3% of Italians (2332 out of 20701) and 14.9% of foreigners (77 out of 516) experienced 3 symptoms. There was a higher rate in foreigners ($P = 0.0119$).

Nine point three percent of Italians (1918 out of 20701) and 10.7% of foreigners (55 out of 516) experienced four symptoms. There was no significant difference between the two populations' proportions, $P = 0.3173$.

Nine percent of Italians (1860 out of 20701) and 8.9% of foreigners (46 out of 516) experienced five symptoms. There was no significant difference between the two populations' proportions, P value = 1.

Quantitative analysis of the prevalence of symptom complexity: The role of psychiatric history: A psychiatric history, compared to no psychiatric history, increased the likelihood of multiple symptoms, with an identical pattern of symptom combinations as described above.

Specifically, regarding the differences between people with psychiatric history (PH) and without PH (NoPH) - a history of psychiatric symptoms (Table 7), proportion tests were performed to compare the groups.

Table 5 Correlations between the mental health features in the Italian sample (*n* = 21217)

Mental health issue	Anxiety	Perceived stress	PTSS	Depression	PTSD-NA
Anxiety	1				
Perceived stress	0.522	1			
PTSS	0.3521	0.3423	1		
Depression	0.5866	0.4867	0.3301	1	
PTSD-NA	0.2097	0.213	0.3636	0.2228	1

Note: All correlations: $P < 0.001$. PTSS: Post-traumatic stress symptoms; PTSD-NA: Post-traumatic stress disorder-negative affect.

Table 6 Italian sample

Combination	Count	Frequency	Percentage
None	0	3500	16.5%
PTSD-NA	1	6725	31.7%
Depression	1	147	0.7%
Perceived stress	1	59	0.3%
Anxiety	1	22	0.1%
Depression, PTSD-NA	2	771	3.6%
PTSS, PTSD-NA	2	2995	14.1%
Perceived stress, PTSD-NA	2	424	2.0%
Perceived stress, Depression	2	31	0.2%
Anxiety, PTSD-NA	2	202	1.0%
Anxiety, Depression	2	45	0.2%
Anxiety, Perceived stress	2	8	0.0%
PTSS, Depression, PTSD-NA	3	693	3.3%
Perceived stress, Depression, PTSD-NA	3	292	1.4%
Perceived stress, PTSS, PTSD-NA	3	586	2.8%
Anxiety, Depression, PTSD-NA	3	357	1.7%
Anxiety, PTSS, PTSD-NA	3	301	1.4%
Anxiety, Perceived stress, PTSD-NA	3	137	0.7%
Anxiety, Perceived stress, Depression	3	43	0.2%
Perceived stress, PTSS, Depression, PTSD-NA	4	480	2.3%
Anxiety, PTSS, Depression, PTSD-NA	4	657	3.2%
Anxiety, Perceived stress, Depression, PTSD-NA	4	537	2.5%
Anxiety, Perceived stress, PTSS, PTSD-NA	4	281	1.3%
Anxiety, Perceived stress, PTSS, Depression, PTSD-NA	5	1906	9.0%

PTSS: Post-traumatic stress symptoms; PTSD-NA: Post-traumatic stress disorder-negative affect.

Thirteen point three percent of PH (805 out of 6057) and 10.6% of NoPH (1604 out of 15160) experienced 3 symptoms. There is a significant difference between the two populations' proportions, P value < 0.0001 .

Twelve point nine percent of PH (782 out of 6057) and 7.9% of NoPH (1191 out of 15160) experienced 4 symptoms. There is a significant difference between the two populations' proportions, P value < 0.0001 .

Table 7 The most frequent symptom combinations per number of symptoms, for people with and without Psychiatric history

Combination	Count	Frequency	Percentage
Psychiatric history			
PTSS, Depression, PTSD-NA	3	257	4.2%
Anxiety, PTSS, Depression, PTSD-NA	4	291	4.8%
Anxiety, Perceived stress, PTSS, Depression, PTSD-NA	5	885	14.6%
No Psychiatric history			
Perceived stress, PTSS, PTSD-NA	3	439	2.9%
Anxiety, PTSS, Depression, PTSD-NA	4	384	2.5%
Anxiety, Perceived stress, PTSS, Depression, PTSD-NA	5	1021	6.7%

PTSS: Post-traumatic stress symptoms; PTSD-NA: Post-traumatic stress disorder-negative affect.

Fourteen point six percent of PH (885 out of 6057) and 6.7% of NoPH (1021 out of 15160) experienced 5 symptoms. There is a significant difference between the two populations' proportions, P value < 0.0001.

DISCUSSION

We report evidence from studies in two different countries, on the presentation of complex symptomatology that crosses diagnostic boundaries, during the first surge of the COVID-19 pandemic. The complex of symptoms that we found correlated in severity. This suggests a common relationship or a single overarching disorder. This offers an alternative and perhaps more complete characterization of psychopathology compared with employing multiple diagnoses for the same patient[9]. Moreover, this pattern is observed within each of the two countries studied, despite different survey methods, and is found within ethnic subpopulations of both countries, attesting to the generalizability of the pattern. The more the number of symptoms or diagnostic categories reported, the greater the proportion of subjects with past psychiatric history, suggesting that the identified complex of symptoms is related to psychiatric vulnerability. The greater proportion of subjects reporting this pattern over time indicates a cumulative effect of prolonged stress conditions driving individuals towards this more complex combination of symptoms.

Because our findings span different diagnostic categories, we propose that this argues for the need for a broader, transdiagnostic perspective[4,21,22]. We note that even prior to the pandemic others suggested a transdiagnostic approach for better treatment[23-26]. Given these earlier considerations, the current study may support the implementation of the treatment and organizational guidelines published by the WPA[27]. Thus, our large binational study provides more robust support for a new perspective, termed by some researchers "COVID Stress Syndrome"[12,28], which crosses DSM 5 and ICD 11 boundaries. In addition, transdiagnostic considerations may be helpful for post-COVID-19 concerns, if multiple stressors are identified as triggers and complex symptomatology characterizes the clinical picture.

"Transdiagnostic" in the context of the COVID-19 pandemic

We searched the literature using Reference Citation analysis, PubMed and Google Scholar, focusing on the term "transdiagnostic" in the context of the COVID-19 pandemic. For the term "transdiagnostic" we identified 1284 references from 2019 to 2022. For the same years, in PubMed, 84 references were identified by the search "transdiagnostic and COVID-19". In Google Scholar, with the same terms and range of years, 5670 references were identified. In reviewing the literature found, we conclude that the "transdiagnostic" term is very popular and used in a too general manner, not specifying exactly which symptoms are associated with a more accurate diagnosis. From our literature search it appears that the term "transdiagnostic" is used for conventional categories (DSM-5 and ICD-11) and for non-conventional (other psychological) phenotypes too, making it hard to understand what the term truly means. Most of the transdiagnostic research papers that uses diagnosis for treatment intervention, relate to the association between depression and anxiety, *e.g.*[29], which is a known comorbidity and not directly related particularly to the COVID-19 mental health symptomatology. In our search we found just a few papers that diagnose three associated symptoms or more[15,30-33], as in our study.

It seems from the literature that the traditional approach of developing programs for prevention and treatment derived from an accurate specific research-based diagnosis as uniquely shown in our research

is not included in most papers that used the “transdiagnostic” perspective. Additionally, unlike the methodology and rationale for the present study, general use of this term is related to treatment, not necessarily explained and derived from an accurate, transdiagnostic, research-based new diagnosis or a group of symptoms that span conventional categories [34,35] as shown in our findings.

Moreover, the transdiagnostic approach is presented in the literature with the promise to unravel better prevention and treatment of mental health disorders. The novelty of our current paper lies in analyzing the COVID-19 situation with its multiplicity of stressors to identify a more accurate diagnosis spanning more than 2 or 3 conventional categories. In our search, a few cutting-edge papers were found, in which associations between conventional categories were investigated with sound methodology *e.g.* [29,31,32]. The benefit of these cutting-edge papers is in showing the long-term impact of the COVID-19 pandemic on mental health. The identification of such a long-term effect emphasizes the relevance of our paper at this time, in learning lessons from the first surge towards the post-pandemic era. We note however, that these cutting-edge papers, too, focus on treatment, and not on the investigation of a more accurate diagnosis of the mental health reaction during the COVID-19 epidemic, as we suggest in the present paper.

Limitations

One limitation of our bi-national research is that we did not assess the full range of the possible neuropsychiatric spectrum, including neuropsychiatric symptoms and patterns evident in individuals recovering from infection. This extended transdiagnostic approach is discussed in our recent review published in the *World Journal of Psychiatry*, suggesting a neuropsychiatric syndrome, Complex Stress Reaction Syndrome, combining emotional-psychological symptoms (Type A) with neuropsychiatric (the non-systemic portion of Long-COVID) symptoms (Type B) [4]. Although the Israeli sample size is modest compared to the Italian sample, the Israeli data were collected by national probability-based representative sampling. We note that the fact that two differently designed studies in two different countries show similar results is a strength of this study and not a limitation. While the data analyzed are from the first surge of the pandemic, the pattern of results provides a novel perspective on diagnostic considerations in the post-COVID era.

CONCLUSION

In sum, our data and the literature suggest multiple symptoms that characterize the mental health reaction to the pandemic, and that the clinical picture during the first surge of the pandemic was transdiagnostic in terms of DSM/ICD diagnostic systems. This occurred more frequently in individuals with prior psychiatric illness and with the continued duration of the pandemic. This unique clinical picture that characterizes the reaction to the pandemic may raise broader thoughts on diagnostic considerations regarding a new category beyond pandemic mental health symptomatology [4]. This suggested category may involve transdiagnostic criteria resulting from multiplicity of stressors. This type of condition may be apparent in the post-COVID era although not recognized to date. Our findings indicate a need for an empirical unbiased approach for reaching a true understanding of the COVID-19 pandemic's psychopathologic consequences in the post-COVID era. Further international studies are essential. Accordingly, we are currently conducting a multi-national study, based on the present empirical paper's findings. This understanding needs to be extended to encompass psychopathology more comprehensively including neuropsychiatric effects. Without a more complete diagnosis, the treatment plan and organizational modifications cannot be complete.

ARTICLE HIGHLIGHTS

Research background

From early stages of the COVID-19 pandemic up to the current post-COVID era there are accumulating reports of a mix clinical picture of the related mental health symptomatology.

Research motivation

We hypothesized that the clinical picture of the COVID-19 related mental health symptomatology span several conventional diagnostic categories and therefore there is a growing risk for misdiagnosing suffering individuals thus reducing the option of developing more accurate research-based programs for prevention and treatment.

Research objectives

To show that the association between 3 or more symptoms from different conventional diagnostic categories are more prevalent.

Research methods

Three consecutive representative samples in Israel has been compared to a very large sample in Italy for 3 or more associated symptoms from different conventional categories using proportion analyses.

Research results

The most frequent 4-symptom combination was Anxiety, post-traumatic stress symptoms (PTSS), Depression, and Post-Traumatic Stress Disorder-Negative Affect (PTSD-NA) (3.2%), compared to the other 4-symptom combinations. The prevalence of the 5-symptom combination, Anxiety, Perceived stress, PTSS, Depression, and PTSD-NA (9.0%, 95%CI: 8.5-9.3) was greater than that of the most prevalent 3- (95%CI: 3.0-3.5) and 4-symptom combinations (95%CI: 2.9-3.4, $P < 0.001$) in Italy.

The prevalence of the four-symptom combination (95%CI: 21.8-26.3) was greater than that of the most prevalent 3-symptom combination (Phobia, Anxiety and Depression, 7.32%, 95%CI: 6.0-8.7, $P < 0.001$) in Israel with an increase over time.

Research conclusions

We report evidence from studies in two different countries, on the presentation of complex symptomatology that crosses diagnostic boundaries, during the first surge of the COVID-19 pandemic. The complex of symptoms that we found correlated in severity. This suggests a common relationship or a single overarching disorder that we termed previously Complex Stress Reaction Syndrome. This offers an alternative and perhaps more complete characterization of psychopathology compared with employing multiple diagnoses for the same patient. Moreover, this pattern is observed within each of the two countries studied, despite different survey methods, and is found within ethnic subpopulations of both countries, attesting to the generalizability of the pattern.

Research perspectives

Further international studies are essential. Accordingly, we are currently conducting a multi-national study, based on the present empirical paper's findings. This understanding needs to be extended to encompass psychopathology more comprehensively including neuropsychiatric effects. Without a more complete diagnosis, the treatment plan and organizational modifications cannot be complete.

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FOOTNOTES

Author contributions: Goldstein Ferber S and Mann JJ contributed to conceptualization; Di Lorenzo G, Rossi R and Trezza V verified the Italian data; Weller A and Goldstein Ferber S verified the Israeli data; Weller A, Goldstein Ferber Trezza V, Di Lorenzo G and Rossi R contributed to data curation; Weller A, Goldstein Ferber Trezza V, Di Lorenzo G and Rossi R contributed to formal analysis; Zalsman G and Shoval G contributed to investigation; Trezza V, Di Lorenzo G, Rossi R, Goldstein Ferber S and Mann JJ contributed to methodology; Weller A, Goldstein Ferber S, Di Lorenzo G, and Rossi R contributed to project administration; Zalsman G, Shoval G, Mann JJ, Weller A, Goldstein Ferber S, Trezza V, Rossi R, and Di Lorenzo G contributed to validation; Goldstein Ferber S contributed to writing - original draft; Mann JJ, Trezza V, Rossi R, Di Lorenzo G, Zalsman G, Shoval G, Weller A and Goldstein Ferber S contributed to writing, review & editing; All authors contributed substantially to the final version of the manuscript.

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