

# Increased Occurrence of PTSD Symptoms in Adolescents with Major Depressive Disorder Soon After the Start of the COVID-19 Outbreak in China: a Cross-Sectional Survey

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## Research article

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# Abstract

## Objective

The Coronavirus Disease 2019 (COVID-19) pandemic continues to threaten the physical and mental health of people across the world. This study aimed to understand the psychological impact of this disease on adolescents with major depressive disorder (MDD) at one month after the start of the outbreak in China.

## Methods

Using the Children's Impact of Event Scale (CRIES-13) questionnaire, we investigated the occurrence of posttraumatic stress disorder (PTSD) in two groups of adolescents: MDD patients who were in stable condition with antidepressant therapy and healthy controls. Total scores and factor subscores were compared between the two groups and subgroups stratified by sex and school grade. Logistic regression was used to identify variables associated with high total CRIES-13 scores.

## Results

Compared to controls (n = 107), the MDD group (n = 90) had higher total CRIES-13 scores and a higher proportion with a total score  $\geq 30$ . They also had a lower intrusion subscore and a higher arousal subscore. In the MDD group, males and females did not differ significantly in total CRIES-13 scores or factor subscores, but junior high school students had higher avoidance subscores than senior high school students. Logistic regression showed high total CRIES-13 scores to be associated with MDD and the experience of "flashbacks" or avoidance of traumatic memories associated with COVID-19.

## Conclusions

It is crucial to understand the psychological impact of COVID-19 on adolescents with MDD in China, especially females and junior high school students. Long-term monitoring of adolescents with a history of mental illness is required to further understand these impacts.

## Trial registration

ChiCTR, ChiCTR2000033402, Registered 31 May 2020, <http://www.chictr.org.cn/index.aspx>

# Introduction

Over the last several months, the COVID-19 pandemic has become the source of enormous stress for people across the world [1–4]. Studies show that individuals who experience such stressful events are more likely to suffer from depression and experience symptoms of posttraumatic stress disorder (PTSD) [5–7]. Compared to adults, adolescents are at higher risk of mental illness after disasters [8]. Therefore, it is important not to overlook the mental health of children and adolescents [9], especially because it could lead to an increased risk of psychiatric disease in adulthood [10].

Psychiatric history and mental illness have been associated with an increased occurrence of PTSD symptoms in the young adults aged 18–21 years old [11]. However, very few cross-sectional studies have addressed the association between pre-trauma mental illness and PTSD. In this study, we investigated the psychological impact of the COVID-19 outbreak on adolescents suffering from major depressive disorder (MDD) in China. We are not aware of any other cross-sectional studies on the occurrence of PTSD symptoms in MDD adolescents during the COVID-19 outbreak.

# Methods

## Study subjects

The results described here were obtained within the context of a larger, prospective cohort study. The study was approved by the Ethics Committee of the West China Hospital of Sichuan University, and registered in the Chinese Clinical Trial Registry (ChiCTR2000033402). Written informed consent was obtained from all participants and their guardians.

Adolescents aged 12–18 years and diagnosed independently by two senior psychiatrists at our hospital with drug naïve, first-episode MDD according to *Diagnostic and Statistical Manual of Mental Disorders IV* (DSM-IV) were consecutively recruited from June 2019 to the time point we did this survey (February 2020). All adolescents are right-handed, primary school education or above, judged by imaging physician that there is no structural abnormality of the brain, can understand the content of the scale, has not received electrical convulsive therapy, has no physical illness and has not taken any other drugs recently. Before the administration of stable antidepressant therapy, we evaluated the severity of depression symptoms using the Chinese version of Beck Depression Inventory-II (BDI-II) [12]. Age- and sex-matched junior and senior school students without COVID-19 (based on our self-report general information form) were enrolled as healthy controls. We excluded all the participants with a history of substance abuse, as well as those suffering from severe physical and mental illnesses, including Axis I and Axis II disorders based on the DSM-IV. Nearly all subjects came from Sichuan province in China.

## Data collection

Between 17 February and 23 February, approximately one month after the outbreak of COVID-19 in China, we collected demographic data using a general information form that we developed, as well as psychopathological data using the Chinese version of the Children's Revised Impact of Event Scale (CRIES-13) questionnaire [13].

The CRIES-13 was used as a brief self-rating scale for children  $\geq 8$  years old. The degree of each stressful symptoms in the last 2 weeks was recorded to 4 grades (not at all, rarely, sometimes, often), respectively scored 0, 1, 3, 5 points. There was no reverse entry, and the three factors were intrusion (item 1,4,8,9), avoidance (item 2,6,7,10), and high arousal (item 3, 5, 11, 12, 13), respectively corresponding to the three symptom groups of B (re-experience), C (avoidance), and D (high arousal) in the DSM-IV diagnostic criteria for PTSD. The severity of the psychological impact caused by a stressful event can be measured using total CRIES-13 scores ranged 0–65 points and a total score  $\geq 30$  indicates severe psychological stress. According to the preliminary investigation, the Cronbach number of CRIES-13 was 0.81, the re-test reliability was 0.79, and the three-factor structure was stable, which confirmed that the table was a good screening tool for assessing the degree of stress response after traumatic events experienced by children[14–16]. All the questionnaires were distributed via WeChat ensured the responses of participants were anonymous to others but can only be seen by the researchers. Additionally, we conducted telephone interviews and semi-structured mental health examinations based on the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (KSADS-PL) [17]. All PTSD diagnoses were confirmed by two independent psychiatrists based on the DSM-IV.

## Statistical analysis

Statistical analyses were performed using Statistical Product and Service Solutions (SPSS) 25.0 (IBM, Armonk, NY, USA), and the significance level was set at  $\alpha = 0.05$ . We analyzed participant data and compared CRIES-13 scores across groups using chi-squared, Mann-Whitney U, Kruskal-Wallis H, Student's *t* or Fisher's exact tests as appropriate.

Bivariate logistic regression analysis was performed to assess the factors influencing the proportion of subjects with a total CRIES-13 score  $\geq 30$ . Participants were stratified into two groups: those with a total score  $< 30$  (CRIES-) and those with a total score  $\geq 30$  (CRIES+). We considered the effects of group (MDD/control), sex (female/male), grade (senior/junior high school), and family structure (with single-parent family serving as reference in the regression). We also considered exposure to infection, which was defined as relatives with COVID-19 (yes/no), or as having family members who work at the frontline in medical facilities (yes/no). We included participants' responses to such questions as "How often do images associated with COVID-19 cross your mind?" and "How often do you have to stop yourself from thinking about COVID-19?" (those responding "not at all" served as reference in the regression).

## Results

### Demographic characteristics

Of the 95 patients and 120 controls initially enrolled, valid questionnaires were received from 90 patients and 107 controls (excluded controls who had undergone psychological counseling with underlying psychological problems and MDD patients who had not been treated). Most of the patients were receiving antidepressant medications at the start of the study, including sertraline (32 patients, 50–150 mg/day), fluoxetine (7 patients, 20–40 mg/day), escitalopram (20 patients, 10–20 mg/day), venlafaxine (22 patients, 150–225 mg/day), agomelatine (4 patients, 25–50 mg/day), and one patient was taking both sertraline (50 mg/day) and agomelatine (25 mg/day). Four patients were receiving psychotherapy instead of antidepressant medication.

The MDD group (72 females) consisted of 47 junior high school students and 43 senior high school students, while the control group (82 females) had 58 junior high school students and 49 senior high school students. Patients and controls differed significantly in family structure and occupation of parents, but not in sex ratio, age, school grade or exposure to infection (Table 1).

Table 1  
Demographic characteristics of adolescents with or without major depressive disorder, stratified by sex and school grade

Characteristic	Total		Stratified by sex								Stratified by school grade			
	MDD <sup>1</sup>	Control	z/x <sup>2</sup>	p	Male (n = 43)		Female (n = 154)		H/t/x <sup>2</sup>	p	Junior (n = 105)		Senior (n = 92)	
					MDD	Control	MDD	Control			MDD	Control	MDD	Control
(n = 90)	(n = 107)	(n = 18)	(n = 25)	(n = 72)	(n = 82)	(n = 47)	(n = 58)	(n = 43)	(n = 49)					
Median age (years)	15	15	-0.69	0.491	15.00	15.00	15.00	15.00	0.61	0.894	14.00	14.00	16.00	17.00
Baseline BDI <sup>2</sup> score	35.81 ± 11.79	NA			33.33 ± 9.11	NA	36.43 ± 12.35	NA	-1.00	0.322	37.65 ± 12.79	NA	33.80 ± 10.38	NA
Sex (Male/Female)	18/72	25/82	0.32	0.569							10/37	15/43	8/35	10/39
Grade (Junior/Senior)	47/43	58/49	0.08	0.781	10/8	15/10	37/35	43/39	0.62	0.892	NA	NA	NA	NA
Family structure			12.28	0.006						0.075				
Single parent	13	8			1	2	12	6			6	4	7	4
Two parents	34	36			6	10	28	26			17	18	17	18
Multi-generational	19	46			5	10	14	36			9	25	10	21
Other	24	17			6	3	18	14			15	11	9	6
Occupation of parents				0.035						0.087				
Medical staff	2	1			0	1	2	0			1	1	1	0
Police	1	1			0	0	1	1			0	1	1	0
Civil servant	8	5			0	0	8	5			4	4	4	1
Teacher	9	3			1	1	8	2			3	1	6	2
Freelancer	14	20			6	6	8	14			7	11	7	9
Farmer	1	9			0	3	1	6			0	4	1	5
Researcher	2	0			1	0	1	0			2	0	0	0
Worker	17	24			2	6	15	18			8	12	9	12
Self-employed	19	31			5	7	14	24			12	17	7	14
Others	17	13			3	1	14	12			10	7	7	6
Respondent has family members who are														
Infected (Yes/No)	0/90	4/103		0.127	0/18	0/25	0/72	4/78		0.249	0/47	2/56	0/43	2/47
Frontline health worker (Yes/No)	3/87	3/104		1.000	0/18	0/25	3/69	3/79		0.925	2/45	1/57	1/42	2/47

Values are n or mean ± SD, unless otherwise noted.

<sup>1</sup> MDD, major depressive disorder

<sup>2</sup> BDI, Beck Depression Inventory

The baseline mean BDI score in the MDD group (before treatment with antidepressants) was 35.81 ± 11.79. We found no significant difference in baseline BDI scores between male and female patients ( $t = -1.00, p = 0.322$ ), or between junior and senior high school students ( $t = 1.56, p = 0.123$ ). They were all received antidepressant therapy at least 6 weeks and based on the BDI scores after treatments, 8 of the patients were remission on the MDD (BDI-II score ≤ 9) [18].

## CRIES-13 scores

The MDD group had significantly higher total CRIES-13 scores than controls (23.5 vs 21,  $z = -2.14$ ,  $p = 0.033$ ), as well as a higher proportion of participants with a total score  $\geq 30$  (34.4% vs 15.9%,  $\chi^2 = 9.13$ ,  $p = 0.003$ ). Patients also had a significantly lower intrusion subscore (7 vs 9,  $z = -2.17$ ,  $p = 0.030$ ) and higher arousal subscore (13 vs 8,  $z = -6.39$ ,  $p < 0.001$ ) (Table 2).

Table 2  
CRIES-13 scores of adolescents with or without major depressive disorder (MDD)

	Total (n = 197)	MDD (n = 90)	Controls (n = 107)	$z/\chi^2$	$p$
<b>Median scores</b>					
Total	22.00	23.50	21.00	-2.14	0.033
Intrusion factor	8.00	7.00	9.00	-2.17	0.030
Avoidance factor	3.00	3.50	3.00	-0.14	0.886
Arousal factor	10.00	13.00	8.00	-6.39	<0.001
<b>Distribution by total score, n (%)</b>					
$\leq 30$	149 (75.6)	59 (65.6)	90 (84.1)	9.13	0.003
$\geq 30$	48 (24.4)	31 (34.4)	17 (15.9)		

Male and female patients did not differ significantly in total scores, factor subscores, or proportion of participants with a total score  $\geq 30$  (Table 3). Among controls, however, females had higher total scores (22.5 vs 16,  $z = -2.89$ ,  $p = 0.004$ ) and arousal subscores (8 vs 4,  $z = -3.79$ ,  $p < 0.001$ ) than males.

Table 3  
CRIES-13 scores of adolescents with or without major depressive disorder (MDD), stratified by sex

	MDD		$z/\chi^2$	$p$	Controls		$z/\chi^2$	$p$
	Male (n = 18)	Female (n = 72)			Male (n = 25)	Female (n = 82)		
<b>Median scores</b>								
Total	22.00	25.00	-0.09	0.928	16.00	22.50	-2.89	0.004
Intrusion factor	4.50	8.00	-0.81	0.421	7.00	9.50	-1.83	0.068
Avoidance factor	4.00	3.00	-0.69	0.488	3.00	3.50	-0.47	0.637
Arousal factor	13.00	13.00	-0.20	0.840	4.00	8.00	-3.79	<0.001
<b>Distribution of total scores, n (%)</b>								
$\leq 30$	12 (66.7)	47 (65.3)	0.01	0.912	21 (84)	69 (84.1)		1.000
$\geq 30$	6 (33.3)	25 (34.7)			4 (16)	13 (15.9)		

Among either patients or controls, the proportion of participants with a total score  $\geq 30$  was not significantly different between junior high school or senior high school students (Table 4). Among patients, junior high school students had significantly higher avoidance subscores than senior high school students (5 vs 2,  $z = -2.20$ ,  $p = 0.028$ ). Among controls, senior high school students had higher total scores (24 vs 19,  $z = -2.06$ ,  $p = 0.040$ ) and intrusion subscores (10 vs 8,  $z = -2.14$ ,  $p = 0.033$ ) than junior high school students.

Table 4  
**CRIES-13 scores of adolescents with and without major depressive disorder (MDD), stratified by school grade**

	MDD				Controls			
	Junior high	Senior high	z/x <sup>2</sup>	p	Junior high	Senior high	z/x <sup>2</sup>	p
	(n = 47)	(n = 43)			(n = 58)	(n = 49)		
<b>Median scores</b>								
Total	26.00	22.00	-0.92	0.357	19.00	24.00	-2.06	0.040
Intrusion factor	6.00	7.00	-0.02	0.981	8.00	10.00	-2.14	0.033
Avoidance factor	5.00	2.00	-2.20	0.028	3.00	3.00	-0.17	0.862
Arousal factor	13.00	13.00	-0.55	0.579	7.00	8.00	-1.95	0.052
<b>Distribution of total scores, n (%)</b>								
≤30	27 (57.4)	32 (74.4)	2.87	0.091	52 (89.7)	38 (77.6)	2.91	0.088
≥ 30	20 (42.6)	11 (25.6)			6 (10.3)	11 (22.4)		

## PTSD diagnosis

Two clinicians performed mental health examinations of all the subjects who had total CRIES-13 scores ≥ 30 (31 patients and 17 controls). Eleven patients were determined by KSADS to have experienced PTSD before the COVID-19 outbreak, while none of the controls was diagnosed with PTSD.

## Factors influencing total CRIES-13 scores

Logistic regression identified the following factors as influencing total CRIES-13 scores: group, responses to CRIES-13 questions such as COVID-19 images cross one's mind, and having to stop oneself from thinking about the pandemic (Table 5). The model was able to classify 85.3% of participants into correct CRIES- and CRIES + groups, corresponding to sensitivity, 60.4%; specificity, 93.3%; positive predictive value, 74.4%; and negative predictive value, 88% (Table 6).

Table 5  
**Logistic regression to identify related to a total CRIES-13 score of at least 30 (n = 197)**

Variable	B	SE	Wald chi-square	OR(95% CI)	p
<b>Group</b> (Patient/Control)	2.92	0.63	21.39	18.54 (5.38–63.88)	< 0.001
<b>Sex</b> (Female/Male)	0.49	0.64	0.60	1.63 (0.47–5.68)	0.441
<b>Grade</b> (Senior high/Junior high school)	0.43	0.50	0.75	1.54 (0.58–4.07)	0.386
<b>Family structure<sup>1</sup></b>			4.64		0.200
Two parents	0.01	0.80	0.00	1.01 (0.21–4.86)	0.990
Multi-generational	1.30	0.86	2.28	3.66 (0.68–19.69)	0.131
Other	0.13	0.92	0.02	1.14 (0.19–6.86)	0.885
<b>Relative(s) infected with COVID-19</b> (Yes/No)	0.98	1.49	0.44	2.68 (0.14–49.56)	0.509
<b>Family member works at frontline</b> (Yes/No)	-0.66	1.79	0.13	0.52(0.02–17.43)	0.714
<b>How often do images associated with COVID-19 cross your mind?<sup>2</sup></b>			27.16		< 0.001
Rarely	1.64	1.17	1.96	5.16 (0.52–51.43)	0.162
Sometimes	4.01	1.16	11.96	54.89 (5.67-531.26)	0.001
Often	5.81	1.34	18.96	333.93 (24.42-4567.19)	< 0.001
<b>How often do you have to stop yourself from thinking about COVID-19?<sup>3</sup></b>			21.97		< 0.001
Rarely	1.66	0.65	6.60	5.24(1.48–18.57)	0.010
Sometimes	3.36	0.74	20.83	28.81(6.81-122.01)	< 0.001
Often	3.38	1.10	9.56	29.23(3.44-248.23)	0.002
<sup>1</sup> Respondents answering “single-parent family” served as the reference group					
<sup>2,3</sup> Respondents answering “not at all” for these questions served as the reference group.					

Table 6  
Classification table of the logistic regression

Observed	Predicted by combination of all factors		% correct
	CRIES-13 -	CRIES-13 +	
CRIES-13 -	139	10	93.3
CRIES-13 +	19	29	60.4
<b>Overall</b>			85.3
CRIES-13 -: respondents with total CRIES-13 scores < 30, CRIES-13 +: respondents with total CRIES-13 scores ≥ 30			

## Discussion

In this study, we examined and compared the effects of the COVID-19 outbreak on the mental health of Chinese adolescents with or without MDD. We found that the MDD group had higher total CRIES-13 scores, as well as a higher proportion of participants with a total score  $\geq 30$  than healthy controls. These results indicate that early in the COVID-19 outbreak, adolescents with MDD were more likely than adolescents without MDD to experience severe psychological stress and symptoms of PTSD. Similar results were observed in United States military personnel deployed in the conflicts in Iraq and Afghanistan and patients with neurotic disorders after the Great East Japan Earthquake on 11 March 2011 [19, 20].

Our study found higher arousal and lower intrusion subscores among patients than controls based on the CRIES-13. The symptoms of arousal observed in the MDD group were inability to concentrate, irritability, insomnia, as well as increased vigilance and fear. This could be due to higher levels of brain arousal and hyper-stable regulation caused by the hyperactivity of the locus coeruleus in the central noradrenergic system [21, 22] [22–23]. The hyper-stable regulation mode can prevent MDD patients from reducing arousal in order to sleep or regulate diurnal variation in mood [23][24]. The lower intrusion levels in MDD patients may be a result of antidepressant treatment, which can decrease the response to psychological stimuli by dampening activation of the amygdala [24, 25] [25–26]. The amygdala is activated when the brain encodes non-spontaneous, intrusive memories, such as "flashbacks" of traumatic events [26, 27] [27–28]. Further studies should examine how arousal and intrusion levels influence risk of PTSD symptoms in adolescents during the COVID-19 outbreak.

Age is a crucial factor associated with psychological stress caused by disasters [28, 29] [37–38]. In our study, junior high school students with MDD showed higher avoidance levels than senior high school students. This may reflect higher "distractibility" and greater tendency to apply maladaptive coping strategies among younger students, who may therefore be more vulnerable to negative effects of stressful situations [30] [39]. So we should focus on intervention of MDD patients in junior high students and try to explore how age factor affect the avoidance level of MDD patients.

Studies have also reported sex differences in the severity of posttraumatic stress symptoms [31, 32] [29–30]. After the 5.12 Wenchuan earthquake in China, women were at higher risk of PTSD [32], and this increased risk of PTSD may be associated with biological, environmental and social factors [33] [31]. Fluctuations in ovarian hormone levels can alter sensitivity to emotional stimuli at certain stages of the menstrual cycle, which could in turn lead to an increased susceptibility to mental illness [34]. A study on adult women showed that fear associated with the COVID-19 outbreak can lead to higher arousal symptoms [35]. Among individuals with PTSD, women show greater reactivity than men in the fear and arousal network in the ventral region of the brainstem [36] [34]. These reports are consistent with our findings that female controls had higher total CRIES-13 scores and arousal subscores than male controls. However, we observed no significant sex differences in total scores or factor subscores among MDD patients. MDD has been associated with sensitization of the neurotransmitter and neuroendocrine systems, resulting in higher reactivity to stress [37], but whether women with MDD are more vulnerable to external stress than men with MDD is unknown. We speculate that the MDD-induced shift in hormone levels may mask sex differences in reactivity to external stimuli.

Adolescents can recover from the effects of their maladaptive cognitive style after disasters sooner than adults can [38]. Nevertheless, there is a positive correlation between history of pre-traumatic mental illness and post-traumatic stress symptoms in both adults and adolescents [38, 39], and our results with adolescents show that larger proportions of patients than controls had PTSD symptoms and total CRIES-13 scores  $\geq 30$ . Therefore, the post-disaster mental status of adolescents with MDD should be carefully monitored to avoid the risk of PTSD. A hallmark of PTSD is the transition from re-experiencing to avoiding memories associated with trauma [26]. Consistent with other studies on the role of avoidance symptoms [40, 41], we observed a significant association between total CRIES-13 scores and responses to questions such as "How often do images associated with COVID-19 cross your mind?" and "How often do you have to stop yourself from thinking about COVID-19?" The mechanisms of how these factors associated with high risk of PTSD occurrence can be studied in the future.

Our cross-sectional study provides what appears to be the first evidence that COVID-19 is having a particularly strong psychological impact on adolescents with MDD, especially females and junior high school students. Whether our findings can be generalized to adolescents outside Sichuan province in China needs to be confirmed. Future work should examine potential influence of antidepressant therapy on the vulnerability of adolescents to COVID-19 stress. Based on the mental health examinations that we conducted on a subset of patients and controls who scored at least 30 on CRIES-13, we did not detect anyone with PTSD that could be attributed to the COVID-19 outbreak. This may be because our study was conducted only one month after the outbreak began in China, and because of the containment measures implemented rapidly by the government. Our continuing analysis of these patients and controls as part of our larger prospective cohort study (ChiCTR2000033402) may detect an association between COVID-19 and PTSD among adolescents with or without MDD. This may help identify adolescents who require psychological and clinical intervention.

## Abbreviations

**BDHI**

Beck Depression Inventory-II

**COVID-19**

Coronavirus Disease 2019

**CRIS-13**

the Children's Impact of Event Scale questionnaire

**DSM-IV**

the Diagnostic and Statistical Manual of Mental Disorders IV

**KSADS-PL**

Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version

**MDD**

Major Depressive Disorder

**PTSD**

Post-Traumatic Stress Disorder

**SPSS**

Statistical Product and Service Solutions

## Declarations

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### Availability of data and material

The data that support the findings of this study are available on request from the corresponding author (Li Yin, yli009@163.com). The data are not publicly available due to privacy or ethical restrictions.

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of West China Hospital of Sichuan University. The research had been performed in accordance with the Declaration of Helsinki. Written informed consents had been attained from all the participants and their guardians based on the principle of self-determination. The participants' rights were fully respected and preserved in the whole process of this study.

### Competing interests

The authors declare that they have no competing interests.

### Consent for publication

Not applicable.

### Authors' contributions

Methodology, Zhang Hang and Xu Hanmei; investigation, Zhang Hang, Xu Hanmei, Huang Lijuan, Wang Xiaolan, Tang Xiaowei, Wang Yanping, Deng Fang, Wo Wang, Tao Yuanmei and Yin Li.

writing—original draft preparation, Zhang Hang and Xu Hanmei ; writing—review and editing, Zhang Hang and Yin li; project administration, Yin Li; funding acquisition, Yin li

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