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Article

Association of Adverse Childhood Experiences with Non-Suicidal Self-Injury and Suicidality: Baseline Survey of the Chinese Adolescent Health Growth Cohort

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Abstract: Many researches have identified that adverse childhood experiences (ACEs) are associated with non-suicidal self-injury (NSSI) and suicidality. However, most studies have been restricted to a few types of ACEs. This study aims to investigate associations of 13 common types of ACEs with NSSI, suicidal ideation (SI) and suicide attempt (SA), as well as the mediation of depressive and anxiety symptoms therein. A total of 1771 students aged 11-16 years who participated in the baseline survey of the Chinese Adolescent Health Growth Cohort study were included for the analysis. ACEs, SI, SA, depressive and anxiety symptoms were recorded by standard questionnaire. Of included participants, 92.0% reported one or more category of ACEs. Smoking, parent-child separation, emotional abuse, physical abuse and being bullied were positively associated with NSSI, with the adjusted odds ratio (aOR) of 2.41(95%CI, 1.01-5.75), 1.80(1.28-2.54), 1.69(1.21-2.37), 2.08(1.44-3.01) and 1.87(1.35-2.59), respectively; smoking (4.03, 1.66-9.81), parent-child separation (1.42, 1.07-1.90), emotional abuse (1.91, 1.41-2.59), physical abuse (1.80, 1.27-2.57), emotional neglect (1.78, 1.28-2.49) and being bullied (2.08, 1.54-2.81) were positively associated with SI; smoking(4.30, 1.67-11.10), emotional abuse (2.42, 1.58-3.72) and being bullied (1.75, 1.17-2.60) were positively associated with SA. The associations of ACEs with NSSI, SI and SA were each partially or completely mediated through depressive and anxiety symptoms. Children and adolescents who had experiences of smoking, physical abuse and being bullied during childhood are consistently and independently associated with NSSI and suicidality, and these associations may be largely mediated through depressive and anxiety symptoms.

Keywords: Adverse childhood experiences; Depressive symptoms; Anxiety symptoms; Non-suicidal self-injury; Suicidal behaviors

1. Introduction

Non-suicidal self-injury (NSSI), suicidal ideation (SI) and suicidal attempts (SA) are major public health concerns among adolescents worldwide [1], and their prevalence may have increased during the COVID-19 pandemic [2-3]. NSSI and suicidality represent the strongest and most consistent predictors of future suicidal behaviors among youth in clinical patients and general populations [4]. Thus, it is of great importance to further understand the complex interplay between these many

recognized risk factors. A substantial body of research has demonstrated independent associations between adverse childhood experiences (ACEs), NSSI, and suicidality [5]. Yet, our current knowledge surrounding these associations has predominantly been derived from adults or clinical patients in high income countries (HICs) [6-8], with only a few studies conducted among community adolescents in low- and middle-income countries (LMICs) [9-10]. Findings from HICs may not be generalized to LMICs due to socio-economic and cultural differences. ACEs include a broad set of potentially traumatic events, such as experiencing violence, abuse, neglect, and other aspects of the child's environment that can undermine their sense of safety, stability, and bonding [11]. However, most prior studies that have examined the associations between ACEs and NSSI and suicidality have been rather limited in their scope, focusing on a narrow range of ACEs, such as childhood maltreatment [12], parent-child separation [13], and experienced violence [14]. It is uncertain whether other types of ACEs are independently associated with NSSI and suicidality. Furthermore, ACEs are linked to depressive and anxiety symptoms [15-16], while depressive and anxiety symptoms are significantly associated with both NSSI and suicidality [17]. However, no study has examined whether there are combined mediation effects of depressive and anxiety symptoms on the associations of ACEs with NSSI, SI and SA [18]. Depressive and anxiety symptoms are the most common mental health difficulties among Chinese children and adolescents [19]. Consequently, to identify the potential mediation effects of depressive and anxiety symptoms on associations of ACEs with NSSI and suicidality are of substantial public health importance, since it will not only help to better understand the development and mechanism of NSSI and suicidality, but also may be meaningful for public policy makers to implement intervention of NSSI and suicidality. Accordingly, the primary purpose of the present study was to investigate the associations between a broad range of ACEs and NSSI and suicidality among Chinese children and adolescents. We hypothesized that not all ACEs will independently associate with NSSI and suicidality after adjusting for demographic characteristics and potential confounders, such as social support, and emotional management ability. The secondary purpose of our study was to estimate the mediation effects of depressive and anxiety symptoms on associations between ACEs and NSSI and suicidality. We hypothesized that the effects of ACEs on NSSI and suicidality would be partially mediated through depressive and anxiety symptoms.

2. Materials and Methods

2.1. Study participants and data collection

This study used the baseline survey data of Chinese Adolescent Health Growth Cohort (CAHGC), an ongoing cohort study established across three study sites (Qidong County, Hengyang City in Hunan province, Guangming District in Shenzhen City and Zhongshan City in Guangdong Province) in China in 2020. The CAHGC aimed to understand the epidemiological characteristics, developmental trajectory and influence of high-risk behaviors (mainly self-harm and aggressive behaviors) among children and adolescents, and to provide evidence on policies and measurements development for reducing these behaviors. The study baseline survey was conducted from the 18th of February to the 14th of July 2021, when participants first completed a questionnaire on their sociodemographic profile, psychosocial variables, behavioral characteristics, and took physical examinations.

We set the students who were at seventh grade as the study population, because the onset of NSSI and suicidality usually occurs in early adolescence [19]. With the help of the local administration in each study site, 4 public schools and 7 private schools were randomly selected for the CAHGC study. All the seventh-grade students in the 11 schools were eligible to participate in the baseline survey, except for 7 students who had severe mental disorders (5 had moderate to severe depression, 1 had schizophrenia, and 1 had bipolar disorder), who were identified by the headteacher and/or health care physicians. Consent forms were sent to a total of 1844 students by the head teacher of 42 classes. The students were asked to take the consent form back home and discuss it with their parents/guardians carefully. Interested students need to provide their parent's/guardian's written informed consent before participation in the baseline survey.

Trained investigators, comprising teachers and postgraduates, administered the questionnaire survey; they were also available at each study site to clarify any participant confusion and to address questions about the questionnaire. Participants were asked to complete the questionnaire

independently within 45 to 60 minutes. Completeness of the questionnaire was reviewed by the trained investigators. Clinical professionals from local medical institutions then did physical examinations. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This human study was approved by Institutional Review Board of Guangzhou Medical University – approval: 2021010002. All parents or guardians provided written informed consent for the minors to participate in this study.

2.2. Measurement

2.2.1. Sociodemographic profile, emotional management ability, and social support

A self-designed questionnaire was used to collect categorical data on socioeconomic, familial, and parenting variables, including regional areas (Qidong County, Guangming District, Zhongshan City), school type (public or private), ethnicity (Han or others), age, sex (male or female), single child (yes or no), main caregiver's educational level (junior high school or below, senior high school or technical school, college or above), parenting style (strict, pamper, indulge/rude/frequently changing or open-minded). Whether participant has begun puberty (yes or no) was measured by items developed with reference to the criteria proposed by Ye [20]. Emotional management ability and social support were measured by the 4-item subscale of the Emotional Intelligence Inventory [21] and the 17-item Adolescents Social Support Scale [22], respectively. The Cronbach α coefficient of the scales were 0.84 and 0.96, respectively.

2.2.2. ACEs

ACEs were defined as having experienced potentially traumatic events that occurred in childhood, which included childhood maltreatment, other common forms of ACEs and smoking in the present study. Childhood maltreatment was evaluated by the Chinese version of Child Trauma Questionnaire (CTQ) [23], which assesses five different forms of childhood trauma (emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect). The CTQ comprises 28 summed items using 5-point Likert responses: 1, never like this; 2, rarely like this; 3, sometimes like this; 4, often like this; and 5, always like this. Respondents were defined as exposed to a category if the participants responded '3, sometimes like this', '4, often like this' or '5, always like this' to any item in that category [9]. The CTQ has been demonstrated to have a good internal consistency, with a Cronbach α coefficient of 0.74 in a previous study [9] and 0.79 in the present study. Questions used to assess for the presence of other forms of ACEs were derived from previous studies [5-6], and include: (a) the divorce of parents (yes or no); (b) being bullied by peers (yes or no); (c) family financial difficulties (household income less than 5,000 RMB per month [24], yes or no); (d) poor living environment (per capita living area of family member less than 20 square meters, yes or no); (e) parent-child separation (separation longer than 6 months before 6 years old [25], yes or no); (f) family history of psychiatric diseases (yes or no), and (g) no close friends (yes or no). The Cronbach α coefficient of these questions were 0.74. Respondents were classified as exposed to the type of ACEs if the participants responded to 'yes' to any of these questions. We defined smoking as a form of ACEs since it may be a proxy variable of having witnessed parental substance abuse [26]. Items used for evaluating smoking were derived from Global Youth tobacco Surveys, and participants who smoked a cigarette on at least 1 day during the past 30 days were classified as smokers [27].

2.2.3. Depressive symptoms

A Chinese version of the Center for Epidemiologic Studies Depression Scale (CESD) was used to measure depressive symptoms [28], which consists of 9 items using 4-point Likert responses: 0, never true; 1, rarely true; 2, often true; and 3, always true, thus, the total scores on CESD range from 0 to 27. The higher scores indicate greater risk of depression or more severe depressive symptoms [28]. Participants were divided into two groups based on the cutoff point proposed by He. Participants with CEDS scores between 10 and 27 were classified as having depressive symptoms. Participants with CEDS scores between 0-9 were classified as not having depressive symptoms [28]. The Cronbach α coefficient of the scale in the present study was 0.83.

2.2.4. Anxiety symptoms

Anxiety symptoms. Anxiety symptoms were measured by using the General Anxiety Disorder-7 (GAD-7) [29], which consists of 7 items using 4-point Likert responses: 0, never true; 1, rarely true; 2, often true; and 3, always true. Total scores on GAD-7 range from 0 to 21, with higher scores indicating greater risk of anxiety or more severe anxiety symptoms. Participants were divided into two groups based on the total scores of the GAD-7: (1) scores between 5 and 21, were defined as having anxiety symptoms; (2) scores between 0 and 4, defined as not having anxiety symptoms [29]. The Cronbach α coefficient of the scale in the present study was 0.92.

2.2.5. NSSI, SI and SA

We used the Chinese version of the Functional Assessment of Self-mutilation (FASM) to assess NSSI during the past 12 months [25]. All participants were asked, "During the past 12 months, have you harmed yourself in a way that was deliberate, but not intended to take your life?". A total of 8 methods were listed, included hitting, hair pulling, head banging, pinching, scratching, biting, burning, and cutting. For those who reported that they had engaged in NSSI, the frequency of NSSI was investigated. In the present study, NSSI was dichotomized (frequency of NSSI of three or more acts in the past year versus fewer than three as yes or no, respectively) for analysis [9]. The internal consistency reliability of FASM was 0.80 in the present study.

SI and SA were measured using items derived from the Global School-Based Student Health Survey [30]. SI was defined as a 'yes' in response to the question "During the past 12 months, did you ever seriously consider attempting suicide?". SA was measured by the question of "During the past 12 months, how many times did you actually attempt suicide?" with SA defined as once or more.

2.3. Statistical Analysis

Frequencies and proportions for categorical variables and mean (SD) for continuous variables were used to describe the characteristics of the participants and NSSI or suicidality by the study variables. We used χ^2 tests or 2-tailed, unpaired t tests to compare the distribution between males and females according to the study variables. To test associations of ACEs with NSSI and suicidality, we used logistic regression to separately estimate the unadjusted odds ratios (ORs), adjusted ORs and 95% CIs of NSSI, SI and SA by 13 types of ACEs. In the adjusted models, we adjusted for regional areas, school type, ethnicity, sex, single child, caregiver's educational level, parenting style, puberty, mutually exclusive ACEs, social support (continuous data), and emotional management ability (continuous data). We also estimated the graded associations of ACEs with NSSI and suicidality, in which an ordinal number of ACEs categories score was created by summing the dichotomous ACEs items (range, 0 [unexposed] to 13 [exposed to 13 types of ACEs assessed]). The total score of ACEs was then converted in to three categories (0-2, 3-4, 5-13) based on its tertile, with 0-2 experiences selected as the referent for analysis purposes.

To test the assumption of the mediating effects of depressive and anxiety symptoms on the association of ACEs with NSSI, SI and SA, we conducted mediation analyses by a logistic decomposition of the total effects into direct and indirect effects using the "ldecomp" command in Stata [31]. We also estimated the indirect effects of depressive and anxiety symptoms separately. Figure 1 shows the theoretical framework underlying our mediation analysis. In the mediation analysis, we only reported the ORs for the ACEs which was independently associated with NSSI and suicidality in logistic regression models.

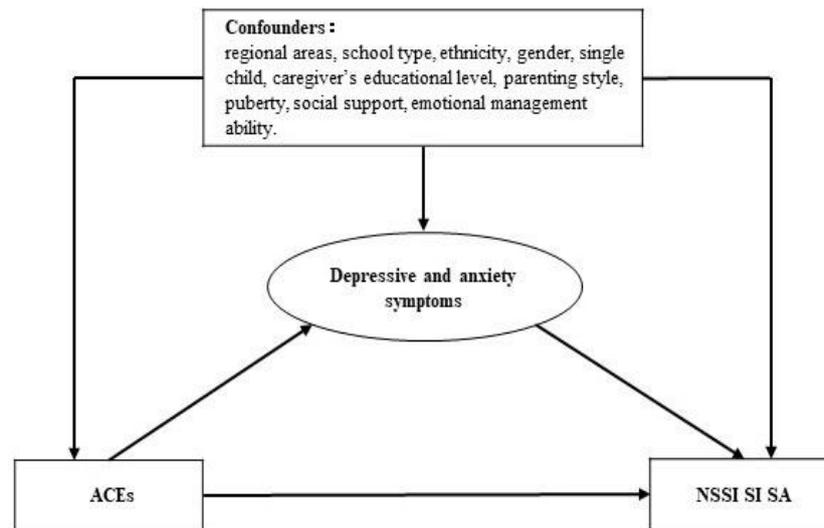


Figure 1. Hypothesized mediation model.

Data were missing in ethnicity (7.8%), caregiver's educational level (2.1%), single child (0.1%), and parenting style (1.0%). We imputed these missing covariates by using the monotone logistic regression method based on other sociodemographic variables, by producing 20 interpolated datasets. The significance level was set at $P=0.05$ and all tests were 2-tailed. Statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp) and Stata (version 14.0, Stata Corp LLC, College Station, TX).

3. Results

3.1. Participant Characteristics

Of 1844 initial potential participants, 40 did not return the consent form, 28 were away from school at the time of the investigation, and 5 submitted an incomplete questionnaire with at least 15% of the items unanswered. The omission of these yielded a final sample of 1771 (96.0%) participants. There were no significant differences in residential area, school type, age and sex between respondents and non-respondents (Table S1 in the Supplementary Materials). Of the 1771 final participants, 994 were males (56.1%) and 777 were females (43.9%), with 60.7% from Zhongshan City. The age of the participants ranged from 11 to 16 years, with the mean (SD) age of 12.9 (0.6) years. All students were in the seventh-grade, 96.6% were Han ethnicity, 17.0% were a single child, 357 (20.2%) reported depressive symptoms and 548 (30.9%) reported anxiety symptoms. Of the 92.0% of the overall sample who experienced 1 or more of the childhood adversities; the mean number of ACEs was 3.5 (SD=1.9, median=3, mode=2, range=1-10) (Table S2 in the Supplementary Materials). Emotional neglect (56.6%), physical neglect (47.1%), parent-child separation (44.0%), and emotional abuse (36.0%) were the most frequently reported ACEs among the participants. Additional characteristics of the participants according to sex are summarized in Table 1.

Table 1. Characteristics of participants with respect to gender.

Variables	Sex		Total (n=1771)	NSSI (n=303)	SI (n=436)	SA (n=147)
	males (n = 994)	females (n = 777)				
Regional areas (n, %) *						
Qidong County	293(29.5)	161(20.7)	454(25.6)	95(31.4)	131(30.0)	49(33.3)
Guangming District	132(13.3)	111(14.3)	243(13.7)	60(19.8)	74(17.0)	36(24.5)
Zhongshan City	569(57.2)	505(65.0)	1074(60.7)	148(48.8)	231(53.0)	62(42.2)
School type (n, %) *						
Public	384(38.6)	353(45.4)	737(41.6)	94(31.0)	165(37.8)	44(29.9)
Private	610(61.4)	424(54.6)	1034(58.4)	209(69.0)	271(62.2)	103(70.1)
Ethnicity (n, %) ^a						
Han	875(88.0)	700(90.1)	1575(88.9)	265(87.5)	378(86.7)	130(88.4)
Other	31(3.1)	27(3.5)	58(3.3)	9(3.0)	15(3.4)	6(4.1)
Age (M, SD)	12.95±0.63	12.91±0.62	12.93±0.62	12.91±0.69	12.95±0.68	12.91±0.70
Single child (n, %) ^{*, a}	194(19.5)	107(13.8)	301(17.0)	44(14.5)	59(13.5)	19(12.9)
Caregiver's educational level (n, %) ^a						
Junior high school or below	578(58.2)	463(59.6)	1041(58.8)	180(59.4)	262(60.2)	90(61.2)
Senior high school or technical school	223(22.4)	186(23.9)	409(23.1)	77(25.4)	113(25.9)	36(24.5)
College or above	167(16.8)	117(15.1)	284(16.0)	41(13.5)	56(12.8)	19(12.9)
Parenting style (n, %) *						
Strict	367(36.9)	211(27.0)	578(32.7)	85(28.1)	117(26.8)	33(22.4)
Pamper	43(4.3)	24(3.1)	67(3.8)	11(3.6)	18(4.1)	5(3.4)
Indulge/Rude/Frequently changing	124(12.5)	96(12.4)	220(12.4)	69(22.8)	98(22.5)	43(29.3)
Open-minded	449(45.2)	439(56.5)	888(50.1)	135(44.6)	197(45.2)	63(42.9)
Puberty (n, %) *	648(65.2)	724(93.2)	1372(77.5)	257(84.8)	359(82.3)	125(85.0)
ACEs (n, %)						
Have no close friends	35(3.6)	31(4.1)	66(3.8)	25(8.6)	27(6.4)	14(9.9)

Smoking *	26(2.6)	6(0.8)	32(1.8)	12(4.0)	18(4.1)	11(7.5)
Parents divorced	73(7.3)	58(7.5)	131(7.4)	31(10.2)	46(10.6)	22(15.0)
Parent-child separation *	464(46.7)	316(40.7)	780(44.0)	174(57.4)	234(53.7)	85(57.8)
Family income <5000 RMB/month *	344(34.6)	321(41.3)	665(37.5)	115(38.0)	167(38.3)	57(38.8)
Family history of psychiatric diseases	13(1.3)	8(1.0)	21(1.2)	8(2.6)	8(1.8)	4(2.7)
Poor living environment	323(32.5)	273(35.1)	596(33.7)	136(44.9)	181(41.5)	74(50.3)
Emotional abuse	324(32.6)	313(40.3)	637(36.0)	187(61.7)	264(60.6)	108(73.5)
Physical abuse *	227(22.8)	109(14.0)	336(19.0)	103(34.0)	137(31.4)	52(35.4)
Sexual abuse *	93(9.4)	32(4.1)	125(7.1)	37(12.2)	51(11.7)	24(16.3)
Emotional neglect	558(56.1)	444(57.1)	1002(56.6)	228(75.2)	326(74.8)	113(76.9)
Physical neglect *	503(50.6)	332(42.7)	835(47.1)	179(59.1)	247(56.7)	95(64.6)
Being bullied	254(25.6)	219(28.2)	473(26.7)	149(49.2)	208(47.7)	82(55.8)
Total number of ACEs (n, %)						
0-2	391(39.3)	325(41.8)	716(40.4)	50(16.5)	92(21.1)	22(15.0)
3-4	354(35.6)	253(32.6)	607(34.3)	112(37.0)	143(32.8)	38(25.9)
≥5	249(25.1)	199(25.6)	448(25.3)	141(46.5)	201(46.1)	87(59.2)
Depressive symptoms (n, %) *	164(16.5)	193(24.8)	357(20.2)	151(49.8)	212(48.6)	99(67.3)
Anxiety symptoms (n, %) *	278(28.0)	270(34.7)	548(30.9)	202(66.7)	262(60.1)	114(77.6)
Emotional management ability (M, SD) *	11.76±3.16	10.99±3.14	11.42±3.18	9.22±3.11	9.25±2.95	8.50±2.99
Social support (M, SD) *	67.93±15.74	66.27±16.03	67.20±15.88	57.84±18.35	57.73±17.50	53.68±18.15

* The distributions of sex with respect to this characteristic were all statistically significant ($P < 0.05$). a. missing data existed.

The 12-month prevalence of NSSI was 17.1%; SI was 24.6%; and SA was 8.3%. Of the 17.1% of the overall sample who engaged in NSSI at least 3 times in the 12 months preceding the survey, 89.1% reported 1-5 methods of NSSI (mean=3.0, SD=1.7, median=3, mode=2, range=1-8). More specifically, self-hitting, self-pinching and self-scratching were the most frequent of NSSI reported in the study population (Table S3 in the Supplementary Materials).

3.2. Association of ACEs with NSSI, SI and SA

Table 2 shows the frequencies and prevalence of NSSI according to the 13 types of ACEs. The prevalence of NSSI ranged from 17.3% among participants whose family income less than 5000 RMB (\$700) per month, to 38.1% in participants who had family history of psychiatric diseases. All 13 forms of ACEs, except of family income less than 5000 RMB (\$700) per month, were significantly associated with NSSI in unadjusted model. However, in the adjusted model, significant associations were only found between smoking, parent-child separation, emotional abuse, physical abuse and being bullied and NSSI, with the adjusted OR of 2.41(95%CI 1.01-5.75) 1.80(95%CI 1.28-2.54), 1.69(95%CI 1.21-2.37), 2.08(95%CI 1.44-3.01) and 1.87 (95%CI 1.35-2.59), respectively (Adjusted model in Table 2).

Table 2. Frequencies, prevalence, and odds ratio of 13 types of ACEs according to NSSI.

ACEs		NSSI (n, %)	Model 1 ^a		Model 2 ^b	
			OR (95%CI)	P-value	OR (95%CI)	P-value
Have no close friend	No(n=1657)	265(16.0)	1.00(reference)		1.00(reference)	
	Yes(n=66)	25(37.9)	3.20(1.92-5.36)	<0.001	1.65(0.86-3.15)	0.131
Smoking	No(n=1739)	291(16.7)	1.00(reference)		1.00(reference)	
	Yes(n=32)	12(37.5)	2.99(1.44-6.18)	0.002	2.41(1.01-5.75)	0.048
Parents divorced	No(n=1640)	272(16.6)	1.00(reference)		1.00(reference)	
	Yes(n=131)	31(23.7)	1.56(1.02-2.38)	0.038	1.04(0.62-1.74)	0.898
Parent-child separation	No(n=991)	129(13.0)	1.00(reference)		1.00(reference)	
	Yes(n=780)	174(22.3)	1.92(1.49-2.46)	<0.001	1.80(1.28-2.54)	0.001
Family income <5000 RMB/month	No(n=1106)	188(17.0)	1.00(reference)		1.00(reference)	
	Yes(n=665)	115(17.3)	1.02(0.49-1.32)	0.873	1.07(0.77-1.50)	0.684
Family history of psychiatric diseases	No(n=1750)	295(16.9)	1.00(reference)		1.00(reference)	
	Yes(n=21)	8(38.1)	3.04(1.25-7.39)	0.010	2.39(0.82-6.99)	0.111
Poor living environment	No(n=1175)	167(14.2)	1.00(reference)		1.00(reference)	
	Yes(n=596)	136(22.8)	1.79(1.39-2.30)	<0.001	1.28(0.90-1.82)	0.174
Emotional abuse	No(n=1134)	116(10.2)	1.00(reference)		1.00(reference)	
	Yes(n=637)	187(29.4)	3.65(2.82-4.72)	<0.001	1.69(1.21-2.37)	0.002
Physical abuse	No(n=1435)	200(13.9)	1.00(reference)		1.00(reference)	
	Yes(n=336)	103(30.7)	2.73(2.07-3.60)	<0.001	2.08(1.44-3.01)	<0.001
Sexual abuse	No(n=1646)	266(16.2)	1.00(reference)		1.00(reference)	
	Yes(n=125)	37(29.6)	2.18(1.45-3.27)	0.003	1.38(0.81-2.36)	0.244
Emotional neglect	No(n=769)	75(9.8)	1.00(reference)		1.00(reference)	
	Yes(n=1002)	228(22.8)	2.76(2.06-3.61)	<0.001	1.32(0.93-1.86)	0.121
Physical neglect	No(n=936)	124(13.2)	1.00(reference)		1.00(reference)	
	Yes(n=835)	179(21.4)	1.79(1.39-2.30)	<0.001	1.42(0.98-2.07)	0.066
Being bullied	No(n=1298)	154(11.9)	1.00(reference)		1.00(reference)	

	Yes(n=473)	149(31.5)	3.42(2.64-4.42)	<0.001	1.87(1.35-2.59)	<0.001
Total number of ACEs	0-2(n=716)	50(7.0)	1.00(reference)		1.00(reference)	
	3-4(n=607)	112(18.5)	3.01(2.12-4.29)	<0.001	2.04(1.39-2.99)	<0.001
	≥5(n=448)	141(31.5)	6.12(4.31-8.68)	<0.001	2.62(1.72-3.98)	<0.001

a. Unadjusted OR. b. Adjusted for regional areas, school type, ethnicity, sex, single child, caregiver's educational level, parenting style, puberty, social support, emotional management ability and exclusive mutually ACEs.

Table 3 shows the frequencies and prevalence of SI according to the 13 types of ACEs. The prevalence of SI ranged from 25.1% in participants whose family income less than 5000 RMB per month, to 56.3% in participants who reported smoking. All ACEs, except of family income less than 5000 RMB (\$700) per month and family history of psychiatric diseases, were significantly associated with SI in unadjusted model. In the adjusted model, significant associations remained between smoking, parent-child separation, emotional abuse, physical abuse, emotional neglect and being bullied and SI, with the adjusted OR of 4.03 (95%CI 1.66-9.81), 1.42(95%CI 1.07-1.90), 1.91(95%CI 1.41-2.59), 1.80(95%CI 1.27-2.57), 1.78(95%CI 1.28-2.49) and 2.08 (95%CI 1.54-2.81), respectively.

Table 3. Frequencies, prevalence, and odds ratio of 13 types of ACEs according to SI.

ACEs		SI (n, %)	Model 1 ^a		Model 2 ^b	
			OR (95%CI)	P-value	OR (95%CI)	P-value
Have no close friend	No(n=1657)	393(23.7)	1.00(reference)		1.00(reference)	
	Yes(n=66)	27(40.9)	2.23(1.35-3.68)	0.001	0.88(0.45-1.74)	0.719
Smoking	No(n=1739)	418(24.0)	1.00(reference)		1.00(reference)	
	Yes(n=32)	18(56.3)	4.06(2.00-8.24)	<0.001	4.03(1.66-9.81)	0.002
Parents divorced	No(n=1640)	390(23.8)	1.00(reference)		1.00(reference)	
	Yes(n=131)	46(35.1)	1.74(1.19-2.53)	0.004	1.13(0.69-1.85)	0.626
Parent-child separation	No(n=991)	202(20.4)	1.00(reference)		1.00(reference)	
	Yes(n=780)	234(30.0)	1.67(1.35-2.08)	<0.001	1.42(1.07-1.90)	0.016
Family income <5000 RMB/month	No(n=1106)	269(24.3)	1.00(reference)		1.00(reference)	
	Yes(n=665)	167(25.1)	1.04(0.84-1.30)	0.708	1.04(0.81-1.21)	0.535
Family history of psychiatric diseases	No(n=1750)	428(24.5)	1.00(reference)		1.00(reference)	
	Yes(n=21)	8(38.1)	1.90(0.78-4.62)	0.149	1.47(0.48-4.51)	0.502
Poor living environment	No(n=1175)	255(21.7)	1.00(reference)		1.00(reference)	
	Yes(n=596)	181(30.4)	1.57(1.26-1.97)	<0.001	0.94(0.67-1.31)	0.716
Emotional abuse	No(n=1134)	172(15.2)	1.00(reference)		1.00(reference)	
	Yes(n=637)	264(41.4)	3.96(3.16-4.96)	<0.001	1.91(1.41-2.59)	<0.001
Physical abuse	No(n=1435)	299(20.8)	1.00(reference)		1.00(reference)	
	Yes(n=336)	137(40.8)	2.62(2.03-3.37)	<0.001	1.80(1.27-2.57)	0.001
Sexual abuse	No(n=1646)	385(23.4)	1.00(reference)		1.00(reference)	
	Yes(n=125)	51(40.8)	2.26(1.55-3.28)	<0.001	1.35(0.81-2.23)	0.249
Emotional neglect	No(n=769)	110(14.3)	1.00(reference)		1.00(reference)	
	Yes(n=1002)	326(32.5)	2.89(2.27-3.68)	<0.001	1.78(1.28-2.49)	0.001
Physical neglect	No(n=936)	189(20.2)	1.00(reference)		1.00(reference)	
	Yes(n=835)	247(29.6)	1.66(1.34-2.07)	<0.001	1.09(0.78-1.52)	0.622

Being bullied	No(n=1298)	228(17.6)	1.00(reference)		1.00(reference)	
	Yes(n=473)	208(44.0)	3.68(2.92-4.64)	<0.001	2.08(1.54-2.81)	<0.001
Total number of ACEs	0-2(n=716)	92(12.8)	1.00(reference)		1.00(reference)	
	3-4(n=607)	143(23.6)	2.09(1.57-2.79)	<0.001	1.32(0.95-1.83)	0.093
	≥5(n=448)	201(44.9)	5.52(4.14-7.36)	<0.001	2.13(1.48-3.07)	<0.001

a. Unadjusted OR. b. Adjusted for regional areas, school type, ethnicity, sex, single child, caregiver's educational level, parenting style, puberty, social support, emotional management ability and exclusive mutually ACEs.

Table 4 shows the frequencies and prevalence of SA according to the 13 types of ACEs. The prevalence of SA ranged from 8.6% in participants whose family income were less than 5000 RMB (\$700) per month, to 34.4% in participants who reported smoking. All the 13 types of ACEs, except of family income less than 5000 RMB (\$700) and had a family history of psychiatric diseases, were significantly associated with SA in unadjusted model. In the adjusted model, significant associations of smoking, emotional abuse and being bullied with SA remained, and the adjusted OR were 4.30(95%CI, 1.67-11.10), 2.42(95%CI, 1.58-3.72) and 1.75(95%CI, 1.17-2.60), respectively (Adjusted in Table 4).

Table 4. Frequencies, percentage, and odds ratio of 13 types of ACEs according to SA.

ACEs	SA (n, %)	Model 1 ^a		Model 2 ^b	
		OR (95%CI)	P-value	OR (95%CI)	P-value
Have no close friend	No(n=1657)	128(7.7)	1.00(reference)	1.00(reference)	
	Yes(n=66)	14(21.2)	3.22(1.74-5.96)	<0.001	1.15(0.52-2.51) 0.732
Smoking	No(n=1739)	136(7.8)	1.00(reference)	1.00(reference)	
	Yes(n=32)	11(34.4)	6.17(2.92-13.07)	<0.001	4.21(1.62-10.98) 0.003
Parents divorced	No(n=1640)	125(7.6)	1.00(reference)	1.00(reference)	
	Yes(n=131)	22(16.8)	2.45(1.49-4.01)	<0.001	1.56(0.88-2.77) 0.126
Parent-child separation	No(n=991)	62(6.3)	1.00(reference)	1.00(reference)	
	Yes(n=780)	85(10.9)	1.83(1.30-2.58)	<0.001	1.19(0.77-1.85) 0.520
Family income <5000 RMB/month	No(n=1106)	90(8.1)	1.00(reference)	1.00(reference)	
	Yes(n=665)	57(8.6)	1.06(0.75-1.50)	0.749	0.98(0.63-1.54) 0.929
Family history of psychiatric diseases	No(n=1750)	143(8.2)	1.00(reference)	1.00(reference)	
	Yes(n=21)	4(19.0)	2.64(0.88-7.96)	0.073	1.74(0.49-6.17) 0.394
Poor living environment	No(n=1175)	73(6.2)	1.00(reference)	1.00(reference)	
	Yes(n=596)	74(12.4)	2.14(1.52-3.01)	<0.001	1.20(0.76-1.89) 0.437
Emotional abuse	No(n=1134)	39(3.4)	1.00(reference)	1.00(reference)	
	Yes(n=637)	108(17.0)	5.73(3.92-8.39)	<0.001	2.39(1.56-3.67) <0.001
Physical abuse	No(n=1435)	95(6.6)	1.00(reference)	1.00(reference)	
	Yes(n=336)	52(15.5)	2.58(1.80-3.71)	<0.001	1.25(0.76-2.08) 0.998
Sexual abuse	No(n=1646)	123(7.5)	1.00(reference)	1.00(reference)	
	Yes(n=125)	24(19.2)	2.94(1.82-4.76)	0.002	1.44(0.78-2.65) 0.244
Emotional neglect	No(n=769)	34(4.4)	1.00(reference)	1.00(reference)	
	Yes(n=1002)	113(11.3)	2.75(1.85-4.08)	<0.001	1.16(0.67-1.99) 0.594
Physical neglect	No(n=936)	52(5.6)	1.00(reference)	1.00(reference)	

Being bullied	Yes(n=835)	95(11.4)	2.18(1.54-3.10)	<0.001	1.10(0.71-1.69)	0.730
	No(n=1298)	65(5.0)	1.00(reference)		1.00(reference)	
Total number of ACEs	Yes(n=473)	82(17.3)	3.98(2.82-5.62)	<0.001	1.73(1.16-2.57)	0.007
	0-2(n=716)	22(3.1)	1.00(reference)		1.00(reference)	
	3-4(n=607)	38(6.3)	2.11(1.23-3.60)	0.007	1.17(0.66-2.08)	0.599
	≥5(n=448)	87(19.4)	7.60(4.68-12.34)	<0.001	2.45(1.38-4.36)	0.002

a. Unadjusted OR. b. Adjusted for regional areas, school type, ethnicity, sex, single child, caregiver's educational level, parenting style, puberty, social support, emotional management ability and exclusive mutually ACEs.

3.3. Mediation analysis

The results from the mediation analyses indicated that the combined indirect effects of depressive and anxiety symptoms on associations of ACEs with NSSI, SI and SA were all significant ($P < 0.05$), with the aOR ranged from 1.12(1.05-1.19) to 1.97(1.58-2.46) (Table 5). The direct effects of emotional abuse on NSSI and being bullied on SA were no longer significant in the mediation model, with the aORs of 1.27(0.89-1.84) and 1.43(0.98-2.12), respectively. Similar results were found in participants stratified by sex (Table S4-5 in the Supplementary Materials).

Table 5. Logistic regression model of direct and indirect effects through mediators on NSSI and suicidality.

	OR (95%CI)				
	Total effect	Direct effect	Indirect effect, Combined	Indirect effect, through	
				Depressive symptoms	Anxiety symptoms
NSSI^a					
Smoking	2.32(1.01-5.26)	1.49(0.66-3.35)	1.55(1.25-1.93)	1.21(1.03-1.42)	1.45(1.21-1.75)
Parent-child separation	1.77(1.28-2.41)	1.54(1.13-2.10)	1.15(1.06-1.23)	1.07(1.03-1.13)	1.11(1.04-1.17)
Emotional abuse	2.08(1.48-2.89)	1.27(0.89-1.84)	1.62(1.38-1.92)	1.27(1.12-1.46)	1.43(1.26-1.65)
Physical abuse	2.25(1.57-3.25)	1.57(1.14-2.18)	1.43(1.27-1.62)	1.20(1.09-1.31)	1.31(1.16-1.46)
Being bullied	2.34(1.79-3.06)	1.52(1.19-1.95)	1.54(1.30-1.82)	1.23(1.12-1.35)	1.39(1.23-1.57)
SI^a					
Smoking	3.82(1.40-10.38)	2.69(1.04-6.96)	1.42(1.16-1.75)	1.26(1.01-1.57)	1.27(1.11-1.46)
Parent-child separation	1.54(1.17-2.01)	1.38(1.05-1.19)	1.12(1.05-1.19)	1.08(1.02-1.15)	1.06(1.02-2.46)
Emotional abuse	1.99(1.54-2.61)	1.35(1.01-1.82)	1.48(1.28-1.72)	1.32(1.20-1.46)	1.25(1.12-1.38)
Physical abuse	1.95(1.46-2.61)	1.46(1.11-1.92)	1.34(1.20-1.49)	1.23(1.09-1.38)	1.17(1.08-1.27)
Emotional neglect	1.79(1.30-2.44)	1.35(1.01-1.82)	1.31(1.16-1.48)	1.23(1.13-1.35)	1.13(1.06-1.20)
Being bullied	2.32(1.84-2.92)	1.63(1.30-2.08)	1.42(1.22-1.63)	1.27(1.17-1.38)	1.22(1.11-2.23)
SA^a					
Smoking	6.05(2.32-15.96)	3.46(1.35-8.94)	1.75(1.34-2.29)	1.40(1.07-1.86)	1.52(1.22-1.90)
Emotional abuse	3.63(2.36-5.64)	1.84(1.22-2.80)	1.97(1.58-2.46)	1.57(1.31-1.88)	1.52(1.27-1.80)
Being bullied	2.59(1.63-3.97)	1.43(0.98-2.12)	1.80(1.49-2.16)	1.46(1.26-1.70)	1.46(1.27-1.67)

a. Adjusted for regional areas, school type, ethnicity, sex, single child, caregiver's educational level, parenting style, puberty, social support, emotional management ability and mutually exclusive ACEs.

4. Discussion

This study used baseline data of a multi-center cohort study to investigate the possible associations of 13 common types of ACEs with NSSI and suicidality, as well as the potential mediation effects of depressive and anxiety symptoms therein. The data revealed that some types of ACEs are independently associated with NSSI, SI and SA. Children and adolescents who had experiences of smoking, physical abuse and being bullied during childhood are consistently associated with higher risk of NSSI, SI and SA. Mediation analyses suggested that ACEs associated with NSSI and suicidality were partially or fully mediated through depressive and anxiety symptoms.

ACEs, defined as experiences that threaten the child's bodily, familial, or social safety or security [11], are highly prevalent. Data from the Behavioral Risk Factor Surveillance System (BRFSS) demonstrated that 61.55% of the US adult population has experienced at least 1 of 8 types of ACEs [32]. Although many of existing literatures on ACEs focused on childhood maltreatment and household dysfunction, there is a lack of consensus on precisely what constitutes ACEs given the interindividual variation in threat perception [33], which led to incomparable of prevalence of ACEs between different studies directly. In the present study, we assessed 13 types of ACEs ranged from broad categories of maltreatment and household dysfunction to more targeted experiences of being bullied, smoking, and economic disadvantage, and data demonstrated that 92.0% of the participants has experienced at least 1 type of ACEs, which was similar with a previous study measured 10 types of ACEs defined by the ACE study [9].

4.1. Associations of ACEs with NSSI, SI and SA

Previous research has demonstrated that many types of ACEs, including physical and sexual abuse [34], parent-child separation [25], and other familiar stressors are associated with NSSI and suicidality. Indeed, an investigation of 1404 college students in China suggested that individuals who experienced sexual abuse in childhood were more at risk of engaging in NSSI and suicidality [35]. Similarly, data from the UK 1958 British Birth Cohort Study also suggested that parental divorce, physical abuse, sexual abuse in childhood were associated with SI at the age of 45 [36]. Our study extends this line of research by exploring associations between broader types of ACEs and NSSI and suicidality within Chinese community populations. This notwithstanding, the associations observed between all ACEs types and NSSI and suicidality in the present study were not all consistent prior research involving clinical [37] and community populations [35]. For instance, whereas significant associations between physical abuse and NSSI have been documented in previous studies [35] this was not the case in our study. Similar with previous studies [9], varied associations were found across different types of ACEs, as ACEs were not significantly associated with NSSI and suicidality after the adjusting for paternal care [38]. The discrepancies in the findings between studies for the associations of ACEs with NSSI and suicidality may be related to study samples, definitions of ACEs, and adjusted variables.

Findings from the present study demonstrated that parent-child separation was associated with NSSI and SI but not with SA, which was consistent with one of our previous studies involving a national representative sample [25]. A similar association was also established for physical abuse. Varied associations of the same type of ACEs with NSSI, SI and SA, may imply the etiology differences between NSSI, SI and SA, although existing literature indicated that the risk factors of NSSI and suicidality are regularly consistent [39]. Smoking in childhood, defined as an ACEs in the present study, was associated with NSSI and suicidality, even after adjusting for many potential confounders and mutually ACEs, which was in line with previous studies [40]. Harrison and colleagues used the UK Biobank data found associations of smoking behaviors with SI and SA, although the subsequence mendelian randomization analysis did not find clear evidence for a causal effect of smoking on SI and SA [40]. Of noted, the frequencies of smokers among present study participants were relatively small, requiring further studies to identify whether the associations of smoking with NSSI and suicidality were occasional or significant. Moreover, although many studies suggested that child smoking could be proxy variable of having witnessed parental smoking or other substance use [26], whether child smoking can be defined as one form of ACEs also need further studies.

Findings of our study indicated that being bullied was associated with NSSI and suicidality, which was also consistent with previous studies that conducted among community population [30] but not with studies among clinical patients [41]. Being bullied may increase the risk of adverse

psychological outcomes in terms of NSSI and suicidality in the short and the long term [41], thus, it would be reasonable to suggest that intervention strategies could be implemented based on the association between being bullied, NSSI and suicidality.

4.2. The mediation of depressive and anxiety symptoms on associations of ACEs with NSSI, SI and SA

Many studies have examined whether the associations between ACEs and NSSI and suicidality are mediated by different variables; in most cases, however, these mediators include factors such as social support or alexithymia [42]. Our study extends knowledge in this area by demonstrating the associations of ACEs with NSSI and suicidality were mediated through depressive and anxiety symptoms. The association between ACEs, depressive and anxiety symptoms, NSSI, SI and SA is complex. Many previous studies have demonstrated that depressive symptoms may be a partial mediator between ACEs and NSSI among young adults [41]. For example, The UK 1958 British Birth Cohort study also found that ACEs predicts SI in midlife and is partially mediated by adolescent internalizing and externalizing disorders [41]. Duan and colleagues found that the association between being bullied, and suicide risk was mediated through negative coping styles and depressive symptoms [43]. Indeed, exposure to ACEs may increase the risk of adverse psychological symptoms. As such, it seems reasonable to suggest that depressive and anxiety symptoms, which are the most prevalent mental symptoms in adolescents [25], may mediate the association of ACEs with NSSI, SI and SA. Interestingly, we found the direct effects of emotional abuse and smoking on NSSI, and being bullied on SA were not significant, while the indirect effects were significant, suggesting the effects were completely mediated through depressive and anxiety symptoms. A possible explanation of the null direct effects of emotional abuse on NSSI and being bullied on SA may be due to sex differences in the prevalence of depressive and anxiety symptoms. In particular, previous studies have indicated that there are sex differences between the mediation effect of depressive symptoms on association of ACEs with NSSI [44]. Taken together, further studies investigating the mediation role of depressive and anxiety symptoms on association of ACEs with NSSI, SI and SA will be needed to delineate these complex associations.

4.3. Strengths and Limitations

This study is the first to examine the associations between a broad set of ACEs and NSSI and suicidality, and the extent to which these relations were mediated by depressive and anxiety symptoms among Chinese community children and adolescents. Although this study was conducted during the COVID-19 pandemic, there was a high response rate across the public and private schools involved; thus, our findings are helpful in exploring the above associations during the time of the COVID-19 pandemic. To this end, examining the associations between 13 types of ACEs and NSSI, SI and SA extends the existing literature on these associations, and our mediation analyses provides a deeper understanding of the nature of these associations. Collectively, these findings may have utility for developing preventions and interventions of NSSI and suicidality.

Several limitations should be acknowledged. Firstly, although our study used data from a large cohort study, the present study itself was a cross-sectional design; therefore, it is difficult to establish causal associations or to account for the temporal nature of the relations examined, and thus it may be inappropriate to examine the mediation of depressive and anxiety symptoms. Nonetheless, mediation analysis has been applied in previous similar study [12], and our findings also pertaining to the association of ACEs with NSSI, SI and SA were similar to several previous cohort studies [36; 41]. Secondly, given the study design, recall bias may have occurred as data were collected by retrospective self-report. The prevalence of ACEs, especially those with less impression could thus be underestimated. This may ultimately influence the strength of the observed associations; indeed, our results may represent a more conservative estimation than was presented [24]. However, the prevalence of ACEs, NSSI, SI, SA, depression and anxiety were comparable with previous studies [2-3; 45], and systematic reviews have demonstrated that data garnered from school-based students regarding self-harm and risk factors is likely to be reliable [45]. Thirdly, our study only focused on the presence of different types of ACEs; it may be important to understand the duration of these ACEs and an individual's subjective experience of the events. This may help to index the extent to which the ACEs impacted participants. Finally, our study only included seventh grade children and adolescents in traditional school environments. Therefore, we cannot assume that the present results

would generalize to other study phases or to those who are absent from school—perhaps due to mental health difficulties. This is important because the prevalence of some types of ACEs focused on in the present study, such as smoking, and being bullied, may change with study phases, and ACEs may be more prevalent in students who with low educational achievement and socioeconomic status [46]. Replication using other populations would help to determine the generality of the findings. Overall, caution should be exercised when applying the results to the total population of Chinese children and adolescents.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Table S1: Comparison of characteristics between respondent and non-respondent participants; Table S2: Childhood adversity statistics; Table S3: Frequency and prevalence of 8 types of NSSI; Table S4: Logistic regression model of direct and indirect effects through mediators on NSSI and suicidality in males; Table S5: Logistic regression model of direct and indirect effects through mediators on NSSI and suicidality in females.

Author Contributions: Dr Tang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Guo & Tang. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Guo. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Guo & Tang. Administrative, technical, or material support: Tang & Yu. Supervision: Tang.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by Institutional Review Board of Guangzhou Medical University (protocol code 2021010002).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy.

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