An Overall Trend of Headache Remission during COVID-19 Pandemic for Chinese Patients with Pre-existing Headache Highlights the Role of Family Supports

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Abstract

Background: Impact of COVID-19 pandemic on Chinese patients with pre-existing headache remains unclear. The present study investigated the impact of COVID-19 pandemic on headache patients in China.

Methods: A survey was conducted through an online survey platform from June 6, 2020. Demographic characteristics, PHQ-9 scores, ISI scores, COVID-19 questionnaires and headache profile section were included in the online questionnaires.

Results: Eventually a total of 15,000 participants from China completed the online questionnaire. Among them, 2806 participants (18.71%) had preexisting headache disorders. Our analysis showed a reality of those participants with remission of headache duration (3.414 ± 6.859 vs 4.033 ± 7.325 , $P=0.000$), headache days per month (1.788 ± 2.989 vs 2.092 ± 3.694 , $P=0.000$), and headache intensity (4.110 ± 1.609 vs 4.290 ± 1.680 , $P=0.000$), during COVID-19. Smoking ($OR=1.397$, 95% CI 1.090 to 1.790, $P=0.008$) and getting support from family members during the social isolation ($OR=1.656$, 95% CI 1.075 to 2.550, $P=0.022$) were the independent factors of remission in headache duration. Education level ($OR=1.478$, 95% CI 1.103 to 1.980, $P=0.009$) and having relative or acquaintance got COVID-19 ($OR=0.643$, 95% CI 0.458 to 0.902, $P=0.011$) were the independent factors of remission in headache severity. And participants living in Wuhan area, having COVID-19 symptoms or COVID-19 diagnosis and having relative or acquaintance got COVID-19 are more likely to get headache deteriorated.

Conclusions: Participants presented an overall trend of headache remission during COVID-19. Family supports played an important role in headache remission.

Background

The coronavirus disease 2019 (COVID-19), first reported in Wuhan, China, has caused a large global pandemic, and is moving quickly via human-to-human transmission, droplets, or direct contact¹. Currently, there are more than 32 million confirmed COVID-19 cases with more than 990,000 deaths worldwide. To minimize the exposure risk and prevent further spread of COVID-19, “social distancing” is advocated, to some extent, disrupting our normal life, work and medical care.

Typical symptoms of COVID-19 include fever, cough, and dyspnea². Besides, neurological symptoms, such as dizziness and headache, have also been reported³. Almost 11–34% of the hospitalized COVID-19 patients present with headache⁴, but clinical features and underlying mechanisms of these headaches remain unclear. In a study from Singapore, most healthcare workers develop de novo personal protective equipment (PPE) -associated headaches or exacerbation of their preexisting headache disorders⁵. Headache patients, particularly migraine, are more vulnerable to such major stressful life events. Anxiety and stress caused by COVID-19 pandemic may aggravate a headache. Additionally, the COVID19 outbreak has drastically affected the medical care of patients with preexisting headache disorders⁵. First, due to the restriction of “social distancing”, neurological physicians have had to adapt by replacing face-

to-face visits with telemedicine visits⁶⁻⁹. On the one hand, telemedicine techniques bring dramatic benefit, to protect both patients and physicians while continuing to help headache patients receive medical care^{6,8}. On the other hand, patients with headache disorders, especially chronic migraine, usually rely on specific treatment, like Onabotulinumtoxin and pericranial nerve blocks¹⁰. Telemedicine limits the application of these treatments, and leads to deterioration in those patients^{7,9}. In a word, it remains controversial whether the use of telemedicine can bring benefit for headache patients or not in the era of COVID-19. Second, headache medication like renin-angiotensin system (RAS) blockers and the non-steroid anti-inflammatory drug (NSAID) ibuprofen, might be connected with an increased risk for COVID-19 infection or a worse COVID19 clinical course¹¹. However, conclusive evidence is lacking currently.

Global situation of COVID-19 pandemic is not optimistic. This is a particularly vulnerable time for patients with preexisting headache disorders, having aroused wide concern among headache specialist. It is imperative to understand the present situation of headache during COVID-19. To our knowledge, no research on headache patients in China during the COVID-19 pandemic has been reported. Thus, the present study aims to investigate the impact of COVID-19 pandemic on headache patients in China, and to further explore potential factors aggravating or relieving headache.

Methods

Design and participants

A survey was conducted through an online survey platform from June 6, 2020, completely voluntary and non-commercial. The questionnaire was anonymous, designed by the research team from Mental Health Center of Renmin Hospital of Wuhan University and School of Computing of Huazhong university of science and technology. All participants sign an informed consent before filling in the questionnaire, and can withdraw from the survey at any time. And all the online questionnaires were expressed in Chinese. Persons in the nation were encouraged to complete and submit the online questionnaires attentively on time. Participants completing all the online questionnaires were recruited.

Variables and instruments

Demographic characteristics

Demographic data included gender, age, education level, chronic disease history, smoking and drinking history.

Depressive symptoms

The Patient Health Questionnaire-9 (PHQ-9), a nine item questionnaire, was applied to assess depressive symptoms. Items are rated on a 4-point Likert-type scale, ranging from 0 (not at all) to 3 (nearly every day). Total score can range from 0 to 27, with high scores meaning high depression¹².

Sleep quality

Insomnia Severity Index (ISI), a brief self-report instrument, was applied to assess subjective sleep quality. The ISI comprises seven items. Each item is rated on a 4-point Likert-type scale, ranging from 0 to 3, and the total score ranges from 0 to 28. A higher score suggests more severe insomnia¹³.

COVID-19 questionnaires

COVID-19 questionnaires included having COVID-19 symptoms or COVID-19 diagnosis, having relative or acquaintance got COVID-19, getting support from family members, getting support from the outside world during the social isolation.

The Impact of Event Scale Revised (IES-R), a self-administered questionnaire, was applied to assess the psychological impact of COVID-19. The IES-R comprises 22 items, ranging from 0 to 4, and the total score ranges from 0 to 88. A higher score suggests more severe symptoms¹⁴.

The headache profile section

The headache profile section included items on history of preexisting headache disorders, characteristics of accompanying symptoms (nausea, vomiting, photophobia, phonophobia and osmophobia, aggravation by or causing avoidance of routine physical activity, lacrimation, rhinorrhea, conjunctival injection, and eye bilges, remission by massage), headache triggers (increased stress, sleep too short, sleep too long, menstruation, bright light, noise or special smell, special foods and alcohol), headache intensity/headache days per month/headache duration at baseline or during COVID-19, factors associated with headache during COVID-19(stress, sleep quality, changes in the law of life and decreased social interaction).

Statistical Analysis

Statistical analysis was performed with SPSS V.25.0 software (IBM, West Grove, Pennsylvania, USA). Categorical data were reported using proportions, while continuous data with means and standard deviations. The chi-square test was used to find out whether differences in proportions are significant. Mann-Whitney U test or the Wilcoxon Signed Rank Test was used to compare non-normally distributed data. Binary logistic regression was first performed to explore variables associated with headache relief. Then multivariate logistic regression analyses were performed to verify the independent influence factor associated with headache relief. A p-value < 0.05 was considered to be statistically significant.

Results

Eventually a total of 15,000 participants from China completed the online questionnaire. Of which, 22 (0.13%) respondents were diagnosed with COVID-19 infections. Overall, the majority of respondents were female (8569/15000, 57.13%), aged 31–40 (6373/15000, 42.49%), and well educated (11425/15000, 76.12% with at least a bachelor degree). Among them, 2806 participants (18.71%) had preexisting headache disorders.

The epidemiology of headache disorders in China

Figure 1 shows demographic features of all headaches. Prevalence of headache peaked during adolescence (under 18 years old), followed by middle age (31–40 years). Headache was more prevalent in females (20.57%) than in males (16.22%).

Figure 2 presents characteristics of accompanying symptoms and headache triggers. 676 of 2806 participants (24.09%) reported accompanying symptoms with nausea or vomiting; 531 (18.92%) with photophobia, phonophobia or osmophobia; 641(18.92%) with aggravation by or causing avoidance of routine physical activity; 1555 (55.42%) with remission by massage; and 294 (10.48%) with lacrimation, rhinorrhea, conjunctival injection or eye bilges. Participants reported increased stress (48.43%), sleep too short (69.60%), sleep too long (8.62%), menstruation (23.52%), bright light, noise or special smell (13.79%), special foods (2.99%) and alcohol (7.34%) as precipitating factor for headache attacks.

Comparison of headache intensity, headache days per month, and headache duration at baseline and during COVID-19

Table 1 presents comparison of headache intensity, duration, frequency (days per month), at baseline and during COVID-19. Our analysis showed a reality of those participants with remission of headache duration (3.414 ± 6.859 vs 4.033 ± 7.325 , $P = 0.000$), headache days per month (1.788 ± 2.989 vs 2.092 ± 3.694 , $P = 0.000$), and headache intensity (4.110 ± 1.609 vs 4.290 ± 1.680 , $P = 0.000$), during COVID-19.

Table 1 Comparison of headache intensity, headache days per month, and headache duration at baseline and during COVID-19			
variables	Baseline	During COVID-19	P value
Headache severity	4.290 ± 1.680	4.110 ± 1.609	0.000
Headache duration (h)	4.033 ± 7.325	3.414 ± 6.859	0.000
Headache days per month	2.092 ± 3.694	1.788 ± 2.989	0.000

Figure 3 presents self-reported factors associated with remission or deterioration in headache during COVID-19. Participants reported decreased stress (19.35%), changes in the law of life (14.18%), good sleep quality (15.00%) or others (5.35%) as factors associated with headache remission, while increased stress (27.48%), bad sleep quality (29.12%), decreased social interaction (10.23%), changes in the law of life (4.45%) or others (1.00%) as factors associated with headache aggravation.

Application of the International Headache Society (IHS) criteria¹⁵ generated the following diagnosis of headache: 378 respondents had migraine, 1385 had tension-type headache (TTH), and 100 had cluster headache (CH). We observed that, remission in headache duration during COVID-19 differentiated significantly among different headache types (Fig. 4). Post hoc analysis using Bonferroni test showed that migraine presented higher remission rate of headache duration, compared with TTH (30.95% vs 25.05%, $P = 0.021$) and CH (30.95% vs 8.00%, $P = 0.000$). Besides, TTH presented higher remission rate of headache duration, compared with CH (25.05% vs 8.00%, $P = 0.000$).

Comparison of demographic characteristics for the remission group, unchanged group and aggravating group.

Table 2 presents comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache duration**.

Table 2

Comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache duration**

characteristics	The remission group ¹ (n = 686)	The unchanged group ² (n = 1936)	The aggravating group ³ (n = 184)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Male, n (%)	251(36.59)	715(36.93)	77(44.85)	0.393			
Age, n (%)				0.253			
< 30	176(25.66)	441(22.78)	53(28.80)				
30–50	463(67.49)	1371(70.82)	120(65.22)				
> 50	47(6.85)	124(6.40)	11(5.98)				
Education level, n (%)				0.035	0.152	0.172	0.018
junior colleague or lower	150(21.87)	374(19.32)	49(26.63)				
University or above	536(78.13)	1562(80.68)	135(73.37)				
Chronic disease history, n (%)	167(24.34)	444(22.93)	52(28.26)	0.253			
Smoking, n (%)	91(13.27)	334(17.25)	47(25.54)	0.000	0.015	0.000	0.005
Drinking, n (%)	279(40.67)	813(41.99)	88(47.83)	0.217			
Living in Wuhan, n (%)	20(2.92)	63(3.25)	13(7.07)	0.018	0.663	0.009	0.008
Having COVID-19 symptoms or COVID-19 diagnosis, n (%)	45(6.56)	86(4.44)	20(10.87)	0.000	0.029	0.048	0.000
Having relative or acquaintance got COVID-19, n (%)	80(11.66)	240(12.40)	38(20.65)	0.004	0.613	0.002	0.002
Getting support from family members, n (%)				0.001	0.015	0.000	0.005
Unchanged or more	659 (96.06)	1811 (93.54)	163 (88.59)				
Less	27(3.94)	125(6.46)	21(11.41)				

characteristics	The remission group ¹ (n = 686)	The unchanged group ² (n = 1936)	The aggravating group ³ (n = 184)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Getting support from the outside world, n (%)				0.028	0.056	0.011	0.120
Unchanged or more	599 (87.32)	1632 (84.30)	147 (79.89)				
Less	87(12.68)	304(15.70)	37(20.11)				
ISI score	6.70 ± 5.30	8.16 ± 5.67	10.22 ± 6.01	0.000	0.000	0.000	0.000
PHQ9 score	5.99 ± 4.74	6.92 ± 4.93	8.74 ± 4.89	0.000	0.000	0.000	0.000
ISER score	17.99 ± 14.18	21.08 ± 14.63	27.71 ± 16.96	0.000	0.000	0.000	0.000

686 of 2806 participants (24.45%) tended to improve in headache duration during COVID-19, 1936 (68.99%) remain unchanged, and 184 (6.56%) worsen. An initial comparative analysis showed significant difference in education level ($P = 0.035$), smoking ($P = 0.000$), place of residence ($P = 0.018$), COVID-19 symptoms or COVID-19 diagnosis ($P = 0.000$), relative or acquaintance got COVID-19 ($P = 0.004$), getting support from family members ($P = 0.001$), getting support from the outside world ($P = 0.028$) during the social isolation, ISI ($P = 0.000$), PHQ-9 ($P = 0.000$) and ISE-R ($P = 0.000$). Post hoc comparisons using Bonferroni test evidenced that the aggravating group presented significantly higher proportion of smoking, living in Wuhan area, having relative or acquaintance got COVID-19, getting less support from family members during the social isolation, and significantly higher ISI, PHQ-9 and ISE-R score, compared with the remission group ($P = 0.000$, $P = 0.009$, $P = 0.002$, $P = 0.000$, $P = 0.000$, $P = 0.000$, $P = 0.000$) and unchanged group ($P = 0.005$, $P = 0.008$, $P = 0.002$, $P = 0.005$, $P = 0.000$, $P = 0.000$, $P = 0.000$). The aggravating group also demonstrated significantly higher proportion of having COVID-19 symptoms or COVID-19 diagnosis, compared with the unchanged group ($P = 0.000$), and higher proportion of getting less support from the outside world during the social isolation, compared with the remission group ($P = 0.011$).

Table 3 presents comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache frequency (days per month)**.

Table 3

Comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache frequency**.

characteristics	The remission group ¹ (n = 737)	The unchanged group ² (n = 1790)	The aggravating group ³ (n = 279)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Male, n (%)	289(39.21)	633(35.36)	21(43.47)	0.015	0.068	0.228	0.010
Age, n (%)				0.431			
< 30	185(25.10)	410(22.91)	75(26.88)				
30–50	502(68.11)	1263(70.56)	190(68.10)				
> 50	50(6.79)	117(6.53)	14(7.82)				
Education level, n (%)				0.260			
junior colleague or lower	152(20.62)	354(19.78)	64(24.01)				
University or above	585(79.38)	1456(80.22)	212(75.99)				
Chronic disease history, n (%)	184(24.97)	385(21.51)	94(33.69)	0.000	0.059	0.005	0.000
Smoking, n (%)	123(16.69)	291(16.26)	58(20.79)	0.169			
Drinking, n (%)	316(42.88)	725(40.50)	139(49.82)	0.012	0.270	0.047	0.003
Living in Wuhan, n (%)	18(2.44)	59(3.30)	19(6.81)	0.003	0.256	0.001	0.004
Having COVID-19 symptoms or COVID-19 diagnosis, n (%)	41(5.56)	75(4.19)	35(12.54)	0.000	0.134	0.000	0.000
Having relative or acquaintance got COVID-19, n (%)	90(12.31)	202(11.28)	66(23.66)	0.000	0.508	0.000	0.000
Getting support from family members, n (%)				0.027	0.407	0.071	0.007
Unchanged or more	690 (93.62)	1691 (94.47)	252 (90.32)				
Less	47(6.38)	99(5.53)	27(9.68)				

characteristics	The remission group ¹ (n = 737)	The unchanged group ² (n = 1790)	The aggravating group ³ (n = 279)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Getting support from the outside world, n (%)				0.258			
Unchanged or more	635 (86.16)	1514 (84.58)	229 (82.08)				
Less	102(13.84)	276(15.42)	50(17.92)				
ISI score	6.99 ± 5.48	8.25 ± 5.66	8.42 ± 5.93	0.000	0.000	0.000	1.000
PHQ9 score	6.18 ± 4.84	7.00 ± 4.88	7.28 ± 5.27	0.000	0.000	0.006	1.000
ISER score	18.79 ± 14.83	21.32 ± 14.57	22.36 ± 16.25	0.000	0.000	0.002	1.000

737 of 2806 participants (26.27%) tended to improve in headache frequency (days per month). during COVID-19, 1790 (63.79%) remain unchanged, and 279 (9.94%) worsen. An initial comparative analysis showed significant difference in gender ($P = 0.015$), chronic disease history ($P = 0.000$), drinking ($P = 0.012$), place of residence ($P = 0.003$), COVID-19 symptoms or COVID-19 diagnosis ($P = 0.000$), relative or acquaintance got COVID-19 ($P = 0.000$), getting support from family members during the social isolation ($P = 0.027$), ISI ($P = 0.000$), PHQ-9 ($P = 0.000$) and ISE-R ($P = 0.000$). Post hoc comparisons using Bonferroni test evidenced that the aggravating group presented significantly higher proportion of having underlying diseases, living in Wuhan area, having COVID-19 symptoms or COVID-19 diagnosis, and having relative or acquaintance got COVID-19, compared with the remission group ($P = 0.005$, $P = 0.001$, $P = 0.000$, $P = 0.000$, $P = 0.000$) and unchanged group ($P = 0.000$, $P = 0.004$, $P = 0.000$, $P = 0.000$). The aggravating group also demonstrated significantly higher proportion of males ($P = 0.010$), drinking ($P = 0.003$) and getting less support from family members during the social isolation ($P = 0.007$), compared with the unchanged group, and higher ISI ($P = 0.000$), PHQ-9 ($P = 0.006$) and ISE-R score ($P = 0.002$), compared with the remission group.

Table 4 presents comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache intensity**.

Table 4

Comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache intensity**.

characteristics	The remission group ¹ (n = 258)	The unchanged group ² (n = 2451)	The aggravating group ³ (n = 97)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Male, n (%)	101(39.15)	901(36.76)	41(42.27)	0.430			
Age, n (%)				0.047			
< 30	77(29.84)	563(22.97)	30(30.93)				
30–50	163(63.18)	1731(70.62)	60(61.86)				
> 50	18(6.98)	157(6.41)	7(7.21)				
Education level, n (%)				0.019	0.005	0.209	0.825
junior colleague or lower	70(27.13)	483(19.71)	20(20.62)				
University or above	188(72.87)	1968(80.29)	77(79.38)				
Chronic disease history, n (%)	68(26.36)	567(23.13)	28(28.87)	0.238			
Smoking, n (%)	53(20.54)	398(16.24)	21(21.65)	0.000	0.000	0.000	0.083
Drinking, n (%)	121(46.90)	1010(41.21)	49(50.52)	0.048	0.078	0.543	0.068
Living in Wuhan, n (%)	11(4.26)	77(3.14)	8(8.25)	0.019	0.334	0.137	0.006
Having COVID-19 symptoms or COVID-19 diagnosis, n (%)	20(7.75)	121(4.94)	10(10.31)	0.015	0.053	0.440	0.030
Having relative or acquaintance got COVID-19, n (%)	47(18.22)	276(11.26)	35(36.08)	0.000	0.001	0.000	0.000
Getting support from family members, n (%)				0.002	0.060	0.170	0.001
Unchanged or more	236 (91.47)	2313 (94.37)	84 (86.60)				
Less	22(8.53)	138(5.63)	13(13.40)				

characteristics	The remission group ¹ (n = 258)	The unchanged group ² (n = 2451)	The aggravating group ³ (n = 97)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Getting support from the outside world, n (%)				0.112			
Unchanged or more	221 (85.66)	2082 (84.94)	75 (77.32)				
Less	37(14.34)	369(15.06)	22(22.68)				
ISI score	7.52 ± 5.57	8.04 ± 5.68	6.50 ± 5.44	0.009	0.494	0.225	0.014
PHQ9 score	6.83 ± 5.34	6.85 ± 4.90	5.80 ± 4.38	0.110			
ISER score	20.82 ± 15.42	20.86 ± 14.85	18.03 ± 13.39	0.294			

258 of 2806 participants (9.19%) tended to improve in headache days during COVID-19, 2451 (87.35%) remain unchanged, and 97 (3.46%) worsen. An initial comparative analysis showed significant difference in age ($P = 0.047$), education level ($P = 0.019$), smoking ($P = 0.000$), drinking ($P = 0.048$), place of residence ($P = 0.019$), COVID-19 symptoms or COVID-19 diagnosis ($P = 0.015$), relative or acquaintance got COVID-19 ($P = 0.000$), getting support from family members during the social isolation ($P = 0.002$) and ISI ($P = 0.009$). Post hoc comparisons using Bonferroni test evidenced that the aggravating group presented significantly higher proportion of having relative or acquaintance got COVID-19, compared with the remission group ($P = 0.000$) and unchanged group ($P = 0.000$). The aggravating group also demonstrated significantly higher proportion of smoking ($P = 0.000$), compared with the remission group, and significantly higher proportion of living in Wuhan area ($P = 0.006$) and getting less support from family members during the social isolation ($P = 0.001$), and lower ISI score ($P = 0.014$), compared with the unchanged group.

Figure 5 shows that participants living in Wuhan area, having COVID-19 symptoms or COVID-19 diagnosis and having relative or acquaintance got COVID-19 are more likely to get headache deteriorated. Participants living in Wuhan area took a higher exacerbation rate of headache duration (13.54% vs 6.31%, $P = 0.005$), headache days (19.79% vs 9.59%, $P = 0.001$) and headache intensity (8.33% vs 3.28%, $P = 0.008$). And participants having COVID-19 symptoms or COVID-19 diagnosis took a higher exacerbation rate of headache duration (13.25% vs 6.18%, $P = 0.001$), headache days (23.18% vs 9.19%, $P = 0.000$) and headache intensity (6.62% vs 3.28%, $P = 0.029$). Participants having relative or acquaintance got COVID-19 also took a higher exacerbation rate of headache duration (10.61% vs 5.96%, $P = 0.001$), headache days (18.44% vs 8.70%, $P = 0.000$) and headache intensity (9.78% vs 2.53%, $P = 0.000$).

Predictors of remission

Table 5, 6, 7 shows details of multivariate logistic regression analyses of factor associated with remission in headache duration, headache days and headache intensity respectively. Smoking (OR = 1.397, 95% CI 1.090 to 1.790, P = 0.008) and getting support from family members during the social isolation (OR = 1.656, 95% CI 1.075 to 2.550, P = 0.022) were the independent factors of remission in headache duration. Participants without a history of smoking or getting unchanged or more support from family members during the social isolation were more likely to have remission in headache duration. ISE-R score had no clinical significance for remission in headache duration (OR = 1.009, 95% CI 1.002 to 1.016), though a p-value < 0.05 was got. Similarly, ISI score (OR = 0.968, 95% CI 0.948 to 0.989) had no clinical significance for remission in headache days, though a p-value < 0.05 was got. Education level (OR = 1.478, 95% CI 1.103 to 1.980, P = 0.009) and having relative or acquaintance got COVID-19 (OR = 0.643, 95% CI 0.458 to 0.902, P = 0.011) were the independent factors of remission in headache severity. Participants of low education or having relative or acquaintance got COVID-19 were more likely to have remission in headache.

Table 5
Predictors of remission in **headache duration**.

Variables	OR (95% CI)	P value
Smoking ¹	1.397(1.090–1.790)	0.008
Getting support from family members ²	1.656(1.075–2.550)	0.022
Getting support from the outside world ³	1.218(0.938–1.580)	0.139
ISI score	1.013(0.992–1.034)	0.232
PHQ9 score	1.006(0.982–1.031)	0.619
ISER score	1.009(1.002–1.016)	0.016
1, non-smoking vs smoking;		
2, Getting Unchanged or more support from family members vs Getting less support from family members;		
3, Getting Unchanged or more support from the outside world vs Getting less support from family members.		

Table 6
Predictors of remission in **headache frequency**

Variables	OR (95% CI)	P value
ISI score	0.968(0.948–0.989)	0.003
PHQ9 score	0.997(0.973–1.022)	0.809
ISER score	0.994(0.987–1.002)	0.131

Table 7
Predictors of remission in **headache intensity**

Variables	OR (95% CI)	P value
Having relative or acquaintance got COVID-19 ¹	0.643(0.458–0.902)	0.011
Education level ³	1.478 (1.103–1.980)	0.009
1, Not having relative or acquaintance got COVID-19 vs having relative or acquaintance got COVID-19;		
2, junior colleague or lower vs University or above.		

Discussion

To our knowledge, the present study was the first research to investigate the impact of COVID-19 pandemic on headache patients in China. Our analysis showed a reality of those headache participants with remission of headache duration, headache days per month, and headache intensity during COVID-19. Smoking, education level and getting support from family members during the social isolation were the independent factors of remission in headache during COVID-19. Besides, participants living in Wuhan area, having COVID-19 symptoms or COVID-19 diagnosis and having relative or acquaintance got COVID-19 are more likely to get headache deteriorated.

A previous door-to-door population-based survey reported the headache epidemiological data among China. Of 5041 respondents, 1425 reported headache in the preceding year, giving a 1-year prevalence of 28.5%. Headache was more prevalent in females (36.8%), than in males (23.8%)¹⁶. Similar to the previous study, our analysis showed a higher prevalence of headache in females (20.57%), compared with that in males (16.22%), while the headache prevalence in the present study was 18.71%, slightly lower than in the previous study. Besides, prevalence of headache peaked during adolescence. As shown in previous studies, headache prevalence among childhood or adolescence varied widely, from 5.9 to 82%, bringing high costs to individual and society^{17–19}. It presented a gradual upward trend throughout childhood, peaking at about 11 to 13 years old^{17–18}. And headache in children or adolescents can result in impaired psychosocial function, as a major factor associated with school absenteeism and poorer quality of life¹⁸. A consensus was reached that the natural pattern of headache may change through childhood to adulthood¹⁸. Hormonal changes, different levels of stress exposure, and the life events and circumstances behind each stress exposure were the possible explanations for the evolution of headaches over time¹⁸. Moreover, those who had headaches in childhood or adolescence may be at a higher risk of getting additional physical or psychological problems in adulthood¹⁹. Given that headache in childhood or adolescents had a high prevalence, and caused various negative effects not only on childhood but also on adulthood, it is vital for us to understand the clinical feature and evolution of headache from childhood to adulthood.

The main target of this research was to investigate the impact of COVID-19 pandemic on headache patients in China. Interestingly, but not surprisingly, our analysis showed a reality of those headache participants with a tendency to improve or remit in headache duration, headache frequency and headache intensity during COVID-19 outbreak. Meanwhile, we inquire some headache patients, as well as friends and colleagues. In line with the present study, they reported a tendency to improve or remit in headache attacks during the social isolation. We also observed that, migraine was more likely to have remission in headache duration, compared with TTH and CH. Further work is required to demonstrated the underlying causes.

Previous studies demonstrated evidences that the risk of headache attacks decreased in holidays or days off²⁰. Due to the war against COVID-19, we got a special long holiday. Then, why does the holiday give participants a remission in headache attacks? Several factors are particularly noteworthy to report. For instance, time off is important for workers or students to recover from load effects accumulated at work or study²¹. Less stress from work or study could be a factor related to headache remission during the social isolation. Additionally, previous studies reported not eating on time as a precipitating factor of headache attacks^{22–23}. The underlying mechanism could be explained by causing relative hypoglycemia, further activating the adrenal medulla²¹. Eat regularly during the special holiday could be another factor related to headache remission. Then, sleep quality is an acknowledged factor affecting headache attacks. Our analysis showed that ISI scores were significantly lower in the remission group than in the aggravating group. Also, it should be particularly emphasized that getting support from family members during the social isolation were the independent factors of remission in headache duration. A previous study demonstrated that patients from functional families appeared to show relatively low levels of distress regardless of the severity of their headache²⁴. COVID-19 outbreak when Spring Festival was approaching, the period for a reunion with family members in China. Families got together during the special holiday, and have more time to communicate and listen to each other. Similarly, with regard to headache participants, they got more opportunities to communicate their headache-related problems with family members and obtained more effective support, thus reduced the headache-related or mental burden. Given that, we call on more family supports involved to help headache patients improve or remit in headache attacks.

Besides getting support from family members, education level and smoking were also independent factors of remission in headache attacks. A previous study showed that remission was positively associated with increased educational level²⁵. On the contrary, another study demonstrated that participants with higher education tended to having more headaches, especially migraine²⁶. The present study found that participants with a junior colleague or lower degree were more likely to have remission in headache severity during COVID-19, compared with participants with a university degree. Smoking was a precipitating factor of headache attacks. Participants not smoking were more likely to have remission in headache duration. Rather curiously multivariate logistic regression analyses showed that having relative or acquaintance got COVID-19 was a protective factor factors of remission in headache severity. By synthesizing the data, we found that the aggravating group presented significantly higher proportion of

participants having relative or acquaintance got COVID-19, compared with the remission group and unchanged group, while the unchanged group presented a significantly lower proportion, compared with the remission group. And participants in the unchanged group greatly outnumber participants in the aggravating group (Table 4), which significantly offset the adverse effect of having relative or acquaintance got COVID-19 on headache severity.

Though participants presented an overall trend of headache remission, adverse impacts of COVID-19-related events on headache cannot be overlooked. Participants living in Wuhan area, having COVID-19 symptoms or COVID-19 diagnosis and having relative or acquaintance got COVID-19 are more likely to get headache deteriorated. COVID-19 outbreak is a stress event, causing varying degrees of anxiety and worry, and some even developed post-traumatic stress disorder. With regard to headache participants, they were more vulnerable when faced stress events. So it is understandable that COVID-19-related events were precipitating factors of headache attacks. Most of participants included in the present study lived outside Wuhan, having no COVID-19 symptoms or COVID-19 diagnosis and having no relative or acquaintance got COVID-19. For most people, they were less affected by the COVID-19 outbreak, and thus tended to have headache unchanged or remission.

A previous study²⁷ reported that the seropositive prevalence rate of antibodies (IgM or IgG) against SARS-CoV-2 was 0.8% in the general Chinese population. In the present study, the overall prevalence of SARS-CoV-2 infection was 0.15%, which roughly matched the general prevalence of COVID-19 in the Chinese population. Given that the sample size is large enough, results reported in the present study are more likely generalizable. However, we acknowledge some limitations of our study. First, since the study was based on a self-administered questionnaire, it could be inevitably affected by the recall bias. Besides, it is difficult for us to identify what types of headache the respondents had. Further work is needed. Second, the number of participants infected with COVID-19 included in our study was very few. We could not exactly report the impact of COVID-19 infection on headache attacks. The prevalence of SARS-CoV-2 infection in headache participants was 0.2% (6/2806). No significant difference was found when compared with the prevalence of SARS-CoV-2 infection in non-headache participants (16/12194, 0.13%). Additionally, headache participants confirmed with SARS-CoV-2 infection showed a higher exacerbation rate of headache intensity, when compared with headache participants not confirmed with SARS-CoV-2 infection (50.00% vs 3.36%, $P = 0.001$). Further study would be needed to identify the impact of COVID-19 infection on headache attacks. Third, sampling error is unavoidable by using this online questionnaire, for example, illiterate, the elderly, children and those who cannot afford to buy a smartphone may have a less participation in the survey. Fourth, some factors such as BMI, marriage status and regular diet were not assessed.

Conclusion

The present study provided the first data about the impact of COVID-19 pandemic on headache patients in China. Adverse impacts of COVID-19-related events on headache patients, especially those living in high-risk area, cannot be overlooked, though participants presented an overall trend of headache

remission during COVID-19. Smoking, education level and getting support from family members during the social isolation were the independent factors of remission in headache. We call on more family supports involved to help headache patients improve or remit in headache attacks.

Abbreviations

COVID-19: coronavirus disease 2019; PPE: personal protective equipment; RAS: renin-angiotensin system; NSAID: non-steroid anti-inflammatory drug; PHQ-9: Patient Health Questionnaire-9; ISI: Insomnia Severity Index; IES-R: Impact of Event Scale Revised; HIS: International Headache Society; TTH: tension-type headache; CH: cluster headache.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the ethics committee of the Remin hospital of Wuhan University, Wuhan, china. The informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

Data used for analysis are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

QG contributed to the study design. QG, SL, RL, LY and ZX contributed to data acquisition and analysis. QG wrote the manuscript. ZX reviewed the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1 Comparison of headache intensity, headache days per month, and headache duration at baseline and during COVID-19

variables	Baseline	During COVID-19	P value
Headache severity	4.290±1.680	4.110±1.609	0.000
Headache duration (h)	4.033±7.325	3.414±6.859	0.000
Headache days per month	2.092±3.694	1.788±2.989	0.000

Table 2 Comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache duration**

characteristics	The remission group ¹ (n=686)	The unchanged group ² (n=1936)	The aggravating group ³ (n=184)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Male, n (%)	251 36.59%	71536.93%	7744.85%	0.393			
Age, n (%)				0.253			
<30	176 25.66%	44122.78%	5328.80%				
30-50	463 67.49%	137170.82%	12065.22%				
>50	476.85%	1246.40%	115.98%				
Education level, n (%)				0.035	0.152	0.172	0.018
junior colleague or lower	150 21.87%	374(19.32)	49(26.63)				
University or above	536 78.13%	1562(80.68)	135(73.37)				
Chronic disease history, n (%)	167 24.34%	44422.93%	5228.26%	0.253			
Smoking, n (%)	9113.27%	33417.25%	4725.54%	0.000	0.015	0.000	0.005
Drinking, n (%)	279 40.67%	81341.99%	8847.83%	0.217			
Living in Wuhan, n (%)	202.92%	633.25%	137.07%	0.018	0.663	0.009	0.008
Having COVID-19 symptoms or COVID-19 diagnosis, n (%)	456.56%	864.44%	2010.87%	0.000	0.029	0.048	0.000
Having relative or acquaintance got COVID-19, n (%)	8011.66%	24012.40%	3820.65%	0.004	0.613	0.002	0.002
Getting support from family				0.001	0.015	0.000	0.005

members, n (%)							
Unchanged or more	659 (96.06)	1811 (93.54)	163 (88.59)				
Less	27±3.94%	125±6.46%	21±11.41%				
Getting support from the outside world, n (%)				0.028	0.056	0.011	0.120
Unchanged or more	599 (87.32)	1632 (84.30)	147 (79.89)				
Less	87±12.68%	304±15.70%	37±20.11%				
ISI score	6.70 ± 5.30	8.16 ± 5.67	10.22 ± 6.01	0.000	0.000	0.000	0.000
PHQ9 score	5.99 ± 4.74	6.92 ± 4.93	8.74 ± 4.89	0.000	0.000	0.000	0.000
ISER score	17.99 ± 14.18	21.08 ± 14.63	27.71 ± 16.96	0.000	0.000	0.000	0.000

Table 3 Comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache frequency**.

characteristics	The remission group ¹ (n=737)	The unchanged group ² (n=1790)	The aggravating group ³ (n=279)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Male, n (%)	289 39.21%	63335.36%	2143.47%	0.015	0.068	0.228	0.010
Age, n (%)				0.431			
<30	185 25.10%	41022.91%	7526.88%				
30-50	502 68.11%	1263 70.56%	19068.10%				
>50	506.79%	1176.53%	147.82%				
Education level, n (%)				0.260			
junior colleague or lower	152 20.62%	354(19.78)	64(24.01)				
University or above	585 79.38%	1456(80.22)	212(75.99)				
Chronic disease history, n (%)	184 24.97%	38521.51%	9433.69%	0.000	0.059	0.005	0.000
Smoking, n (%)	123 16.69%	29116.26%	5820.79%	0.169			
Drinking, n (%)	316 42.88%	72540.50%	13949.82%	0.012	0.270	0.047	0.003
Living in Wuhan, n (%)	182.44%	593.30%	196.81%	0.003	0.256	0.001	0.004
Having COVID-19 symptoms or COVID-19 diagnosis, n (%)	415.56%	754.19%	3512.54%	0.000	0.134	0.000	0.000
Having relative or acquaintance got COVID-19, n (%)	90 12.31%	20211.28%	6623.66%	0.000	0.508	0.000	0.000
Getting				0.027	0.407	0.071	0.007

support from family members, n (%)							
Unchanged or more	690 (93.62)	1691 (94.47)	252 (90.32)				
Less	47±6.38	99±5.53	27±9.68				
Getting support from the outside world, n (%)				0.258			
Unchanged or more	635 (86.16)	1514 (84.58)	229 (82.08)				
Less	102 ±13.84	276±15.42	50±17.92				
ISI score	6.99 ± 5.48	8.25 ± 5.66	8.42 ± 5.93	0.000	0.000	0.000	1.000
PHQ9 score	6.18 ± 4.84	7.00 ± 4.88	7.28 ± 5.27	0.000	0.000	0.006	1.000
ISER score	18.79 ± 14.83	21.32 ± 14.57	22.36 ± 16.25	0.000	0.000	0.002	1.000

Table 4 Comparison of demographic characteristics for the remission group, unchanged group and aggravating group according to **headache intensity**.

characteristics	The remission group ¹ (n=258)	The unchanged group ² (n=2451)	The aggravating group ³ (n=97)	P value	P value Post hoc		
					1 vs 2	1 vs 3	2 vs 3
Male, n (%)	101 39.15%	90136.76%	4142.27%	0.430			
Age, n (%)				0.047			
<30	7729.84%	56322.97%	3030.93%				
30-50	163 63.18%	173170.62%	6061.86%				
>50	186.98%	1576.41%	77.21%				
Education level, n (%)				0.019	0.005	0.209	0.825
junior colleague or lower	7027.13%	483(19.71)	20(20.62)				
University or above	188 72.87%	1968(80.29)	77(79.38)				
Chronic disease history, n (%)	6826.36%	56723.13%	2828.87%	0.238			
Smoking, n (%)	5320.54%	39816.24%	2121.65%	0.000	0.000	0.000	0.083
Drinking, n (%)	121 46.90%	101041.21%	4950.52%	0.048	0.078	0.543	0.068
Living in Wuhan, n (%)	114.26%	773.14%	88.25%	0.019	0.334	0.137	0.006
Having COVID-19 symptoms or COVID-19 diagnosis, n (%)	207.75%	1214.94%	1010.31%	0.015	0.053	0.440	0.030
Having relative or acquaintance got COVID-19, n (%)	4718.22%	27611.26%	3536.08%	0.000	0.001	0.000	0.000
Getting support from family members, n (%)				0.002	0.060	0.170	0.001

Unchanged or more	236 (91.47)	2313 (94.37)	84 (86.60)				
Less	22±8.53	138±5.63	13±13.40				
Getting support from the outside world, n (%)				0.112			
Unchanged or more	221 (85.66)	2082 (84.94)	75 (77.32)				
Less	37±14.34	369±15.06	22±22.68				
ISI score	7.52 ± 5.57	8.04 ± 5.68	6.50 ± 5.44	0.009	0.494	0.225	0.014
PHQ9 score	6.83 ± 5.34	6.85 ± 4.90	5.80 ± 4.38	0.110			
ISER score	20.82 ± 15.42	20.86 ± 14.85	18.03 ± 13.39	0.294			

Table 5 Predictors of remission in **headache duration**.

Variables	OR (95% CI)	P value
Smoking ¹	1.397(1.090-1.790)	0.008
Getting support from family members ²	1.656(1.075-2.550)	0.022
Getting support from the outside world ³	1.218(0.938-1.580)	0.139
ISI score	1.013(0.992-1.034)	0.232
PHQ9 score	1.006(0.982-1.031)	0.619
ISER score	1.009(1.002-1.016)	0.016

1, non-smoking vs smoking;

2, Getting Unchanged or more support from family members vs Getting less support from family members;

3, Getting Unchanged or more support from the outside world vs Getting less support from family members.

Table 6 Predictors of remission in **headache frequency**

Variables	OR (95% CI)	P value
ISI score	0.968(0.948-0.989)	0.003
PHQ9 score	0.997(0.973-1.022)	0.809
ISER score	0.994(0.987-1.002)	0.131

Table 7 Predictors of remission in **headache intensity**

Variables	OR (95% CI)	P value
Having relative or acquaintance got COVID-19 ¹	0.643(0.458-0.902)	0.011
Education level ³	1.478 (1.103-1.980)	0.009

1, Not having relative or acquaintance got COVID-19 vs having relative or acquaintance got COVID-19;
2, junior colleague or lower vs University or above.

Figures

Figure 1

Basic demographic features of all headaches.

Figure 2

Characteristics of accompanying symptoms and headache triggers.

Figure 3

Self-reported factors associated with remission (A) or deterioration (B) in headache during COVID-19.

Figure 4

Remission rate of headache duration among TTH, migraine and CH.

Figure 5

Exacerbation factors of headache duration (A), headache frequency (B) and headache intensity (C).