Mental Health in Persons With Chronic Myeloid Leukemia During the SARS-CoV-2 Pandemic: The Need for Increased Access to Health Care Services

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Mental health problems in the general population have been reported during the SARS-CoV-2 pandemic; however, there were rare data in persons with chronic myeloid leukemia (CML). Therefore, we performed a cross-sectional study on mental health evaluated using the 9-item Patient Health Questionnaire (PHQ-9; depression), the 7-item Generalized Anxiety Disorder (GAD-7; anxiety), and the 22-item Impact of Event Scale—Revised (IES-R; distress), including subscales of avoidance, intrusion, and hyper-arousal in persons with CML, non-cancer persons, and immediate family members of persons with cancer as controls (≥16 years) by an online survey. Data from 3,197 persons with CML and 7,256 controls were collected. In multivariate analyses, CML was significantly associated with moderate to severe depression (OR = 1.6; 95% Confidence Interval [CI], 1.4, 1.9; p < 0.001), anxiety (OR = 1.4 [1.1, 1.7]; p = 0.001), avoidance (OR = 1.3 [1.1, 1.5]; p < 0.001), and hyper-arousal (OR = 1.5 [1.3, 1.6]; p < 0.001). Moreover, delay in regular monitoring was significantly associated with depression (OR = 1.3 [1.0, 1.7]; p = 0.024), anxiety (OR = 1.3 [1.0, 1.8]; p = 0.044), avoidance (OR = 1.2 [1.0, 1.4]; p = 0.017), and intrusion (OR = 1.2 [1.0, 1.4]; p = 0.057); tyrosine kinase-inhibitor dose reduction or discontinuation, depression (OR = 1.9 [1.3, 2.8]; p = 0.001), distress (OR = 2.0 [1.4, 2.8]; p < 0.001), avoidance (OR = 1.6 [1.2, 2.1]; p = 0.004), intrusion (OR = 1.6 [1.1, 2.1]; p = 0.006), and hyper-arousal...
(OR = 1.3 [1.0, 1.8]; p = 0.088). We concluded that persons with CML during the SARS-CoV-2 pandemic have worse mental health including depression, anxiety, and distress symptoms. Decreasing or stopping monitoring or dose resulted in adverse mental health consequences.

Keywords: SARS-CoV-2, chronic myeloid leukemia, mental health, depression, anxiety, distress

INTRODUCTION

There are many reports of increased prevalence and severity of mental health problems including those of depression, anxiety, and distress during the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic in the general population, medical health care workers (1–9), and persons with chronic diseases (10, 11). Several studies reported that cancer patients experienced mental health problems or worse health-related quality of life (HRQoL) (12–21), which were associated with delay in cancer care or reduced therapy intensity. However, the impact of the pandemic on the mental health of persons with leukemia is rare, and there is none in persons with chronic myeloid leukemia (CML).

The mental health of persons with CML is of concern because they require long-term tyrosine kinase-inhibitor (TKI) therapy response monitoring and TKI dose adjustments (22). Data from before the pandemic indicate that persons with CML experience more severe depression and/or anxiety to daily life challenges compared with controls (23–27). Several studies reported prevalence and/or severity of SARS-CoV-2-infection and of coronavirus infectious disease 2019 (COVID-19) in persons with CML (28–31) compared with controls. There are no data on the mental health of persons with CML during the SARS-CoV-2 pandemic. Therefore, we performed a cross-sectional survey to explore the prevalence of depression, anxiety, and distress symptoms in 3,197 subjects with CML during the pandemic. Results were compared with concurrent controls, which were non-cancer persons and immediate family members of persons with cancer including CML. We were especially interested in the effects on mental health of adjustments in the frequency of monitoring response to TKI therapy and/or dose.

Questionnaire

The questionnaire consisted of five dimensions (Supplementary Contents 1, 2). The first dimension included a brief introduction of the survey and a question about whether having filled out the questionnaire before. The second dimension included 10 questions assessing demographics. The third included 15 questions about CML-related data such as diagnosis, therapy, and response. The fourth included 11 questions about behavior and experience at the peak of the COVID-19 pandemic in China, the end of January to end of March (32–34). The fifth included three self-reported validated measurement tools in Chinese version including the 9-item Patient Health Questionnaire (PHQ-9), the 7-item Generalized Anxiety Disorder (GAD-7), and the 22-item Impact of Event Scale—Revised (IES-R) to assess the prevalence and severity of depression, anxiety, and distress during the end of January to April. The questionnaire was the same for age and subjects with CML except for CML-related questions (the third dimension). Comorbidities were defined as coexisting diseases except CML and COVID-19.

Assessment of Mental Health

The PHQ-9 (range, 0–27) was used to assess depression symptoms with the total scores categorized as follows: controls (0–4), mild (5–9), moderate (10–14), and severe (15–27) (35). The GAD-7 (range, 0–21) was used to assess anxiety symptoms with the total scores categorized as follows: controls (0–4), mild (5–9), moderate (10–14), and severe (15–21) (36). The IES-R (range, 0–88) was used to assess subjective distress (excessive panic and anxiety) caused by traumatic events including trauma-related distressing memories and persistent negative emotions resulting from the pandemic, which is composed of three subscales to measure the avoidance, intrusion, and hyper-arousal. The total IES-R score was categorized as follows: subclinical (0–8), mild (9–25), moderate (26–43), and severe (44–88) (37). Respondents who had the scores greater than the cutoff threshold of 10 in PHQ-9, 10 in GAD-7, and 26 in IES-R indicate moderate to severe depression, anxiety, and distress, respectively, and IES-R score ≥ 26 is associated with post-traumatic stress disorder (PTSD) symptoms (35, 38, 39).

Statistical Analyses

Descriptive analysis results were presented as median (range) or number (percent). Categorical variables were compared with the chi-square test and continuous variables with the Mann–Whitney test. The k-means clustering method was used to cluster the three subscales of distress including avoidance, intrusion, and hyper-arousal symptoms derived from the IES-R. To identify the variables associated with the
TABLE 1 | Respondents’ characteristics.

|                          | CML   | Controls | P-value |
|--------------------------|-------|----------|---------|
| N                        | 3,197 | 7,257    |         |
| Male, n (%)              | 1,831 (57) | 3,296 (45) | <0.001 |
| Age, y, median (range)   | 43 (16–92) | 30 (16–89) | <0.001 |
| Urban household registration, n (%) | 1,888 (59) | 4,200 (58) | 0.260 |
| Marital status, n (%)    |       |          | <0.001 |
| Unmarried                | 495 (16) | 3,391 (47) |       |
| Married                  | 2,486 (78) | 3,730 (51) |       |
| Divorced or widowed      | 216 (7) | 136 (2) |       |
| Education, n (%)         |       |          | <0.001 |
| Junior middle school and below | 1,012 (32) | 403 (6) |       |
| Senior middle school     | 786 (25) | 610 (8) |       |
| University and above     | 1,399 (44) | 6,244 (86) |       |
| Comorbidity(ies), n (%)  |       |          | <0.001 |
|                          | 732 (23) | 545 (8) |       |
| Residence in Hubei province, n (%) | 322 (10) | 785 (11) | 0.254 |
| Living in rural area, n (%) | 1,030 (32) | 1,313 (18) | <0.001 |
| Cohabitating with family or friends, n (%) | 3,037 (95) | 6,223 (86) | <0.001 |
| Following pandemic information frequently, n (%) | 1,422 (44) | 3,554 (49) | <0.001 |
| Sharing feelings actively, n (%) | 2,542 (80) | 6,028 (83) | <0.001 |
| Exposure to someone with COVID-19, n (%) | 9 (0.3) | 162 (2) | <0.001 |
| Family member with an acute respiratory symptom, n (%) | 3 (0.1) | 40 (1) | 0.001 |
| Having acute respiratory symptom, n (%) | 396 (12) | 622 (9) | <0.001 |
| Fatigue                  | 233 (7) | 285 (4) | <0.001 |
| Cough                    | 117 (4) | 252 (4) | 0.633  |
| Fever                    | 68 (2) | 95 (1) | 0.002  |
| Sore throat              | 85 (3) | 186 (3) | 0.777  |
| Dyspnea                  | 34 (1) | 32 (0.4) | <0.001 |
| Other                    | 43 (1) | 48 (1) | 0.001  |
| Suspected being infected with COVID-19 | 87 (3) | 251 (4) | 0.049 |
| Going to the hospital     | 84 (3) | 102 (1) | <0.001 |
| Performing lung CT scan  | 65 (2) | 82 (1) | <0.001 |
| Having qRT-PCR test      | 26 (1) | 54 (1) | 0.709  |
| Disease phase at diagnosis of CML, n (%) |       |          |         |
| Chronic                  | 2,989 (94) | NA | NA |
| Accelerated              | 128 (4) | NA | NA |
| Blast                    | 20 (1) | NA | NA |
| Unknown                  | 60 (2) | NA | NA |
| Interval from diagnosis to starting TKI therapy, mo, median (range) | 0 (0–211) | NA | NA |
| CML duration, mo, median (range) | 52 (4–325) | NA | NA |
| TKI therapy duration, mo, median (range) | 49 (1–228) | NA | NA |
| Current treatment, n (%) |       |          |         |
| Imatinib                 | 1,864 (58) | NA | NA |
| Dasatinib                | 409 (13) | NA | NA |
| Nilotinib                | 693 (22) | NA | NA |

Table continued...

poor mental health in responses with CML and controls, covariates including age, sex, education level, marital status, household registration (rural vs. urban), comorbidity(ies), residence in Hubei province or elsewhere, cohabitation, behavior and experience (such as following pandemic information frequently, sharing feelings actively), and having an acute respiratory symptom during the pandemic were used to analyze the association with the moderate to severe depression, anxiety, and distress, as well as the presence of avoidance, intrusion, and hyper-arousal by the k-means clustering analysis. To identify the covariates associated with the poor mental health in persons with CML, CML-related data including disease phase, CML and TKI therapy duration, TKI used, TKI therapy line, treatment response, interruption or delay in disease monitoring, and interruption or dose...
reduction of TKI therapy were used to analyze. Covariates with \( p < 0.2 \) in univariate analysis were included in the multivariate binary logistic regression analyses. \( P < 0.05 \) was considered statistically significant. Analyses were conducted with SPSS Version 22.0 software.

**RESULTS**

From April 28 to May 12, 2020, data of 3,581 respondents with CML and 7,556 controls from 32 provinces and municipalities across China were collected. Questionnaires from subjects <16 years (\( n = 121 \)), duplicates (\( n = 513 \)), subjects with CML diagnosed after February 2020 (\( n = 42 \)), and persons with COVID-19 (\( n = 8 \)) were excluded. The updated dataset consisted of 3,197 respondents with CML and 7,256 controls.

**Respondent Covariates**

Respondent covariates are shown in Table 1. Among the 3,197 respondents with CML, 1,831 (57%) were male. The median age was 43 years (range, 16–92 years); 732 (23%) had \( \geq 1 \) comorbidity(ies); 2,989 (94%) were in the chronic phase at diagnosis; and 1,864 (58%) were receiving imatinib, 409 (13%) dasatinib, and 693 (22%), nilotinib. The median TKI therapy duration was 49 months (range, 1–228 months). A total of 427 (13%) reported that they had a negative cytogenetic analysis, which was defined as a complete cytogenetic response (CCyR); 1,782 (56%) had \( BCR-ABL_1 \) gene levels \( \leq 0.1\% \) or a negative gene detection, which was defined as at least a major molecular response (MMR). Response to TKI therapy was unknown to 694 (22%) respondents. A total of 1,457 CML respondents (47%) had delay in regular monitoring because of fear of SARS-CoV-2 infection in the hospital or during travel (\( n = 866; 27\% \)), travel restriction (\( n = 768; 24\% \)), clinic or laboratory closure (\( n = 279; 9\% \)), or other reasons (\( n = 29; 1\% \)). Two hundred three (6%) respondents had TKI dose reduction or discontinuation because of the travel restriction (\( n = 147; 5\% \)), fear of SARS-CoV-2 infection in the hospital or during travel (\( n = 108; 3\% \)), clinic closure (\( n = 41; 1\% \)), no access to TKI from patient assistance program (\( n = 39; 1\% \)) or clinical trial (\( n = 10; 0.3\% \)), or other reasons (\( n = 32; 1\% \)).

Compared with controls, more respondents with CML were male (\( p < 0.001 \)), older (\( p < 0.001 \)), and married (\( p < 0.001 \)), had lower education level (\( p < 0.001 \)), and had a comorbidity(ies) (\( p < 0.001 \)). Proportions of respondents from Hubei province were comparable (\( p = 0.25 \)). During the SARS-CoV-2 pandemic, more respondents with CML were rural residents (\( p < 0.001 \)) and cohabited with their family members or friends (\( p < 0.001 \)). Fewer respondents with CML followed pandemic information frequently (\( p < 0.001 \)), shared feelings actively (\( p < 0.001 \)), reported being exposed to someone with COVID-19 (\( p < 0.001 \)), or had a family member with an acute respiratory symptom (\( p < 0.001 \)). In contrast, more reported that they had an acute respiratory symptom (\( p < 0.001 \)), fewer suspected that they were infected with SARS-CoV-2 (\( p = 0.049 \)), more went to a hospital (\( p < 0.001 \)), and had a lung computed tomography (CT) scan (\( p < 0.001 \)).

**Comparison of Mental Health Between the Respondents With CML and Controls**

Data from respondents with CML indicated a higher prevalence of depression (PHQ-9 score \( \geq 5 \), 33%, 95% confidence interval [CI], [31, 33%] vs. 31% [30, 32%], \( p = 0.069 \)), anxiety (GAD-7 score \( \geq 5 \), 25% [24, 27%] vs. 23% [24, 27%], \( p = 0.008 \)), and distress (IES-R score \( \geq 9 \), 49% [47, 51%] vs. 45% [44,
46%, \( p < 0.001 \)) and higher proportions of moderate to severe depression (PHQ-9 score \( \geq 10, 11\% [10, 12\%] \) vs. \( 8\% [7, 8\%], p < 0.001 \)), anxiety (GAD-7 score \( \geq 10, 7\% [6, 8\%] \) vs. \( 5\% [5, 6\%], p < 0.001 \)), and distress (IES-R score \( \geq 26, 14\% [13, 15\%] \) vs. \( 10\% [10, 11\%], p < 0.001 \)) compared with controls. There was a higher prevalence of avoidance (26% [24, 27%] vs. 22% [21, 23%], \( p < 0.001 \)), intrusion (28% [26, 29%] vs. 25% [24, 26%, \( p = 0.005 \)), and hyper-arousal (27% [26, 29%] vs. 20% [19, 21%, \( p < 0.001 \)) by k-means clustering analyses (Figure 1, Table 2).

Univariate analyses results are shown in Supplementary Table 1. In multivariate analyses, having CML was significantly associated with moderate to severe depression (odds ratio \( [OR = 1.6 [1.4–1.9]; p < 0.001 \)), anxiety (\( OR = 1.4 [1.1–1.7]; p = 0.001 \)), and distress (\( OR = 1.3 [1.1–1.5]; p < 0.001 \)), as well as hyper-arousal (\( OR = 1.5 [1.3–1.6]; p < 0.001 \)). In addition, having comorbidity(ies), following the pandemic information frequently, and having an acute respiratory symptom were significantly associated with moderate to severe depression, anxiety, distress, avoidance, intrusion, and hyper-arousal. Female sex, increasing age, unmarried, divorced, or widowed marital status, and living in Hubei province were significantly associated with \( \geq 1 \) symptom of mental health described above; however, for those who were sharing feelings actively, there was no or mild depression (Table 3).

We collected data from subjects with CML on the disease phase at diagnosis, with the interval from diagnosis to starting TKI therapy, CML duration, TKI therapy duration, current therapy, the number of TKI therapy lines given, response (MMR vs. <MMR), delay in regular monitoring, and tyrosine kinase-inhibitor dose reduction or discontinuation. Univariate analysis results of CML persons and controls are shown in Supplementary Tables 2, 3; in multivariate analyses, delay in monitoring response to TKI therapy was significantly associated with reporting moderate to severe depression (\( OR = 1.3 [1.0–1.7]; p = 0.024 \)) and anxiety (\( OR = 1.3 [1.0–1.8]; p = 0.044 \), avoidance (\( OR = 1.2 [1.0–1.4]; p = 0.017 \)), and intrusion (\( OR = 1.2 [1.0–1.4]; p = 0.057 \)). TKI therapy interruption or dose reductions were significantly associated with reporting moderate to severe depression (\( OR = 1.9 [1.3–2.8]; p = 0.001 \)), distress (\( OR = 2.0 [1.4–2.8] p < 0.001 \)), avoidance (\( OR = 1.6 [1.2–2.1]; p = 0.004 \)), intrusion (\( OR = 1.6 [1.1–2.1]; p = 0.006 \)), and hyper-arousal (\( OR = 1.3 [1.0–1.8]; p = 0.088 \)). CML disease phase, TKI, TKI therapy duration, and therapy response were not significantly associated with mental health. Other covariates associated with mental health in subjects with CML were similar to those in controls (Tables 4, 5).

**Comparison of Mental Health Between Low- and High-Risk Respondents With CML and Controls**

Next we categorized CML respondents into low-risk (no risk covariate; \( n = 1,664, 52\% \)), intermediate-risk (1 risk; \( n = 1,412, 44\% \)), or high-risk (2 risks, \( n = 121, 4\% \)) cohorts based on delay in monitoring response to TKI therapy, TKI therapy interruption, or dose reduction or both during the pandemic. There were significant differences in mental health among the three CML risk cohorts or between the low-risk CML cohort and controls. The high-risk CML cohort had the highest prevalence and most severe depression (PHQ-9 score \( \geq 5, 47\% [38, 56\%] \) vs. \( 35\% [32, 37\%] \) vs. \( 31\% [28, 33\%], p < 0.001 \)) and anxiety (\( GAD-7 score \geq 5, 42\% [33, 52\%] \) vs. \( 28\% [25, 30\%] \) vs. \( 22\% [20, 25\%], p < 0.001 \)) and the highest prevalence of avoidance (\( IES-R score \geq 9, 65\% [56, 74\%] \) vs. \( 50\% [47, 53\%] \) vs. \( 47\% [44, 49\%], p < 0.001 \)) and IES-R score \( \geq 10, 16\% [10, 23\%] \) vs. \( 8\% [6, 10\%] \) vs. \( 6\% [5, 7\%], p < 0.001 \)), and distress (\( IES-R score \geq 9, 65\% [56, 74\%] \) vs. \( 50\% [47, 53\%] \) vs. \( 47\% [44, 49\%], p < 0.001 \)) and IES-R score \( \geq 10, 16\% [10, 23\%] \) vs. \( 8\% [6, 10\%] \) vs. \( 6\% [5, 7\%], p < 0.001 \)), and the highest prevalence of avoidance (\( 44\% [35, 53\%] \) vs. \( 28\% [25, 30\%] \) vs. \( 23\% [21, 25\%], p < 0.001 \)), intrusion (\( 47\% [38, 56\%] \) vs. \( 30\% [27, 32\%] \) vs. \( 25\% [23, 27\%], p < 0.001 \)), and hyper-arousal (\( 39\% [30, 48\%] \) vs. \( 28\% [26, 31\%] \) vs. \( 26\% [24, 28\%], p = 0.004 \)) among the respondents with CML.

**TABLE 2** Comparison of mental health of respondents with CML and controls.

|               | Controls | \( P^1\)-value | \( P^2\)-value |
|---------------|----------|----------------|---------------|
| **Depression**|          |                |               |
| \( \geq 5 \)  | 1,054 (33) | 1,664 (52)     | 1,412 (44.2)  |
| \( \geq 10 \) | 347 (11)  | 144 (9)        | 178 (13)      |
| **Anxiety**   |          |                |               |
| \( \geq 5 \)  | 813 (25)  | 373 (22)       | 389 (28)      |
| \( \geq 10 \) | 226 (7)   | 97 (6)         | 110 (8)       |
| **Distress**  |          |                |               |
| \( \geq 9 \)  | 1,558 (49) | 774 (47)       | 705 (50)      |
| \( \geq 26 \) | 450 (14)  | 202 (12)       | 211 (15)      |
| **Avoidance** |          |                |               |
| \( \geq 26 \) | 818 (26)  | 375 (23)       | 390 (28)      |
| **Intrusion** |          |                |               |
| \( \geq 26 \) | 889 (28)  | 412 (25)       | 420 (30)      |
| **Hyper-arousal** |    | 47 (39)       | 47 (39)       |

\( P^1 \) is the comparison of mental health between the respondents with CML and controls; \( P^2 \) is the comparison of mental health between low-risk CML cohort and controls.

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### TABLE 3 | Multivariate analyses of mental health of respondents with CML and controls.

|                          | Depression | Anxiety | Distress | Avoidance | Intrusion | Hyper-arousal |
|--------------------------|------------|---------|----------|-----------|-----------|---------------|
|                          | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value |
| Respondents with CML (ref. controls) | 1.6 (1.4, 1.9) | < 0.001 | 1.4 (1.1, 1.7) | 0.001 | 1.3 (1.1, 1.5) | < 0.001 | 1.5 (1.3, 1.6) | < 0.001 |
| Female (ref. male)       | 1.3 (1.1, 1.5) | 0.008 | 1.2 (1.1, 1.4) | 0.002 | 1.2 (1.1, 1.3) | < 0.001 | 1.4 (1.3, 1.5) | < 0.001 | 1.2 (1.1, 1.4) | < 0.001 |
| Age (years)*             | 0.8 (0.8, 0.9) | < 0.001 | 0.9 (0.8, 0.9) | 0.002 | 1.1 (1.0, 1.1) | < 0.001 | 1.1 (1.0, 1.1) | 0.001 |
| Marital status           | < 0.001 | < 0.001 | 0.017 |
| Married (ref.)           |            |         |          |           |           |           |
| Unmarried                | 1.4 (1.1, 1.7) | 0.002 | 0.9 (0.7, 1.1) | 0.351 | 0.9 (0.8, 1.0) | 0.101 |
| Divorced or widowed      | 2.3 (1.7, 3.2) | < 0.001 | 2.1 (1.4, 3.0) | < 0.001 | 1.4 (1.0, 1.9) | 0.034 |
| Comorbidity(ies) (ref. none) | 1.9 (1.6, 2.3) | < 0.001 | 2.0 (1.6, 2.5) | < 0.001 | 1.5 (1.3, 1.8) | < 0.001 | 1.3 (1.1, 1.5) | < 0.001 | 1.5 (1.3, 1.7) | < 0.001 |
| Residence in Hubei province (ref. elsewhere) | 1.6 (1.3, 2.1) | < 0.001 | 1.5 (1.2, 1.8) | < 0.001 | 1.4 (1.2, 1.7) | < 0.001 | 1.6 (1.4, 1.8) | < 0.001 | 1.3 (1.1, 1.5) | 0.004 |
| Following pandemic information frequently (ref. none) | 2.3 (2.0, 2.7) | < 0.001 | 2.9 (2.4, 3.5) | < 0.001 | 3.6 (3.1, 4.1) | < 0.001 | 2.4 (2.2, 2.7) | < 0.001 | 2.9 (2.6, 3.2) | < 0.001 | 2.5 (2.3, 2.7) | < 0.001 |
| Sharing feelings actively (ref. none) | 0.7 (0.6, 0.8) | < 0.001 |         |          |           |           | 1.2 (1.0, 1.3) | 0.033 |
| Having acute respiratory symptom (ref. none) | 3.6 (3.0, 4.3) | < 0.001 | 3.1 (2.5, 3.8) | < 0.001 | 2.6 (2.2, 3.1) | < 0.001 | 2.0 (1.8, 2.3) | < 0.001 | 2.6 (2.3, 3.0) | < 0.001 | 2.8 (2.4, 3.2) | < 0.001 |

*Linear with estimates for every 10-year increase.

### TABLE 4 | Multivariate analyses of mental health of respondents with CML.

|                          | Depression | Anxiety | Distress | Avoidance | Intrusion | Hyper-arousal |
|--------------------------|------------|---------|----------|-----------|-----------|---------------|
|                          | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value |
| Female (ref. male)       | 1.3 (1.0, 1.6) | 0.029 | 1.7 (1.3, 2.2) | < 0.001 | 1.5 (1.2, 1.8) | < 0.001 | 1.3 (1.1, 1.7) | < 0.001 | 1.3 (1.1, 1.6) | 0.001 |
| Age (years)*             | 0.8 (0.7, 0.9) | < 0.001 | 0.8 (0.7, 0.9) | < 0.001 |
| Marital status           | 0.061 | < 0.001 |
| Married (ref.)           |            |         |          |           |           |           |
| Unmarried                | 0.8 (0.6, 1.2) | 0.341 | 0.5 (0.3, 0.8) | 0.008 |
| Divorced or widowed      | 1.5 (1.0, 2.3) | 0.041 | 1.9 (1.2, 3.0) | 0.006 |
| Comorbidity(ies) (ref. none) | 1.9 (1.4, 2.4) | < 0.001 | 1.9 (1.4, 2.6) | < 0.001 | 1.3 (1.0, 1.7) | 0.021 | 1.2 (1.0, 1.5) | 0.071 | 1.4 (1.1, 1.7) | 0.001 | 1.4 (1.2, 1.7) | < 0.001 |
| Residence in Hubei province (ref. elsewhere) | 1.3 (1.0, 1.7) | 0.030 | 1.4 (1.1, 1.8) | 0.011 |
| Following pandemic information frequently (ref. none) | 2.4 (1.9, 3.0) | < 0.001 | 4.1 (3.0, 5.7) | < 0.001 | 4.0 (3.2, 5.1) | < 0.001 | 2.7 (2.3, 3.2) | < 0.001 | 3.1 (2.6, 3.6) | < 0.001 | 2.9 (2.4, 3.4) | < 0.001 |
| Sharing feelings actively (ref. none) | 1.2 (1.0, 1.5) | 0.084 |
| Having acute respiratory symptom (ref. none) | 3.7 (2.8, 4.8) | < 0.001 | 2.7 (1.9, 3.7) | < 0.001 | 2.7 (2.1, 3.5) | < 0.001 | 2.3 (1.8, 2.9) | < 0.001 | 2.7 (2.2, 3.4) | < 0.001 | 2.6 (2.1, 3.3) | < 0.001 |
| Delay in regular monitoring (ref. none) | 1.3 (1.0, 1.7) | 0.024 | 1.3 (1.0, 1.8) | 0.044 |
| TKI dose reduction or discontinuation (ref. none) | 1.9 (1.3, 2.8) | 0.001 | 2.0 (1.4, 2.8) | < 0.001 | 1.6 (1.2, 2.1) | 0.004 | 1.6 (1.1, 2.1) | 0.006 | 1.3 (1.0, 1.8) | 0.088 |

*Linear with estimates for every 10-year increase, TKI, tyrosine kinase-inhibitor.
### TABLE 5 | Multivariate analyses of mental health of controls.

|                         | Depression | Anxiety | Distress | Avoidance | Intrusion | Hyper-arousal |
|-------------------------|------------|---------|----------|-----------|-----------|---------------|
|                         | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value |
| Female (ref. male)      |            |         |           |           |           |         |           |           |           |         |           |         |
| Age (years)*            | 0.8 (0.7, 1.0) | 0.010   | 1.1 (1.0, 1.2) | 0.001 | 1.1 (1.0, 1.1) | 0.008 | 1.2 (1.0, 1.3) | 0.008 |
| Marital status          |            |         |           |           |           |         |           |           |           |         |           |         |
| Unmarried               | 1.7 (1.3, 2.1) | <0.001 | 1.2 (1.0, 1.6) | 0.066 | 0.9 (0.8, 1.1) | 0.386 | 1.1 (1.0, 1.3) | 0.112 |
| Divorced or widowed     | 3.7 (2.3, 6.1) | <0.001 | 2.0 (1.1, 3.7) | 0.028 | 1.9 (1.2, 3.0) | 0.011 | 1.4 (0.9, 2.2) | 0.094 |
| Education               |            |         |           |           |           |         |           |           |           |         |           |         |
| Junior middle school and below (ref.) |          |         |           |           |           |         |           |           |           |         |           |         |
| Senior middle school    | 0.6 (0.4, 1.0) | 0.046   |           |           |           |         |           |           |           |         |           |         |
| University and above    | 0.6 (0.4, 0.9) | 0.009   |           |           |           |         |           |           |           |         |           |         |
| Co-morbidity(ies) (ref. none) | 2.0 (1.5, 2.6) | <0.001 | 2.1 (1.5, 2.8) | <0.001 | 1.7 (1.3, 2.1) | <0.001 | 1.4 (1.2, 1.7) | 0.001 | 1.3 (1.1, 1.7) | 0.004 | 1.7 (1.3, 2.0) | <0.001 |
| Residence in Hubei province (ref. elsewhere) | 1.6 (1.2, 2.2) | 0.001 | 1.6 (1.3, 2.0) | 0.001 | 1.4 (1.2, 1.7) | 0.001 | 1.6 (1.4, 1.9) | <0.001 | 1.4 (1.3, 1.7) | 0.001 |
| Following pandemic information frequently (ref. none) | 2.2 (1.8, 2.7) | <0.001 | 2.3 (1.8, 2.9) | <0.001 | 3.3 (2.8, 3.9) | <0.001 | 2.3 (2.0, 2.5) | <0.001 | 2.8 (2.5, 3.2) | <0.001 | 2.3 (2.0, 2.6) | <0.001 |
| Sharing feelings actively (ref. none) | 0.8 (0.5, 0.8) | <0.001 | 3.4 (2.6, 4.4) | <0.001 | 2.5 (2.0, 3.1) | <0.001 | 1.9 (1.6, 2.3) | <0.001 | 2.5 (2.1, 2.9) | <0.001 | 2.9 (2.4, 3.4) | <0.001 |
| Having acute respiratory symptom (ref. none) | 3.8 (2.8, 4.5) | <0.001 | 3.4 (2.6, 4.4) | <0.001 | 2.5 (2.0, 3.1) | <0.001 | 1.9 (1.6, 2.3) | <0.001 | 2.5 (2.1, 2.9) | <0.001 | 2.9 (2.4, 3.4) | <0.001 |

*Linear with estimates for every 10-year increase.

### TABLE 6 | Multivariate analyses of mental health of respondents of low-risk group with CML and controls.

|                         | Depression | Anxiety | Distress | Avoidance | Intrusion | Hyper-arousal |
|-------------------------|------------|---------|----------|-----------|-----------|---------------|
|                         | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value | OR (95%CI) | P-value |
| Respondents with CML (ref. controls) |            |         |           |           |           |         |           |           |           |         |           |         |
| Female (ref. male)      |            |         |           |           |           |         |           |           |           |         |           |         |
| Age (years)*            | 0.8 (0.7, 0.9) | <0.001 | 1.2 (1.0, 1.4) | 0.021 | 1.2 (1.1, 1.3) | 0.001 | 1.4 (1.3, 1.6) | <0.001 | 1.2 (1.1, 1.3) | 0.004 |
| Marital status          |            |         |           |           |           |         |           |           |           |         |           |         |
| Unmarried               | 1.4 (1.1, 1.7) | 0.002 | 1.2 (0.9, 1.4) | 0.167 | 0.9 (0.8, 1.0) | 0.157 | 1.1 (1.0, 1.3) | 0.059 | 1.3 (0.9, 1.8) | 0.111 |
| Divorced or widowed     | 3.0 (2.0, 4.4) | <0.001 | 2.1 (1.3, 3.4) | 0.002 | 1.7 (1.2, 2.4) | 0.006 |           |         |           |         |           |         |
| Education               |            |         |           |           |           |         |           |           |           |         |           |         |
| Senior middle school    | 0.9 (0.6, 1.2) | 0.353   |           |           |           |         |           |           |           |         |           |         |
| University and above    | 0.7 (0.5, 0.9) | 0.003   |           |           |           |         |           |           |           |         |           |         |
| Comorbidity(ies) (ref. none) | 2.0 (1.6, 2.5) | <0.001 | 2.0 (1.6, 2.6) | <0.001 | 1.7 (1.4, 2.0) | <0.001 | 1.3 (1.1, 1.6) | 0.001 | 1.4 (1.2, 1.6) | <0.001 | 1.6 (1.3, 1.8) | <0.001 |
| Residence in Hubei province (ref. elsewhere) | 1.3 (1.0, 1.7) | 0.048 | 1.6 (1.3, 2.2) | <0.001 | 1.5 (1.3, 1.9) | <0.001 | 1.4 (1.2, 1.7) | <0.001 | 1.6 (1.4, 1.9) | <0.001 | 1.3 (1.1, 1.6) | 0.001 |
| Following pandemic information frequently (ref. none) | 2.2 (1.8, 2.6) | <0.001 | 2.6 (2.1, 3.2) | <0.001 | 3.4 (2.9, 4.0) | <0.001 | 2.4 (2.1, 2.6) | <0.001 | 2.8 (2.5, 3.2) | <0.001 | 2.4 (2.2, 2.7) | <0.001 |
| Sharing feelings actively (ref. none) | 0.7 (0.5, 0.8) | <0.001 | 3.0 (2.4, 3.6) | <0.001 | 2.5 (2.1, 3.0) | <0.001 | 1.9 (1.6, 2.3) | <0.001 | 2.6 (2.2, 3.0) | <0.001 | 2.8 (2.4, 3.3) | <0.001 |
| Having acute respiratory symptom (ref. none) | 3.6 (2.9, 4.4) | <0.001 | 3.0 (2.4, 3.6) | <0.001 | 2.5 (2.1, 3.0) | <0.001 | 1.9 (1.6, 2.3) | <0.001 | 2.6 (2.2, 3.0) | <0.001 | 2.8 (2.4, 3.3) | <0.001 |

*Linear with estimates for every 10-year increase.*
DISCUSSION

The high- and intermediate-risk CML cohorts defined by harboring both or either of the two CML-related risk covariates including delay in monitoring response to TKI therapy and TKI therapy interruption or dose reduction during the pandemic had significantly higher prevalence of depression, anxiety, distress, avoidance, intrusion, and hyper-arousal compared with low-risk CML cohort harboring no-risk covariate. Even in the low-risk CML cohort, hyper-arousal was more common compared with controls. These data suggest that persons with CML are psychologically more vulnerable with trauma-related distressing memories and persistent negative emotions resulting from the pandemic.

During the pandemic, although the likelihood of developing a COVID-19 infection in persons with CML is very low (28–31), negative impact on different aspects of CML management including TKI therapy response monitoring, TKI therapy, and enrollment in and compliance with clinical trials is also reported (29). These highlighted the importance of adequate access to health care services such as patient education of having appropriate personal self-protection equipment, establishing a safe area in the hospital or clinic, and telemedicine and mailed medicine to avoid monitoring and therapy interruptions1,2,3 (44–50).

Our study has several limitations. First, it is cross-sectional. We lacked baseline pre-pandemic data so we cannot be certain

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1https://www.hematology.org/covid-19/covid-19-and-cml
2https://covid19.aichannel.com/guidelines-nhs/files/clinical-guide-for-the-management-of-non-coronavirus-patients-requiring-acute-treatment-cancer
3https://www.who.int/news-room/q-a-detail/q-a-coronaviruses
that the observed changes in mental health were related to the pandemic. Second, there were potential selection biases in the respondents. It is not possible to assess the participation rate since it is unclear how many subjects received the link for the online survey. Third, the survey was conducted when the pandemic in China was mostly controlled, which might result in recall bias.

Our data indicate that persons with CML are more vulnerable than controls to mental health problems. This results in delay in monitoring TKI therapy response and in TKI therapy interruptions and dose reductions. The results of our study may help physicians identify vulnerable persons with CML and help them by increasing access to health care services.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Peking University People's Hospital. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

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Our data indicate that persons with CML are more vulnerable than controls to mental health problems. This results in delay in monitoring TKI therapy response and in TKI therapy interruptions and dose reductions. The results of our study may help physicians identify vulnerable persons with CML and help them by increasing access to health care services.

AUTHOR CONTRIBUTIONS

The study was designed by QJ, WL, and LM. MB, SY, YZ, XL, HZ, RL, BL, LZ, ZL, XD, DS, LM, WL, and QJ collected the data. QJ, MB, SY, and TW analyzed the data. QJ, RG, MB, and SY helped prepare the typescript. All authors contributed to manuscript revision, read, and approved the submitted version.

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SUPPLEMENTARY MATERIAL

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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