Impact of COVID-19 outbreak on the mental health status of undergraduate medical students in a COVID-19 treating medical college: A prospective longitudinal study

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Background. COVID-19 pandemic is found to affect the mental health of the population. Undergraduate medical students are especially prone to mental health disorders and hence could be more vulnerable to the impact of the pandemic.

Methods. A prospective longitudinal study was conducted on 217 undergraduate medical students in a medical college at Chennai, India. Depression, anxiety, and stress levels were recorded using Depression Anxiety Stress Scale 21 Items (DASS21) before and during COVID-19 outbreak in India in December 2019 and June 2020 respectively. In the follow-up survey, in addition to DASS21, Pittsburgh Sleep Quality Index to assess sleep quality and a self-administered questionnaire to assess the impact of COVID-19 related stressors were used. The self administered questionnaire assessed the status of COVID-19 testing, interactions with COVID-19 patients, self-perceived levels of concerns and worries related to academics [COVID-19-AA (academic apprehensions)] and those pertaining to the self and family/friends [COVID-19-GA (general apprehensions)]. Cross-sectional and longitudinal comparison of overall scores of depression, anxiety, and stress and scores stratified by gender, year of study, place of residence and monthly family income were performed. Predictors for depression, anxiety, and stress during COVID-19 were investigated using adjusted binary logistic regression analysis and results were expressed as adjusted odds ratio with 95% confidence interval (CI). A P value <0.05 was considered statistically significant.

Results. The average scores for depression, anxiety, and stress during the baseline survey were 7.55±7.86, 4.6±6.19 and 7.31±7.34 with the prevalence (95% CI) of 33.2% (27-39.9%), 21.2% (16-27.2%) and 20.7% (15.5-26.7%); in follow-up survey, the mean scores were 8.16±8.9, 6.11±7.13 and 9.31±8.18 with 35.5% (29.1-42.2%), 33.2% (27-39.9%) and 24.9% (19.3-31.2%) of the study population showing symptoms of depression, anxiety, and stress respectively. There was a significant increase in both the prevalence and levels of anxiety and stress (P<0.001), with depression remaining unchanged during COVID-19, irrespective of gender, year of study, place of residence and family's monthly income. Poor sleep quality, higher levels of baseline depression, anxiety, and stress, higher COVID-19-GA, absence of COVID-19 patients in family/friends and direct interactions with COVID-19 patients were found to be significant predictors of negative mental health in undergraduate medical students. COVID-19-AA was not significantly associated with depression, anxiety, and stress.

Conclusion. COVID-19 pandemic appears to negatively affect the mental health of the undergraduate medical students with the prevalence and levels of anxiety and stress being increased, and depression symptoms remaining unaltered. Addressing and mitigating the negative effect of COVID-19 on the mental health of this population is crucial.

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3 **19 treating Medical College: A prospective**
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Abstract

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Methods. A prospective longitudinal study was conducted on 217 undergraduate medical students in a medical college at Chennai, India. Depression, anxiety, and stress levels were recorded using Depression Anxiety Stress Scale 21 Items (DASS21) before and during COVID-19 outbreak in India in December 2019 and June 2020 respectively. In the follow-up survey, in addition to DASS21, Pittsburgh Sleep Quality Index to assess sleep quality and a self-administered questionnaire to assess the impact of COVID-19 related stressors were used. The self administered questionnaire assessed the status of COVID-19 testing, interactions with COVID-19 patients, self-perceived levels of concerns and worries related to academics [COVID-19-AA (academic apprehensions)] and those pertaining to the self and family/friends [COVID-19-GA (general apprehensions)]. Cross-sectional and longitudinal comparison of overall scores of depression, anxiety, and stress and scores stratified by gender, year of study, place of residence and monthly family income were performed. Predictors for depression, anxiety, and stress during COVID-19 were investigated using adjusted binary logistic regression analysis and results were expressed as adjusted odds ratio with 95% confidence interval (CI). A P value <0.05 was considered statistically significant.

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Conclusion. COVID-19 pandemic appears to negatively affect the mental health of the undergraduate medical students with the prevalence and levels of anxiety and stress being increased, and depression symptoms remaining unaltered. Addressing and mitigating the negative effect of COVID-19 on the mental health of this population is crucial.

Keywords: COVID-19, Undergraduate medical students, Longitudinal study, Mental health, Depression, Anxiety, Stress, Sleep quality, DASS21, PSQI

Introduction

The World Health Organization (WHO) announced COVID-19 outbreak initially, as a public health emergency of international concern (PHEIC) on January 30, 2020 and later declared as a pandemic on March 11, 2020 (WHO 2020). In India, the first COVID-19 case was reported in Kerala on January 30, 2020, and by May 19, the number of cases had crossed one hundred thousand. By September 7, India became the world's second worst hit nation with 4.2 million confirmed COVID-19 cases following United States of America and has recorded 71,642 deaths (Times, 2020). Within India, the state of Maharashtra was the worst hit state followed by Andhra Pradesh and Tamil Nadu, contributing to 21.6%, 11.8% and 11% of the total cases respectively (Newsdesk, 2020). The Government of India declared a nationwide lockdown on 25th March 2020, as a measure to mitigate the spread of infection. However, prolonged lockdown is not only unfavorable to the individuals, it also significantly affects the nation's economy. As a way to revive and restore the affected economy, a phase-wise upliftment of lockdown was announced from June 1, easing of some restrictions, while the lockdown was maintained for the containment zones alone.

Public health emergencies during epidemic/pandemic like SARS, MERS and Ebola outbreak were associated with increased psychological distress in the affected population (Batawi et al. 2019; Lee et al. 2007; Lotsch et al. 2017). Maladaptive behaviors, emotional and defensive reactions were some of the psychological responses to pandemic (Taylor 2019). Social isolation was found to be strongly associated with anxiety, depression, self-harm, and suicidal tendencies (Matthews et al. 2019). Studies indicated that social distancing for a longer duration could affect the mental health negatively (Reynolds et al. 2008). Isolation, boredom, frustrations, worries about contracting the infection, lack of freedom, concerns for family/friends are some of the factors that could affect mental well-being during quarantine (Brooks et al. 2020). Poor sleep quality and increased psychological distress were also well-documented during earlier pandemics (Chen et al. 2006; Johal 2009). In particular, poor sleep was associated with negative emotions, depressive symptoms and increased the risk of mental illness (Agargun & Kara 1997; Tao et al. 2017).

In a recent study conducted during COVID-19 outbreak in India, one fifth of adults were found to suffer from depression and stress and one fourth from anxiety (Saikarthik et al. 2020). Mental health of medical students was found to be even poorer, when compared to general population (Bergmann et al. 2019). Medical education is the most demanding of all the other professional programs in terms of both academics and emotional component of the students (Wolf 1994). Globally, one in three medical students were found to have anxiety, which was higher than the general population (Tian-Ci Quek et al. 2019). Level of depression, suicidal ideation, suicide rates, substance abuse and mental health disorders were also found to be higher among medical students (Hays et al. 1996; Molodynski et al. 2020; Schwenk et al. 2010). Although medical students have better access to mental health care, they were less likely to seek mental health help

121 compared to general population, mainly due to stigma surrounding mental health disorders. This
122 may lead to untoward and harmful coping methods like excess alcohol consumption and
123 substance abuse (Chew Graham et al. 2003; Rosenthal & Okie 2005).
124
125 Swine flu (H1N1) outbreak in 2009 was the last outbreak of an infectious disease in a pandemic
126 scale to which India was exposed (WHO 2009). Undergraduate medical students in India are
127 usually in the age group of late teens to mid-twenties, and hence the current COVID-19 infection
128 is the first exposure to them as adults on a pandemic level. In addition, medical students are
129 facing challenges such as sudden changes in their training routine, including teaching and
130 assessment via online sessions, decreased patient contact and interactions with peers to name a
131 few. These changes result in increased screen time, possible hinderance to their training and
132 increased risk of contracting the infection mainly among the students in clinical postings. All
133 these factors could eventually exert a toll on the mental and emotional well-being of the medical
134 students as they are on an unknown territory.
135
136 Earlier studies show that the negative impact of epidemic/pandemic on the mental health are
137 higher in healthcare workers (Lee et al. 2018; Lu et al. 2006; McAlonan et al. 2007).
138 Unfortunately, only limited studies were done on the impact of epidemic/pandemic on the mental
139 health of medical students. Studies on the impact of COVID-19 pandemic on medical students
140 are limited to cross-sectional surveys assessing attitude, awareness, knowledge, precautionary
141 measures, concerns, risk perceptions, impact on education and confidence, and fear of COVID-
142 19 (Agarwal et al. 2020; Ahmed et al. 2020b; Choi et al. 2020; Khasawneh et al. 2020; Nguyen
143 et al. 2020; Taghrir et al. 2020). Literature search showed only a single study about the
144 psychological impact of COVID-19 on medical students, which cross-sectionally assessed their
145 anxiety levels (Cao et al. 2020).
146
147 Globally, few longitudinal studies compared mental health before and during COVID-19, and
148 found an increase in anxiety and depression symptoms in college students in China (Li et al.
149 2020a), the United States (Huckins et al. 2020) and a deterioration of mental health in the general
150 population in the United Kingdom (Pierce et al. 2020). To our knowledge, there are no studies
151 analyzing the impact of COVID-19 on mental health of undergraduate medical students
152 prospectively to assess cause and relationship. From these observations, we hypothesized that
153 COVID-19 outbreak and quarantine would have a serious negative impact on the mental health
154 of undergraduate medical students. Hence, we conducted a prospective longitudinal study to
155 investigate the mental health of undergraduate medical students over a duration of 6 months by
156 analyzing data collected before and during COVID-19 outbreak in India. The study was
157 conducted in a medical college in Chennai, Tamil Nadu, which is a center for treating COVID-
158 19 patients. We did an extensive investigation of possible confounders and predictors of mental
159 health disorders including demographics, sleep quality, apprehensions related to and caused by

160 COVID-19 in terms of academics and concerns for the self, family, friends, and interpersonal
161 relationships.
162
163 **Materials & Methods**
164 **Participants and setting**
165 The study was originally planned to be a cross-sectional survey for assessing the mental health of
166 the undergraduate medical students in the institution. There were 300 medical students in the
167 institution enrolled for undergraduate medical degree. The Bachelor of Medicine and Bachelor of
168 Surgery (M.B.B.S) is a 5.5 years undergraduate medical course offered in India in which the first
169 2.5 years concentrate mostly on basic medical sciences (pre and para-clinical subjects) and the
170 next 2 years on clinical subjects followed by 1 year of Compulsory Rotatory Resident Internship
171 (CRRI). All 300 students studying in pre-clinical (1st year), para-clinical (1.5 years after pre-
172 clinical year) and clinical years (pre-final year, final year, and resident interns) were included for
173 the study and convenience sampling method was used. The students were explained about the
174 objective of the study and were informed that the participation was voluntary, and confidentiality
175 will be maintained. 276 students out of the total 300 students agreed to take part in the study
176 from whom written consent was obtained before the beginning of the study.
177
178 **Baseline (Before COVID-19) survey**
179 Basic sociodemographic details such as age, gender, year of study, area of current residence and
180 family gross monthly income were collected, and the mental health status was assessed using
181 Depression Anxiety Stress Scale 21 items (DASS21). Students below 18 years of age and those
182 with self-reported history of any pre-existing chronic medical conditions including mental health
183 disorders were excluded (5 were underage and 2 reported history of bronchial asthma). The
184 remaining 269 participants who were included for the study were contacted during their free
185 time, after classes and were encouraged to answer the survey sincerely and doubts were clarified.
186 Email id and mobile number were collected from all the participants. This part of the study was
187 conducted during the first two weeks of December 2019, which was before COVID-19 outbreak
188 in India.
189
190 **Follow-up (During COVID-19) survey**
191 With the unexpected changes to normalcy caused by the COVID-19 outbreak and subsequent
192 lockdown, the authors decided to prospectively study the mental health status of the medical
193 students to assess the effects of COVID-19 on mental health of the study population. After
194 obtaining permission from Institutional Ethics Committee (IEC), the original data from the cross-
195 sectional study was decided to be taken as 'before COVID-19 data' (baseline) and another
196 survey was conducted on June 2020 (June 10 to 20) to collect 'during COVID-19' data (follow-
197 up).
198

199 The follow-up survey was conducted via Google form whose link was sent through personal
200 email IDs of the students which were collected during the baseline survey. This protocol was
201 exercised in order to follow strict social distancing protocol and to avoid direct contact. The
202 follow-up survey included 5 sections; first section had a detailed description of the purpose of
203 the study, along with the informed consent. This section explained the importance and benefits of
204 the survey in the current pandemic, highlighting the voluntary nature of participation and
205 assurance of confidentiality of the collected data. Only after consenting to the study, the
206 participants could access the remaining sections. The successive sections collected responses for
207 demographic details, self-administered questionnaire, DASS21 and Pittsburgh Sleep Quality
208 Index (PSQI). Out of the 269 participants from the baseline survey, 30 randomly selected
209 students were included in a pilot study (described below) and were hence excluded from the
210 follow-up survey. Out of the remaining 239 participants, 222 students responded, from which 5
211 responses were excluded because of being incomplete (response rate 90.8%). The final sample
212 size of this prospective longitudinal study was 217. A flowchart illustrating the sample selection
213 from baseline to follow-up survey is shown in Figure 1.
214

215 **Survey instruments**
216 To fulfil the objective of our longitudinal study, besides DASS21, 'during COVID-19' data also
217 included a self-administered questionnaire to assess the impact of COVID-19 related stressors
218 and PSQI to assess the sleep quality of the students.
219

220 **Assessment of the impact of COVID-19 related stressors**
221 A self-administered questionnaire was prepared by the authors after an extensive literature
222 search, discussion with peers and local experts (Wang et al. 2020; Wong et al. 2007). It included
223 12 close-ended questions out of which, Items 1-3 focused on the subjects' status of COVID-19
224 testing (Yes/No) and their interactions with COVID-19 patients (Yes/No/I don't know). The
225 remaining nine items were designed to assess self-perceived levels of concerns and worries for
226 the self (4-6) and family/friends (7-8) and those related to academics (9-12), due to COVID-19
227 outbreak and quarantine (Supplemental file- Other). The responses were measured on a Likert
228 scale of score 1 to 5, with 1 being the least and 5 being the maximum. This questionnaire was
229 first tested empirically on 30 students (15 each from pre/para clinical years and clinical years) as
230 a pilot study (Hill & century 1998). The collected feedback and responses were analyzed, and
231 corrections were made in the form of changes in articulation and simplification of vocabulary
232 with the help of experts in this field.
233

234 **Identification of latent variables from the self-administered questionnaire**
235 An exploratory factor analysis (EFA) was performed on the 9 items (item 4-12) to determine the
236 validity of the questionnaire and to identify latent variables that could enable the objective of the
237 study. The EFA was conducted using principal component analysis with varimax rotation for
238 factor extraction.

239 The extracted factors were analyzed for retention using Kaiser criterion (Eigen value >1), Scree
240 test and counter-validated using parallel analysis. The Eigen values obtained from parallel
241 analysis, which are values generated randomly with the same number of variables and sample
242 size, were compared with the factor solution generated by EFA with our data. Eigen values of the
243 factors that were higher than the values obtained from parallel analysis decided the number of
244 factors. The two-factor solution thus obtained had 5 items in one (items 4-8) and 4 items in
245 another (items 9-12). The factors were named COVID-19-related general apprehensions
246 (COVID-19-GA) and COVID-19-related academic apprehensions (COVID-19-AA) respectively
247 (Table S1). Reliability analysis was performed for each of the factors separately which presented
248 with a high reliability, with the Cronbach's alpha score of 0.89 for COVID-19-GA and 0.91 for
249 COVID-19-AA. COVID-19-GA was scored by totaling the scores of the five individual items
250 with the total score ranging from 5 to 25 and higher scores denote higher general apprehension.
251 Similarly, COVID-19-AA was scored by summing up the scores of the four individual items
252 with the scores ranging from 4 to 20 and higher scores denote higher academic related
253 apprehension.
254
255 **Estimation of mental health status**
256 Mental health status of the medical students was assessed using Lovibond and Lovibond's
257 Depression Anxiety Stress Scale 21 items (DASS21) (Lovibond et al. 1995). This scale
258 comprises of 21 items with seven each for depression, anxiety, and stress subscales. The total sub
259 scores range from 0 to 42 and is categorized into normal, mild, moderate, severe, and extremely
260 severe. In this study, DASS21 sub scores were categorized dichotomously, with the participants
261 being divided in to those who showed symptoms of depression, anxiety and stress and those who
262 did not, based on the cut-off sub-scores of 9, 7 and 14 respectively (Cheung et al. 2015;
263 Lovibond et al. 1995).
264
265 **Estimation of sleep quality**
266 Subjective sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI) which
267 includes 21 items that assess seven components viz. subjective sleep quality, sleep duration,
268 sleep latency, habitual sleep efficiency, use of sleep medications, sleep disturbance, and daytime
269 dysfunction over the duration of two weeks prior to assessment. Global PSQI scores are obtained
270 by summing up the seven individual sub scores and it ranges from 1 to 21 with higher scores
271 (>5) denoting poor sleep quality (Buysse et al. 1989; Rahe et al. 2015).
272
273 Previous studies have shown high reliability of both DASS21 and PSQI among Indian
274 undergraduate medical student population (Shad et al. 2015; Yadav et al. 2016). In our study,
275 both the scales showed good internal consistency and DASS21 scale demonstrated good test-
276 retest reliability. Cronbach alpha score for reliability for PSQI was 0.72 and for DASS21 scale
277 0.94 (depression subscale 0.85, anxiety subscale 0.84, stress subscale 0.87) and 0.94 (depression

278 subscale 0.87, anxiety subscale 0.81, stress subscale 0.85) for baseline and follow-up survey,
279 respectively.
280
281 **Ethical consideration**
282 Ethical approval was obtained from the IEC, Madha Medical College and Research Institute in
283 Chennai (MMCRI/IEC/H/018/2020) and research was done in accordance with the Helsinki
284 Declaration for research on human participants.
285
286 **Statistical analysis**
287 Descriptive statistics was performed for all the variables. The scores of depression, anxiety,
288 stress, and sleep quality were expressed as mean ± standard deviation (SD). Initially, unadjusted
289 univariate association between the demographic variables and depression, anxiety and stress
290 were performed. Mann Whitney U test and Kruskal Wallis test for continuous variables and Chi-
291 square test for categorical variables were used for cross-sectional analysis. Wilcoxon signed rank
292 test for continuous variables and McNemar's test for categorical variables were used for
293 longitudinal analysis. Spearman's correlation test was performed to assess the correlation
294 between the scores obtained from the survey instruments in both the surveys.
295 To explore the contributory factors associated with depression, anxiety, and stress during
296 COVID-19 outbreak (dependent variable), adjusted binary logistic regression analysis was
297 performed. Independent variables included were scores of PSQI, COVID-19-GA, COVID-19-
298 AA, dependent variable from baseline survey (depression, anxiety and stress sub-scores in
299 respective regression models) as covariates (continuous variables) and responses for the items 1-
300 3 from the self-administered questionnaire as independent factors (categorical variables). Cross-
301 sectional association between sleep quality and study parameters were analyzed using adjusted
302 binary logistic regression. The effect of each of the independent variable was adjusted for
303 sociodemographic variables which were considered to be potential confounders viz. age, gender,
304 year of study, current residence, and family monthly income, in separate binary regression
305 models. The results were expressed as adjusted odds ratio (aOR), 95% confidence interval (95%
306 CI) and P value (statistical significance set at two-tailed P<0.05).
307 All the statistical analysis was performed using SPSS version 26 (IBM, New York, USA) and
308 Parallel analysis was performed using scripts from O'Connor BP (O'Connor 2000)
309
310 **Results**

311 This longitudinal study includes 217 undergraduate medical students (78 males and 139

312 females); the average age was 20±1.6 years. 5.1% got tested for COVID-19, and they all tested

313 negative. 14.3% had friends and family who tested positive for COVID-19 and 12% declared to

314 have had direct contact with COVID-19 patients (Figure 2). The distribution of responses to the

315 items of COVID-19-GA and COVID-19-AA is shown in Figure 2 and percentage distribution of

316 depression, anxiety and stress in baseline and follow-up survey and PSQI in follow-up survey is

317 shown in Figure 3.

318

319 **Cross-sectional relationship between sociodemographic variables and depression, anxiety,**

320 **and stress**

321 The cross-sectional and longitudinal relationship between sociodemographic variables and

322 depression, anxiety, and stress are shown in Table 1. There was no significant cross-sectional

323 relationship between the demographic variables and both baseline and follow-up depression,

324 anxiety, and stress scores except in the baseline survey where depression levels were higher in

325 the students from rural sector than urban sector (P=0.039). The association between demographic

326 variables and depression, anxiety, and stress analyzed by binary logistic regression showed that

327 age was a protective factor for depression in the follow-up survey (OR 0.737, 95% CI 0.565-

328 0.961) (Table S2). Other than this, there were no significant associations between demographic

329 variables and mental health in both baseline and follow-up survey (Tables S2-4).

330

331 **Comparison of baseline and follow-up depression, anxiety and stress stratified by**

332 **sociodemographic variables**

333 The overall prevalence (with 95% confidence interval) of depression, anxiety and stress before

334 COVID-19 was 33.2% (27-39.9%), 21.2% (16-27.2%) and 20.7% (15.5-26.7%) and during

335 COVID-19 outbreak was 35.5% (29.1-42.2%), 33.2% (27-39.9%) and 24.9% (19.3-31.2%)

336 respectively. There was a significant increase in the prevalence and mean scores of anxiety and

337 stress when compared to baseline scores (P<0.001) (Table 1). In terms of prevalence, when

338 compared to baseline values, the prevalence of anxiety was significantly increased during

339 COVID-19 in females (P=0.003), pre-clinical, para-clinical (P=0.014) and clinical year students

340 (P=0.019), students from urban residence (P=0.005) and those with gross family income above

341 100,000 INR per month (P=0.007). In terms of mean DASS21 scores, there was a statistically

342   significant increase in anxiety with mild effect size and stress levels with moderate to strong

343   effect size in medical students in the follow-up survey compared to baseline levels irrespective of

344   gender, year of study, current residence and gross family income per month (below 50,000 INR

345   and above 100,000 INR) (P<0.05). Out of the entire study population, the levels of depression

346   have increased significantly in male students and students from urban residence when compared

347   to before COVID-19 levels albeit with mild effect size (Table 1).

348

349   **Difference in ranks of DASS21 scores between baseline and follow-up survey**

350   The difference in ranks of DASS21 scores between baseline and follow-up survey is shown in

351   Table 2. There was no significant change in depression (P=0.146) in medical students between

352   the two surveys; however, anxiety and stress has increased (P<0.001), showing an increase in

353   median scores in the follow-up survey (Tables 1, 2). The incidence of depression, anxiety, and

354   stress based on DASS21 sub-scores were found to be 2.3 (5 out of 217), 11.98 (26 out of 217)

355   and 4.15 (9 out of 217) per 100 per 6 months, respectively. 97 (44.7%), 89 (41.01%) and 142

356   (65.44%) students scored higher in depression, anxiety, and stress in the follow-up survey when

357   compared to their responses before COVID-19 outbreak. While 60 (28.04%), 69 (31.79) and 7

358   (3.22%) students scored lesser in depression, anxiety, and stress in follow-up survey (Table 2).

359

360   **Correlation between the scores of the survey instruments from baseline and follow-up**

361   **survey**

362   The results of Spearman correlation analysis of the scores of the survey instruments from

363   baseline and follow-up survey is shown in Table 3. There were significant positive correlations

364   between PSQI and baseline and follow-up depression, anxiety, and stress. The correlation

365   between the baseline and follow-up depression, anxiety, and stress scores indicates that a higher

366   baseline score was associated with higher follow-up score and vice versa (P<0.001). There was a

367   relatively weak, but significant positive correlation between depression levels before COVID-19

368   and COVID-19-related general apprehensions (r=0.152, P=0.025) (Table 3).

369

370   **Adjusted binary logistic regression analysis of sleep quality**

371   Cross-sectional association between sleep quality and mental health in the follow-up survey is

372   shown in Figure 4. Students with higher depression, anxiety, and stress scores during COVID-19

373   outbreak were found to be more likely to have poor sleep quality (P<0.001).

374

375   **Adjusted binary logistic regression analysis of follow-up depression, anxiety, and stress**

376   The results of binary logistic regression analysis for follow-up depression, anxiety, and stress are

377   shown in Figures 5-7. Poor sleep quality was found to be significantly associated with an

378   increase in depression, anxiety, and stress (P<0.001). Higher baseline scores of depression,

379   anxiety, and stress were associated with higher levels of the same in follow-up survey (P<0.001).

380   Higher COVID-19-related general apprehension was associated with higher levels of anxiety

381   (P=0.016), and stress (P=0.005). Students who did not have any direct interactions with COVID-

382   19 patients were found to be less likely to have symptoms of depression (P=0.017) and stress

383   (P=0.004) when compared to those who did. Similarly, absence of COVID-19 patients in family

384   and friends was found to be associated with decreased levels of stress (P=0.004).

385

386   # Discussion

387   The present study investigated the mental health status of undergraduate medical students in a

388   medical college, which is a government-approved center for treating COVID-19 patients. The

389   medical college is in Chennai, TamilNadu, which is one of the top 5 COVID-19 affected

390   metropolitan cities in India. Longitudinal data analysis was used to test our hypothesis that

391   COVID-19 outbreak and quarantine has a negative impact on the mental health of undergraduate

392   medical students.

393

394   We found that 35.5% (95% CI 29.1-42.2%), 33.2% (95% CI 27-39.9%) and 24.9% (95% CI

395   19.3-31.2%) of the undergraduate medical students, including resident interns showed symptoms

396   of depression, anxiety, and stress respectively during COVID-19 outbreak with the majority with

397   moderate depression (15.2%), moderate anxiety (17.5%), and mild stress (13.4%). Based on the

398   severity ranking, subjects with moderate and above ranking may present with a possible problem

399   that may require intervention (Crawford & Henry 2003; Lovibond et al. 1995; Page et al. 2007;

400   Stormon et al. 2019). In this study, 23.9%, 26.7% and 11.5% of the study population presented

401   with moderate to extremely severe levels of depression, anxiety, and stress respectively (Figure

402   3). The six-month incidence of anxiety was found to be comparatively higher (11.98%) followed

403   by stress (4.15%) and depression (2.3%). There were no other longitudinal studies conducted in

404   medical students during COVID-19 pandemic assessing the incidence of mental health disorders;

405   however, a study conducted in the general public in China found the one-month incidence of

406   mental health disorders to be relatively low (Yali et al. 2020). Though the incidence rate seemed

407   to be relatively low in our study, 44.7%, 41.01% and 65.44% of the study population scored

408   higher in depression, anxiety, and stress sub scores during COVID-19 (Table 2). When compared
409   to baseline survey that was recorded before COVID-19 outbreak in India, there was a significant
410   increase in prevalence and levels of anxiety and stress, while that of the depression remained
411   unchanged during COVID-19. Similar studies conducted longitudinally in college students found
412   a significant increase in depression and anxiety when compared to before COVID-19 levels. (Li
413   et al. 2020a, Huckins et al. 2020). This negative impact of the pandemic could be attributed to
414   sudden challenges faced by the medical students in terms of academics, uncertainties about
415   future, fear of infection, news about shortage of personal protective equipment, quarantine
416   induced boredom, frustrations, lack of freedom, and fears caused by rumors and misleading news
417   in the media (Bao et al. 2020; Ferrel & Ryan 2020).
418
419   Investigation of the influence of demographics on mental health showed that the increase in
420   anxiety and stress levels in our study population was not affected by gender, year of study,
421   current residence, or family income. We also found no significant cross-sectional difference in
422   depression, anxiety, and stress between the groups of demographic variables during COVID-19.
423   Binary logistic regression analysis of anxiety and stress and demographic variables as
424   independent variables showed no significant association. In contrary, cross-sectional studies
425   done on medical students in China and Brazil during this pandemic found significant
426   associations between mental health disorders and place of residence, parental income/financial
427   support, and gender (Cao et al. 2020; Sartorao Filho et al. 2020). Our results show that the
428   response of the medical students to COVID-19 pandemic in terms of the levels of anxiety and
429   stress is similar, irrespective of gender, year of study, current residence, and financial status of
430   the family. Depression in the study population, on the other hand, remained unchanged during
431   COVID-19 in all the categories except in male and urban population. Binary logistic regression
432   showed that increase in age could decrease the likelihood of depression (OR 0.737, 95% CI
433   0.565-0.961) which is consistent to previous studies during COVID-19 (Ahmed et al. 2020a;
434   González-Sanguino et al. 2020). However, in our study, the range of age was narrow (18-26
435   years) and mostly corresponded to the year of study, which had no significant association with
436   depression. Hence, this observation becomes redundant. We found a significant increase in
437   depression levels in male students but not in female students. This finding is contradictory to the
438   study by Sartorao Filho et al., which found female medical students to be more at risk of
439   developing depression symptoms during this pandemic (Sartorao Filho et al. 2020). Females are
440   more proactive in their response and awareness about the epidemic when compared to males, and
441   our results could be a possible implication of this (Brittni Frederiksen 2020). Despite higher
442   levels of depression in the students from rural areas before COVID-19, their depression levels
443   remained unchanged in the follow-up survey. However, the students from the urban areas
444   presented with an increase in depression when compared to before COVID-19 levels. Nearly
445   53% of India's cases were recorded in Mumbai, Delhi, Ahmedabad, Pune, and Chennai alone,
446   which were listed as top five COVID-19 cities (Shylendra 2020). Urban areas are highly
447   populated, and the epidemic is more active in these areas than in rural areas. This led to the

448   implementation of frequent lockdown measures by the respective State Governments in the
449   COVID-19 hotspots, which are mainly urban centers. This could have possibly increased the
450   psychological distress in the students from urban locations.
451
452   Since we did not find significant differences in mental health among most of the groups of
453   demographic variables in both baseline and follow-up survey, it is likely that the worsening of
454   mental health status of the medical students found in our study is associated with COVID-19-
455   related factors. To further elucidate this, we used adjusted binary logistic regression analysis to
456   explore possible predictors. Our extensive literature survey showed all the collected demographic
457   variables to have a potential influence on the outcome. Hence, despite not finding significant
458   associations between demographics and mental health, we adjusted the effects of each potential
459   predictor for all the recorded demographic variables in the regression models (Cao et al. 2020;
460   Sartorao Filho et al. 2020; Heinze & Dunkler 2017)
461
462   An important finding in our study is the independent bidirectional association between poor
463   sleep quality and mental health. In our study, 34.6% of the study population suffered from poor
464   sleep quality which was found to be a significant independent predictor of depression (aOR
465   1.337, 95% CI 1.19-1.502), anxiety (aOR 1.227, 95% CI 1.106-1.363) and stress (aOR 1.371,
466   95% CI 1.209-1.555) during COVID-19 (Figures 5-7), similar to a previous study by Cellini N et
467   al., in Italy (Cellini et al. 2020). Medical students are especially prone to poor sleep quality
468   because of the physically and emotionally challenging and intense training they undertake
469   (Wong et al. 2005). Poor sleep affects neurocognitive and psychomotor performance, emotional
470   wellbeing, working capacity, academic performance, physical and mental health as well as
471   quality of life (Al-Khani et al. 2019; Flores 2009; Giri et al. 2013; Mume et al. 2011). Due to
472   lockdown measures and travel restrictions, students are facing decreased physical activity, lack
473   of schedule, altered living conditions, increased screen time and time spent in social media, and
474   altered sleep wake schedule including increased daytime nap duration (Majumdar et al. 2020).
475   All these factors in addition to higher demands of medical curriculum could lead to poor sleep,
476   which in turn affects mental wellbeing. Conversely, we also found that higher depression (aOR
477   1.114, 95% CI 1.07-1.159), anxiety (aOR 1.120, 95% CI 1.065-1.178) and stress levels (aOR
478   1.126, 95% CI 1.078-1.176) during COVID-19 were significant predictors of poor sleep quality
479   (Figure 4). Poor sleep is long since been considered an important symptom of mental health
480   disorders. Sleep disturbance is a primary symptom of major depressive disorder (Jindal & Thase
481   2004). Anxiety and stress negatively affect the body's ability to fall and stay asleep (Coplan et al.
482   2015; Kalmbach et al. 2018). In addition, increased time spent in social media and digital devices
483   is a way by which young adults cope with social isolation, and it is associated with increased
484   tendencies to develop sleep disturbances (Sivertsen et al. 2019). Thus, our findings show that
485   poor sleep quality is both a cause and an effect of increased depression, anxiety, and stress
486   symptoms in medical students during this pandemic. Thus, worsening of one could exacerbate
487   the other.

488 Students with higher baseline levels of depression, anxiety, and stress were found to be more
489 likely to have depression (aOR 1.27, 95% CI 1.185-1.361), anxiety (aOR 1.176, 95% CI 1.099-
490 1.259) and stress (aOR 1.810, 95% CI 1.483-2.208) during COVID-19 outbreak (Figures 5-7).
491 There was also significant positive correlation between baseline and follow-up depression,
492 anxiety, and stress scores (Table 3). These results are consistent with a similar study conducted
493 on college students in China (Li et al. 2020a). Studies show associations between pre-existing
494 mental health problems and mental health disorders in medical students (Yates et al. 2008).
495 Previous studies indicate that COVID-19 has a higher negative impact on people with mental
496 health disorders when compared to those without any (Asmundson et al. 2020; Taylor et al.
497 2020). Medical students are proven to be at a higher risk of developing mental health disorders
498 during the course of their training period (Moffat et al. 2004). With the added stressors related to
499 the pandemic, it might be difficult to cope, especially for those students who had higher levels of
500 depression, anxiety, and stress to begin with, leading to exacerbation of symptoms.
501
502 A surprising finding in our study was that COVID-19-related academic apprehensions were not
503 significantly associated with depression, anxiety, and stress. This is in contrary to a recent study
504 conducted in medical students in China, which found moderate positive correlation between
505 worries about academic delay and anxiety (Cao et al. 2020). Although social desirability
506 response bias could be an attributing factor, our finding could be a reflection of the feel of
507 assurance by the students because of drastic student-centered efforts taken by the medical college
508 and universities in continuing medical education. Another reason could be that, since these
509 lockdown instigated changes were in effect for around three months, the students would have
510 adapted to this new normalcy in their training better than anticipated. On the other hand, higher
511 COVID-19-GA scores were found to be a significant predictor for higher levels of anxiety (aOR
512 1.097, 95% CI 1.018-1.182) and stress (aOR 1.128, 95% CI 1.037-1.227) (Figures 6, 7). In a
513 study conducted on medical students in Pakistan, around 76% of the participants conveyed being
514 worried about contracting COVID-19 during clinical postings and even more worried about
515 insufficient care and improper treatment, if they contracted the infection (Ahmed et al. 2020b).
516 In a recent study conducted on adult Indian population, individuals with increased self-perceived
517 risk of contracting COVID-19 were found to be more likely to have mental health disorders
518 (Saikarthik et al. 2020). A longitudinal study conducted in China in college students, found fear
519 of infection to be significantly associated with anxiety and depression (Li et al. 2020a). Our
520 results demonstrated that medical students' self-perceived levels of worries for the self, family,
521 and friends about contracting COVID-19; surviving if contracted with COVID-19; and COVID-
522 19 affecting interpersonal relationships have a negative impact on their mental health. Student
523 population is highly active in social media, which is filled with high amounts of misinformation,
524 adding fear, and affecting mental well-being. Frequent use of social media was associated with
525 higher prevalence of mental health problems during COVID-19 (Gao et al. 2020). At the same
526 time, social media could be used for communications among peers and family, thereby offering
527 much needed social support.

528 In this study, we found no significant association between being tested for COVID-19 and
529 depression, anxiety, and stress. The possible reason could be that all of those who got tested for
530 COVID-19 were found negative. We also found that students without any COVID-19 patients
531 among their family and friends (aOR 0.259, 95% CI 0.069-0.968) and those who were not sure
532 about having any direct interactions with COVID-19 patients (aOR 0.280 95% CI 0.092-0.856)
533 were found to be less likely to have symptoms of stress (Figure 7). Students without any direct
534 interactions with COVID-19 patients were less likely to have symptoms of depression (aOR 0.31
535 95% CI 0.106-0.905) (Figure 5) when compared to those who did. These findings were in line
536 with the study by Cao et al. in China (Cao et al. 2020). The R naught (R0) of SARS-CoV-2 is 2.2
537 (2-2.5), i.e. each infected person spreads the infection to 2.2 individuals, in other words it is more
538 contagious than seasonal flu (Li et al. 2020b). This high contagious nature of the novel SARS-
539 CoV-2 virus could be related to our findings.
540
541 **Strengths and Limitations of the study**

542 The longitudinal nature of this study is its major strength which outweighs the limitation of
543 relatively small sample size. The study investigated the mental health status of the same medical
544 students before and during COVID-19 pandemic, which enabled in studying the pattern,
545 temporal order and predictors of changes in their mental health status. To our knowledge, this is
546 the first study to analyze the effects of COVID-19 outbreak on the mental health of
547 undergraduate medical students longitudinally. We elaborately studied the influence of
548 demographic variables, stressors related to COVID-19 by categorizing them into general and
549 academic apprehensions as well as sleep quality, on mental health. With the known impact of
550 negative mental health on medical students' career and life, we believe the results of our study is
551 important due to the insights provided, that will help the medical educators to address and devise
552 strategies to overcome the pandemic-induced negative impact on undergraduate medical
553 students' mental health.
554
555 Our study is not without limitations. Though our study population includes students who were
556 tested for COVID-19, none turned out positive. Thus, our results cannot be extrapolated to
557 medical students infected with the virus. Despite promising confidentiality, there could have
558 been possible response bias by the students in answering the survey.
559

Conclusions
561 Prevalence and levels of anxiety and stress increased, and depression symptoms remained
562 unaltered during COVID-19 outbreak and quarantine. Poor sleep quality, higher levels of
563 depression, anxiety, and stress before COVID-19, increased worries for the self, family, and
564 friends about contracting and surviving, if contracted with COVID-19, and about COVID-19
565 affecting interpersonal relationships, presence of COVID-19 patients in family and friends and
566 direct interactions with COVID-19 patients were found to be significant predictors of negative
567 mental health in medical students.

568 Neglecting the mental health of the medical students would lead to long-term detrimental effects,
569 which not only will affect the quality of life of medical students and future physicians, but also
570 the overall performance of the healthcare system. An effective plan to safeguard the mental
571 health of this already vulnerable population of undergraduate medical students is crucial. We
572 strongly believe our findings would help the medical educators in addressing and mitigating the
573 rise in mental health disorders, which could prove worse than the current pandemic itself. Further
574 studies to analyze the temporal pattern of changes in mental health status of the medical students
575 are warranted.
576
577

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582

583 **Reference**
584 **Agargun M, and Kara, Solmaz. 1997**. Sleep disturbances and suicidal behavior in patients with
585 major depression. *The Journal of clinical psychiatry*. 58:245-251.
586 **Agarwal V, Gupta L, Davalbhakta S, Misra D, Agarwal V, and Goel AJ. 2020.**
587 Undergraduate medical students in India are underprepared to be the young-taskforce against
588 Covid-19 amid prevalent fears. *medRxiv*
589 **Ahmed MZ, Ahmed O, Aibao Z, Hanbin S, Siyu L, and Ahmad AJ. 2020a.** Epidemic of
590 COVID-19 in China and associated Psychological Problems. *Asian journal of psychiatry*.
591 102092.
592 **Ahmed N, Khan A, Naveed HA, Moizuddin SM, and Khan J. 2020b. Concerns** of
593 undergraduate medical students towards an outbreak of COVID-19. *International Journal of
594 Current Medical And Pharmaceutical Research*. 6(3): 5055-62
595 **Al-Khani AM, Sarhandi MI, Zaghloul MS, Ewid M, and Saquib NJ. 2019.** A cross-sectional
596 survey on sleep quality, mental health, and academic performance among medical students in
597 Saudi Arabia. *BMC research notes*. 12(1):665.
598 **Asmundson GJ, Paluszek MM, Landry CA, Rachor GS, McKay D, and Taylor SJ. 2020.**
599 Do pre-existing anxiety-related and mood disorders differentially impact COVID-19 stress
600 responses and coping? *Journal of Anxiety Disorders*. 102271.
601 **Bao Y, Sun Y, Meng S, Shi J, and Lu LJTL. 2020.** 2019-nCoV epidemic: address mental
602 health care to empower society. *The Lancet*. 395:e37-e38.
603 **Batawi S, Tarazan N, Al-Raddadi R, Al Qasim E, Sindi A, Johni SA, Al-Hameed FM,
604 Arabi YM, Uyeki TM, Alraddadi. 2019.** Quality of life reported by survivors after
605 hospitalization for Middle East respiratory syndrome (MERS). *Health and quality of life
606 outcomes*. 17(1):1-7.

607 **Bergmann C, Muth T, and Loerbroks AJ.** 2019. Medical students' perceptions of stress due to
608 academic studies and its interrelationships with other domains of life: a qualitative study.
609 *Medical education online*. 24:1603526.
610 **Brittni Frederiksen IG, Alina Salganicoff, and Usha Ranji. 2020.** Coronavirus: A Look at
611 Gender Differences in Awareness and Actions. *Kaiser Family Foundation-Women's Health*
612 *Policy*. Available at https://www.kff.org/coronavirus-covid-19/issue-brief/coronavirus-a-look-at-
613 gender-differences-in-awareness-and-actions/ (accessed 28 July 2020).
614 **Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, and Rubin GJ.**
615 **2020.** The psychological impact of quarantine and how to reduce it: rapid review of the evidence.
616 *The Lancet*. 395 (10227); 912-20
617 **Buysse DJ, Reynolds CF, Monk TH, Berman SR, and Kupfer DJ. 1989.** The Pittsburgh
618 Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research*.
619 28:193-213.
620 **Cao W, Fang Z, Hou G, Han M, Xu X, Dong J, and Zheng J. 2020.** The psychological impact
621 of the COVID-19 epidemic on college students in China. *Psychiatry research*. 112934.
622 **Cellini N, Canale N, Mioni G, and Costa SJ. 2020.** Changes in sleep pattern, sense of time and
623 digital media use during COVID-19 lockdown in Italy. *Journal of Sleep Research*. e13074.
624 **Chen R, Chou K-R, Huang Y-J, Wang T-S, Liu S-Y, and Ho L-YJ. 2006.** Effects of a SARS
625 prevention programme in Taiwan on nursing staff's anxiety, depression and sleep quality: a
626 longitudinal survey. *International journal of nursing studies*. 43(2):215-225.
627 **Cheung T, Yip PS. 2015.** Depression, anxiety and symptoms of stress among Hong Kong
628 nurses: a cross-sectional study. *International journal of environmental research and public*
629 *health*. 12(9):11072-11100.
630 **Chew-Graham CA, Rogers A, and Yassin N. 2003.** 'I wouldn't want it on my CV or their
631 records': medical students' experiences of help-seeking for mental health problems. *Medical*
632 *education*. 37(10):873-880.
633 **Choi B, Jegatheeswaran L, Minocha A, Alhilani M, Nakhoul M, and Mutengesa E. 2020.**
634 The impact of the COVID-19 pandemic on final year medical students in the United Kingdom: a
635 national survey. *BMC medical education*. 20(1):1-11.
636 **Coplan JD, Aaronson CJ, Panthangi V, and Kim YJ. 2015.** Treating comorbid anxiety and
637 depression: Psychosocial and pharmacological approaches. *World journal of psychiatry*.
638 5(4):366.
639 **Crawford JR, and Henry JD. 2003.** The Depression Anxiety Stress Scales (DASS): Normative
640 data and latent structure in a large non-clinical sample. *British journal of clinical psychology*.
641 42(2):111-131.
642 **Fawzy M, and Hamed SA. 2017.** Psychological stress among medical students in Assiut
643 University, Egypt. *Psychiatry Research*. 255 (10.1016).
644 **Ferrel MN, and Ryan. 2020.** The impact of COVID-19 on medical education. *Cureus*. 12(3)
645 Flores SJ. 2009. Sleepiness or excessive daytime somnolence. *Geriatric Nursing*. 30 (1):53-60.

646 **Gao J, Zheng P, Jia Y, Chen H, Mao Y, Chen S, Wang Y, Fu H. 2020.** Mental health
647 problems and social media exposure during COVID-19 outbreak. *Plos One.* 15(4):e0231924.
648 **Giri P, Baviskar M, Phalke D. 2013.** Study of sleep habits and sleep problems among medical
649 students of Pravara Institute of Medical Sciences Loni, Western Maharashtra, India. *Annals of*
650 *medical and health sciences research.* 3(1):51-54.
651 **González-Sanguino C, Ausín B, Ángel Castellanos M, Saiz J, López-Gómez A, Ugidos C,**
652 **Muñoz M. 2020.** Mental health consequences during the initial stage of the 2020 Coronavirus
653 pandemic (COVID-19) in Spain. *Brain, Behavior, and Immunity.* 87: 172-176
654 **Hays LR, Cheever T, and Patel P. 1996.** Medical student suicide, 1989-1994. *American*
655 *journal of psychiatry.* 153 (4):553-555.
656 **Heinze G, and Dunkler D. 2017.** Five myths about variable selection. *Transplant International.*
657 30 (1):6-10.
658 **Hill R. 1998.** What sample size is "enough" in internet survey research. *Interpersonal*
659 *Computing and Technology: An electronic journal for the 21st century.* 6(3):1-12.
660 **Huckins JF, DaSilva AW, Wang W, Hedlund E, Rogers C, Nepal SK, Wu J, Obuchi M,**
661 **Murphy EI, and Meyer ML. 2020.** Mental health and behavior of college students during the
662 early phases of the COVID-19 pandemic: Longitudinal smartphone and ecological momentary
663 assessment study. *Journal of medical Internet research.* 22(6):e20185.
664 **Jindal RD, and Thase ME. 2004.** Treatment of insomnia associated with clinical depression.
665 *Sleep medicine reviews.* 8(1):19-30.
666 **Johal SS. 2009.** Psychosocial impacts of quarantine during disease outbreaks and interventions
667 that may help to relieve strain. *NewZealand Medical Journal.* 122 (1296):47 - 52
668 **Kalmbach DA, Anderson JR, and Drake CL. 2018.** The impact of stress on sleep: Pathogenic
669 sleep reactivity as a vulnerability to insomnia and circadian disorders. *Journal of sleep research.*
670 27(6):e12710.
671 **Khasawneh AI, Humeidan AA, Alsulaiman JW, Bloukh S, Ramadan M, Al-Shatanawi TN,**
672 **Awad HH, Hijazi WY, Al-Kammash KR, Obeidat N, Saleh T, and Kheirallah KA. 2020.**
673 Medical Students and COVID-19: Knowledge, Attitudes, and Precautionary Measures. A
674 Descriptive Study from Jordan. *Frontiers in public health.* 8: 253
675 **Kumar SG, Kattimani S, Sarkar S, and Kar SS. 2017.** Prevalence of depression and its
676 relation to stress level among medical students in Puducherry, India. *Industrial psychiatry*
677 *journal.* 26(1):86-90
678 **Lee AM, Wong JG, McAlonan GM, Cheung V, Cheung C, Sham PC, Chu C-M, Wong P-C,**
679 **Tsang KW, and Chua SE. 2007.** Stress and psychological distress among SARS survivors 1
680 year after the outbreak. *The Canadian Journal of Psychiatry.*52(4):233-240.
681 **Lee SM, Kang WS, Cho A-R, Kim T, and Park JK. 2018.** Psychological impact of the 2015
682 MERS outbreak on hospital workers and quarantined hemodialysis patients. *Comprehensive*
683 *psychiatry.* 87:123-127.

684   **Li HY, Cao H, Leung DY, Mak YW. 2020a.** The Psychological Impacts of a COVID-19
685   Outbreak on College Students in China: A Longitudinal Study. *International Journal of*
686   *Environmental Research and Public Health*.17(11):3933.
687   **Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KS, Lau EH, and Wong JY.**
688   **2020b.** Early transmission dynamics in Wuhan, China, of novel coronavirus–infected
689   pneumonia. *England Journal of Medicine*. 382:1199-120
690   **Lotsch F, Schnyder J, Goorhuis A, Grobusch MP. 2017.** Neuropsychological long-term
691   sequelae of Ebola virus disease survivors–a systematic review. *Travel medicine and infectious*
692   *disease*. 18:18-23.
693   **Lovibond PF, Lovibond SH, and therapy. 1995.** The structure of negative emotional states:
694   Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and
695   Anxiety Inventories. *Behaviour research and therapy*. 33(3):335-343.
696   **Lu Y-C, Shu B-C, Chang Y-Y. 2006.** The mental health of hospital workers dealing with severe
697   acute respiratory syndrome. *Psychotherapy and psychosomatics*.75(6):370-375.
698   **Majumdar P, Biswas A, and Sahu S. 2020.** COVID-19 pandemic and lockdown: cause of sleep
699   disruption, depression, somatic pain, and increased screen exposure of office workers and
700   students of India. *Chronobiology International*:1-10.
701   **Matthews T, Danese A, Caspi A, Fisher HL, Goldman-Mellor S, Kepa A, Moffitt TE,**
702   **Odgers CL, and Arseneault L. 2019.** Lonely young adults in modern Britain: findings from an
703   epidemiological cohort study. *Psychological medicine*. 49(2):268-277.
704   **McAlonan GM, Lee AM, Cheung V, Cheung C, Tsang KW, Sham PC, Chua SE, and Wong**
705   **JG. 2007.** Immediate and sustained psychological impact of an emerging infectious disease
706   outbreak on health care workers. *The Canadian Journal of Psychiatry*. 52(4):241-247.
707   **Moffat KJ, McConnachie A, Ross S, and Morrison JM. 2004.** First year medical student
708   stress and coping in a problem-based learning medical curriculum. *Medical education*.
709   38(5):482-491.
710   **Molodynski A, Lewis T, Kadhum M, Farrell SM, Lemtiri Chelieh M, Falcão De Almeida T,**
711   **Masri R, Kar A, Volpe U, Moir F, Torales J, Castaldelli-Maia JM, Chau SWH, Wilkes C,**
712   **and Bhugra D. 2020.** Cultural variations in wellbeing, burnout and substance use amongst
713   medical students in twelve countries. *International Review of Psychiatry*:1-6.
714   10.1080/09540261.2020.1738064
715   **Mume CO, Olawale KO, and Osundina AF. 2011.** Excessive daytime sleepiness, nocturnal
716   sleep duration and psychopathology among Nigerian university students. *South African Journal*
717   *of Psychiatry*. 17(4):108-111.
718   **Newsdesk TH. 2020.** Coronavirus India lockdown Day 167 updates | September 8, 2020.
719   Available at https://www.thehindu.com/news/national/coronavirus-india-lockdown-september-8-
720   2020-live-updates/article32548682.ece (accessed 12 September 2020).
721   **Nguyen HT, Do BN, Pham KM, Kim GB, Dam HT, Nguyen TT, Nguyen TT, Nguyen YH,**
722   **Sørensen K. 2020.** Fear of COVID-19 Scale—Associations of Its Scores with Health Literacy

723 and Health-Related Behaviors among Medical Students. *International Journal of Environmental*
724 *Research and Public Health*. 17(11):4164.
725 **O'connor, BP. 2000.** SPSS and SAS programs for determining the number of components using
726 parallel analysis and Velicer's MAP test. *Behavior research methods, instruments, & computers*.
727 32(3):396-402.
728 **Page AC, Hooke GR, and Morrison DL. 2007.** Psychometric properties of the Depression
729 Anxiety Stress Scales (DASS) in depressed clinical samples. *British Journal of Clinical*
730 *Psychology*. 46(3):283-297.
731 **Pierce M, Hope H, Ford T, Hatch S, Hotopf M, John A, Kontopantelis E, Webb R, Wessely**
732 **S, and McManus SJ. 2020.** Mental health before and during the COVID-19 pandemic: a
733 longitudinal probability sample survey of the UK population. *The Lancet Psychiatry*.
734 **Rahe C, Czira ME, Teismann H, and Berger KJ. 2015.** Associations between poor sleep
735 quality and different measures of obesity. *Sleep medicine*. 16(10):1225-1228.
736 **Ren Y, Zhou Y, Qian W, Li Z, Liu Z, Wang R, Qi L, Yang J, Song X, Zeng L, and Zhang**
737 **X. 2020.** Letter to the Editor "A longitudinal study on the mental health of general population
738 during the COVID-19 epidemic in China". *Brain, behavior, and immunity*. 87:132-133.
739 10.1016/j.bbi.2020.05.004
740 **Reynolds DL, Garay J, Deamond S, Moran MK, Gold W, Styra R. 2008.** Understanding,
741 compliance and psychological impact of the SARS quarantine experience. *Epidemiology &*
742 *Infection*. 136(7):997-1007.
743 **Rosenthal JM, and Okie SJ. 2005.** White coat, mood indigo-depression in medical school. *New*
744 *England journal of medicine*. 353(11):1085.
745 **Saikarthik J, Saraswathi I, and Siva T. 2020.** Risk factors and protective factors of mental
746 health during COVID-19 outbreak and lockdown in adult Indian population-A cross-sectional
747 study. *medRxiv*
748 **Sartorao Filho CI, Rodrigues WCdLV, de Castro RB, Marcal AA, Pavelqueires S, Takano**
749 **L, de Oliveira WL, and Neto CIS. 2020.** Impact Of Covid-19 Pandemic On Mental Health Of
750 Medical Students: A Cross-Sectional Study Using GAD-7 And PHQ-9 Questionnaires. *medRxiv*
751 **Schwenk TL, Davis L, and Wimsatt LA. 2010.** Depression, Stigma, and Suicidal Ideation in
752 Medical Students. *JAMA*.304(11):1181-1190.
753 **Shad R, Thawani R, and Goel A. 2015.** Burnout and sleep quality: a cross-sectional
754 questionnaire-based study of medical and non-medical students in India. Cureus. 7(10)
755 **Shylendra H. 2020.** How is Covid-19 playing out in rural India? Available at
756 https://www.thehindubusinessline.com/opinion/how-is-covid-19-playing-out-in-rural-
757 india/article31671013.ece (accessed 27 July 2020).
758 **Sivertsen B, Vedaa O, Harvey AG, Glozier N, Pallesen S, Aarø LE, Lønning KJ, and**
759 **Hysing MJ. 2019.** Sleep patterns and insomnia in young adults: a national survey of Norwegian
760 university students. *Journal of sleep research*. 28(2):e12790.
761 **Stormon N, Ford PJ, Kisely S, Bartle E, and Eley DS. 2019.** Depression, anxiety and stress in
762 a cohort of Australian dentistry students. *European Journal of Dental Education*. 23(4):507-514.

Taghrir MH, Borazjani R, and Shiraly RJ. 2020. COVID-19 and Iranian Medical Students; A Survey on Their Related-Knowledge, Preventive Behaviors and Risk Perception. *Archives of Iranian medicine*. 23(4):249-254.

Tao S, Wu X, Zhang Y, Zhang S, Tong S, Tao FJ. 2017. Effects of sleep quality on the association between problematic mobile phone use and mental health symptoms in Chinese college students. *International journal of environmental research and public health*. 14(2):185.

Taylor S. 2019. The psychology of pandemics: Preparing for the next global outbreak of infectious disease: Cambridge Scholars Publishing.

Taylor S, Landry CA, Paluszek MM, Fergus TA, McKay D, Asmundson GJ. 2020. COVID stress syndrome: Concept, structure, and correlates. *Depression and anxiety*. 37(8):706-714.

The New York Times. The Coronavirus update: Skyrocketing cases push India to No. 2 on the pandemic list. Available at: https://www.nytimes.com/2020/09/07/world/covid-19-coronavirus.html (Accessed on 12 September 2020)

Tian-Ci Quek T, Tam W-S, X Tran B, Zhang M, Zhang Z, Su-Hui Ho C, Chun-Man Ho R. 2019. The global prevalence of anxiety among medical students: a meta-analysis. *International journal of environmental research and public health*. 16(15):2735.

Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, Ho R. 2020. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. *International journal of environmental research and public health.* 17(15):1729.

WHO. 2009. World now at the start of 2009 influenza pandemic. Available at https://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/ (accessed 02 August 2020).

WHO. 2020. Archived: WHO Timeline - COVID-19. Available at https://www.who.int/news-room/detail/27-04-2020-who-timeline---covid-19 (accessed 29 July 2020).

Wolf TM. 1994. Stress, coping and health: enhancing well-being during medical school. *Medical education.* 28(1):8-17. 10.1111/j.1365-2923.1994.tb02679.x

Wong J, Patil N, Beh S, Cheung E, Wong V, Chan L, and Lieh Mak F. 2005. Cultivating psychological well-being in Hong Kong's future doctors. *Medical teacher.* 27(8):715-719.

Wong TW, Gao Y, Tam WWS. 2007. Anxiety among university students during the SARS epidemic in Hong Kong. *Journal of the International Society for the Investigation of Stress.* 23(1):31-35.

Yadav R, Gupta S, and Malhotra AK. 2016. A cross sectional study on depression, anxiety and their associated factors among medical students in Jhansi, Uttar Pradesh, India. *Int J Community Med Public Health*. 3(5):1209-1214.

Yates J, James D, and Aston I. 2008. Pre-existing mental health problems in medical students: a retrospective survey. *Medical Teacher*. 30(3):319-321. 10.1080/01421590701797630

Relationship between demographic variables and baseline and follow-up depression, anxiety and stress scores

[a] P value: Wilcoxon signed rank test, [b] P value: McNemar test, [c] P value: Mann Whitney U test, [d] P value: Chi square test, [e] P value: Kruskal Wallis test, r value: effect size of Wilcoxon signed rank test

N (%): Number of subjects with depression, anxiety and stress

Subjects with depression: depression sub-score > 9,

Subjects with anxiety: anxiety sub-score > 7,

Subjects with stress: stress sub-score > 14

Significant P value in bold letters

1 Table 1: Relationship between demographic variables and baseline and follow-up depression, anxiety and stress
2 scores

Groups		Depression				Anxiety				Stress			
		Baseline	Follow-up	P value	Effect size (r)	Baseline	Follow-up	P value	Effect size (r)	Baseline	Follow-up	P value	Effect size (r)
Total sample (217)	Mean ± SD	7.55 ± 7.86	8.16 ± 8.9	0.146 a	- 0.070	4.6 ± 6.19	6.11 ± 7.13	**<0.001** a	-0.185	7.31 ± 7.34	9.31 ± 8.18	**<0.001** a	- 0.495
	N (%)	72 (33.2)	77 (35.5)	0.609 b		46 (21.2)	72 (33.2)	**<0.001** b		45 (20.7)	54 (24.9)	**<0.001** b	
Gender Male (78)	Mean ± SD	7.28 ± 8.4	8.54 ± 9.17	**0.023** a	- 0.181	4.62 ± 6.04	6.41 ± 7.5	**0.010** a	-0.208	7.95 ± 7.54	10.08 ± 8.5	**<0.001** a	- 0.528
	N (%)	21 (26.9)	29 (37.2)	0.152 b		20 (25.6)	27 (34.6)	0.118 b		18 (23.1)	23 (29.5)	0.063 b	
Female (139)	Mean ± SD	7.71 ± 7.57	7.94 ± 8.77	0.953 a	- 0.004	4.59 ± 6.29	5.94 ± 6.93	**0.004** a	-0.173	6.95 ± 7.22	8.88 ± 7.99	**<0.001** a	- 0.479
	N (%)	51 (36.7)	48 (34.5)	0.743 b		26 (18.7)	45 (32.4)	**0.003** b		27 (19.4)	31 (22.3)	0.344 b	
	Pc	0.409	0.433			0.986	0.505			0.446	0.304		
	Pd	0.143	0.696			0.230	0.737			0.524	0.240		
Year of study Pre/paraclinical years (150)	Mean ± SD	7.35 ± 7.77	7.84 ± 9.04	0.354 a	- 0.054	4.88 ± 6.13	6.31 ± 7.52	**0.009** a	-0.151	7.08 ± 7.36	9.05 ± 8.29	**<0.001** a	- 0.496
	N (%)	50 (33.3)	51 (34)	1.000 b		34 (22.7)	49 (32.7)	**0.014** b		30 (20)	35 (23.3)	0.180 b	
Clinical years (67)	Mean ± SD	8 ± 8.11	8.87 ± 8.59	0.203 a	- 0.110	3.97 ± 6.32	5.67 ±	**0.003** a	-0.253	7.82 ± 7.33	9.88 ± 7.95	**<0.001** a	- 0.495

N (%)	22 (32.8)	26 (38.8)	0.503 b		12 (17.9)	6.18 23 (34.3)	0.019 b		15 (22.4)	19 (28.4)	0.219 b	
Pc	0.621	0.266			0.079	0.759			0.350	0.339		
Pd	0.943	0.494			0.428	0.810			0.689	0.429		
Current residence Rural (76) Mean ± SD	9.36 ± 9.38	8.71 ± 8.87	0.587 a	0.044	4.92 ± 6.54	6.66 ± 7.96	0.010 a	-0.210	8.05 ± 7.61	10.16 ± 8.58	<0.001 a	-0.473
N (%)	28 (36.8)	29 (38.2)	1.000 b		18 (23.7)	26 (34.2)	0.057 b		19 (25)	22 (28.9)	0.453 b	
Urban (141) Mean ± SD	6.58 ± 6.75	7.86 ± 8.93	**0.022** a	-0.136	4.43 ± 6.01	5.82 ± 6.65	**0.004** a	-0.171	6.91 ± 7.18	8.85 ± 7.95	**<0.001** a	-0.509
N (%)	44 (31.2)	48 (34)	0.627 b		28 (19.9)	46 (32.6)	**0.005** b		26 (18.4)	32 (22.7)	0.07 b	
Pc	**0.039**	0.244			0.806	0.769			0.245	0.297		
Pd	0.400	0.546			0.511	0.813			0.255	0.310		
Family monthly income < 50,000 INR (72) Mean ± SD	9.67 ± 9.73	9.78 ± 10.45	0.696 a	-0.033	5.08 ± 7.14	7.06 ± 8.36	**0.023** a	-0.190	8.50 ± 7.86	10.86 ± 8.97	**<0.001** a	-0.513
N (%)	31 (43.1)	29 (40.3)	0.824 b		19 (25.6)	26 (33.3)	0.210 b		18 (25)	24 (33.3)	0.07 b	
50,000-100,000 INR (84) Mean ± SD	6.83 ± 7.01	7.86 ± 8.62	0.194 a	-0.100	5.17 ± 6.74	5.88 ± 6.7	0.193 a	-0.100	6.88 ± 7.05	8.81 ± 7.92	**<0.001** a	-0.492
N (%)	26 (32.1)	29 (37.2)	0.481 b		18 (23.1)	26 (33.3)	0.134 b		15 (17.9)	15 (17.9)	1.000 b	
>100,000 INR Mean ± SD	6.05 ± 5.84	6.66 ± 6.88	0.471 a	-0.065	3.25 ± 3.47	5.31 ±	**0.001** a	-0.298	6.49 ± 7.02	8.16 ± 7.38	**<0.001** a	-0.481

(61)										
N (%)	15 (24.6)	19 (31.1)	0.523 [b]	9 (14.8)	6.02 20 (32.8)	0.007 [b]	12 (19.7)	15 (24.6)	0.250 [b]
P^e	0.175	0.375		0.383	0.616		0.229	0.193	
P^d	0.068	0.533		0.262	0.790		0.532	0.084	

[a] P value: Wilcoxon signed rank test, [b] P value: McNemar test, [c] P value: Mann Whitney U test, [d] P value: Chi square test, [e] P value: Kruskal Wallis test, r value: effect size of Wilcoxon signed rank test

N (%): Number of subjects with depression, anxiety and stress

Subjects with depression: depression sub-score > 9,

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significant P value in bold letters

Difference in the ranks of DASS21 scores between baseline and follow-up surveys

ª follow-up < baseline ᵇ follow-up > baseline ᶜ follow-up = baseline

1   Table 2: Difference in the ranks of DASS21 scores between baseline and follow-up surveys

Score difference	Negative Ranks[a] (N)	Positive Ranks[b] (N)	Ties[c] (N)	Median score (50th percentile)		Wilcoxon signed-rank test P-value
				Baseline	Follow-up	
Depression	60	97	60	6	6	0.146
Anxiety	69	89	59	2	4	**<0.001**
Stress	7	142	68	6	8	**<0.001**

4   [a] follow-up < baseline, [b] follow-up > baseline, [c] follow-up = baseline

Correlation between scores of survey instruments from baseline and follow-up survey

The results are expressed as ρ (Rho) value; (* P<0.05); (** P<0.001)

1   Table 3: Correlation between scores of survey instruments from baseline and follow-up survey

Variables	COVID-19-AA	COVID-19-GA	PSQI	Depression (baseline)	Depression (follow-up)	Anxiety (baseline)	Anxiety (follow-up)	Stress (baseline)	Stress (follow-up)
COVID-19-AA	1.000	-	-	-	-	-	-	-	-
COVID-19-GA	-0.026 (0.703)	1.000	-	-	-	-	-	-	-
PSQI	0.030 (0.664)	0.032 (0.638)	1.000	-	-	-	-	-	-
Depression (baseline)	-0.025 (0.710)	**0.152*** **(0.025)**	**0.422**** **(<0.001)**	1.000	-	-	-	-	-
Depression (follow-up)	0.019 (0.782)	0.072 (0.292)	**0.520**** **(<0.001)**	**0.673**** **(<0.001)**	1.000	-	-	-	-
Anxiety (baseline)	-0.010 (0.886)	0.126 (0.063)	**0.296**** **(<0.001)**	**0.566**** **(<0.001)**	**0.511**** **(<0.001)**	1.000	-	-	-
Anxiety (follow-up)	0.012 (0.857)	0.088 (0.199)	**0.389**** **(<0.001)**	**0.594**** **(<0.001)**	**0.712**** **(<0.001)**	**0.502**** **(<0.001)**	1.000	-	-
Stress (baseline)	0.011 (0.873)	0.130 (0.055)	**0.474**** **(<0.001)**	**0.710**** **(<0.001)**	**0.783**** **(<0.001)**	**0.575**** **(<0.001)**	**0.765**** **(<0.001)**	1.000	-
Stress (follow-up)	-0.007 (0.914)	0.130 (0.056)	**0.460**** **(<0.001)**	**0.690**** **(<0.001)**	**0.771**** **(<0.001)**	**0.571**** **(<0.001)**	**0.729**** **(<0.001)**	**0.961**** **(<0.001)**	1.000

2   The results are expressed as ρ (Rho) value; (* P<0.05); (** P<0.001)

Figure 1

Flow chart illustrating the sample selection from baseline to follow-up

DASS21: Depression, Anxiety, Stress Scale 21 items.

PSQI: Pittsburgh Sleep Quality Index.
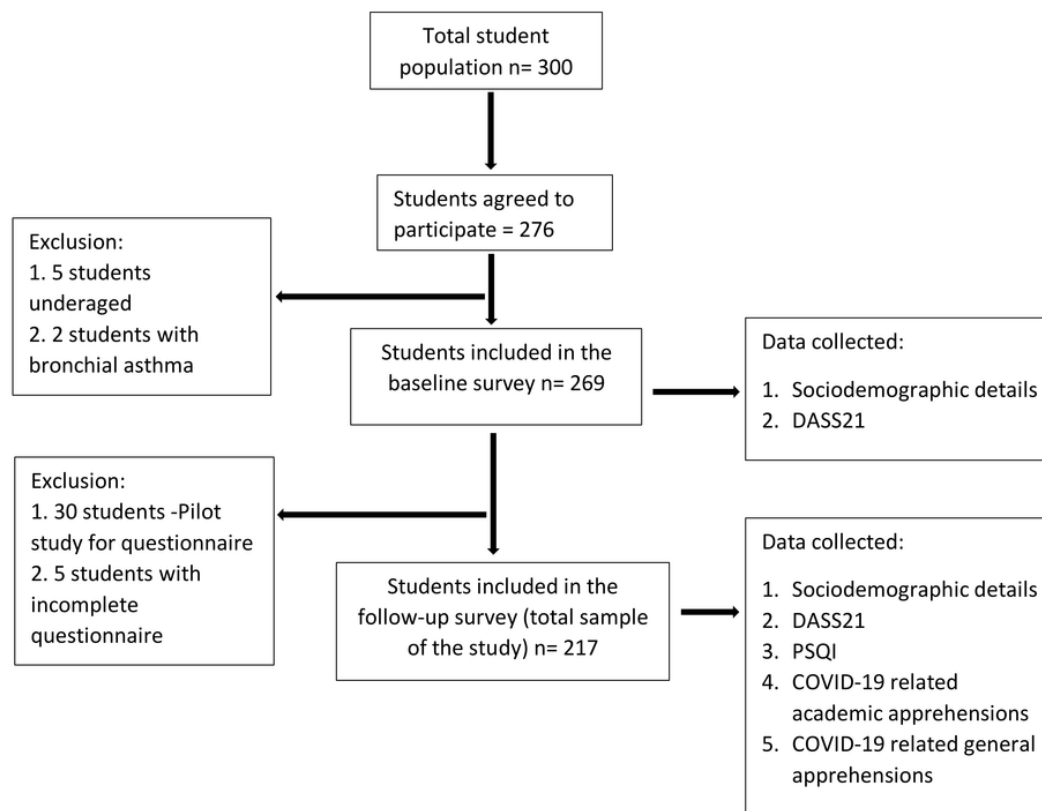
Figure 2

Distribution of responses to self-administered questionnaire (in %)

Items 4 to 12: Likert scale score, 1 through 5; from minimum to maximum COVID-19-GA scores (5 to 25) = 4+5+6+7+8); COVID-19-AA scores (4 to 20) = 9+10+11+12
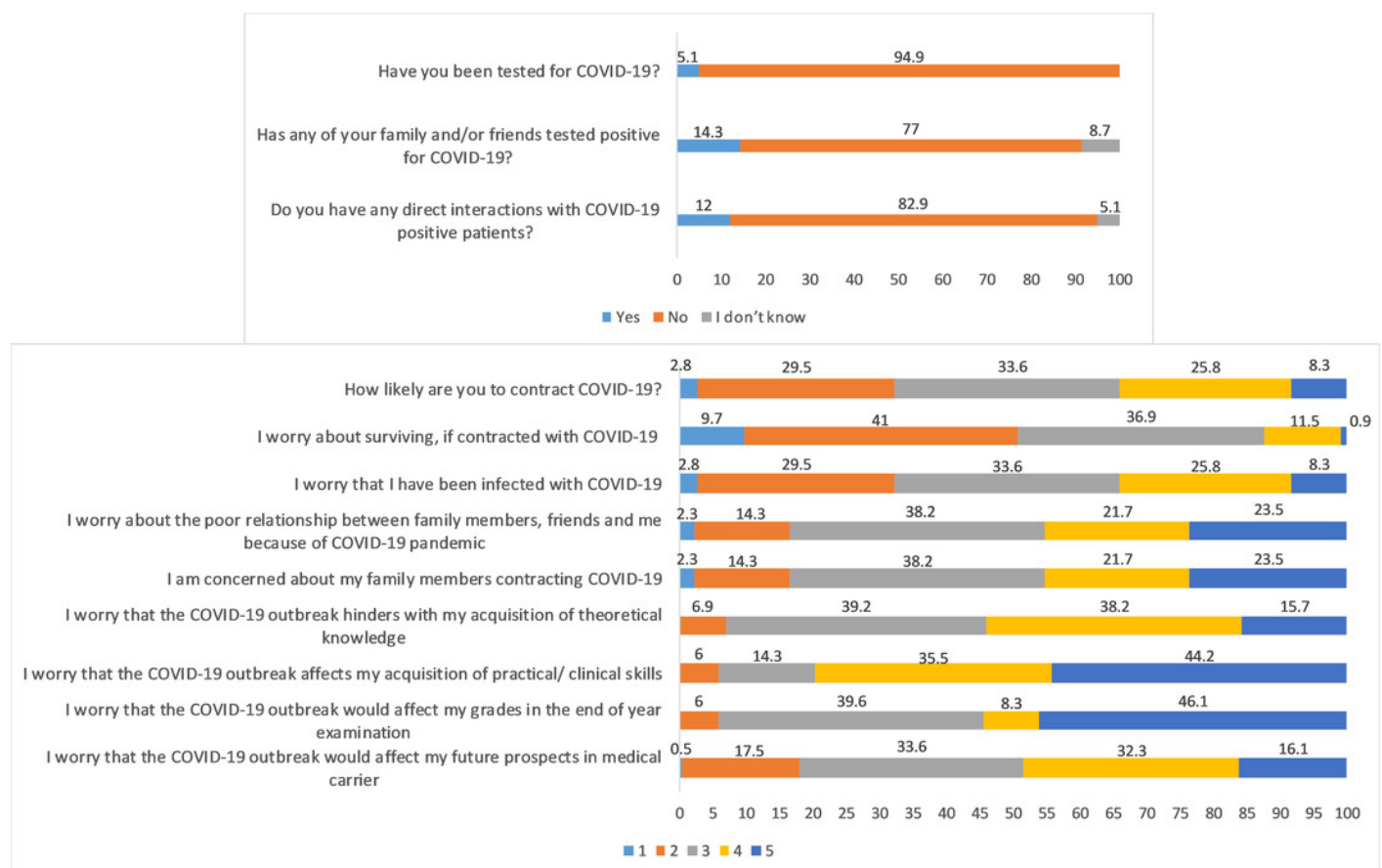
Figure 3

Percentage distribution of baseline and follow-up depression, anxiety and stress levels and sleep quality in follow-up survey

* Severity ranking scores DASS-42. Depression: normal; 0-9, mild. 10-13, moderate; 14-20, severe; 21-27, extremely severe ≥ 28. Anxiety: normal; 0-7, mild; 8-9, moderate; 10-14, severe; 15-19, extremely severe ≥ 20. Stress: normal; 0-14, mild; 15-18, moderate; 19-25, severe; 26-33, extremely severe ≥ 34. DASS21 mean scores are doubled to calculate severity ranking (Lovibond et al. 1995)

** global PSQI score above 5 is considered to be poor sleep quality (Buysse et al. 1989)
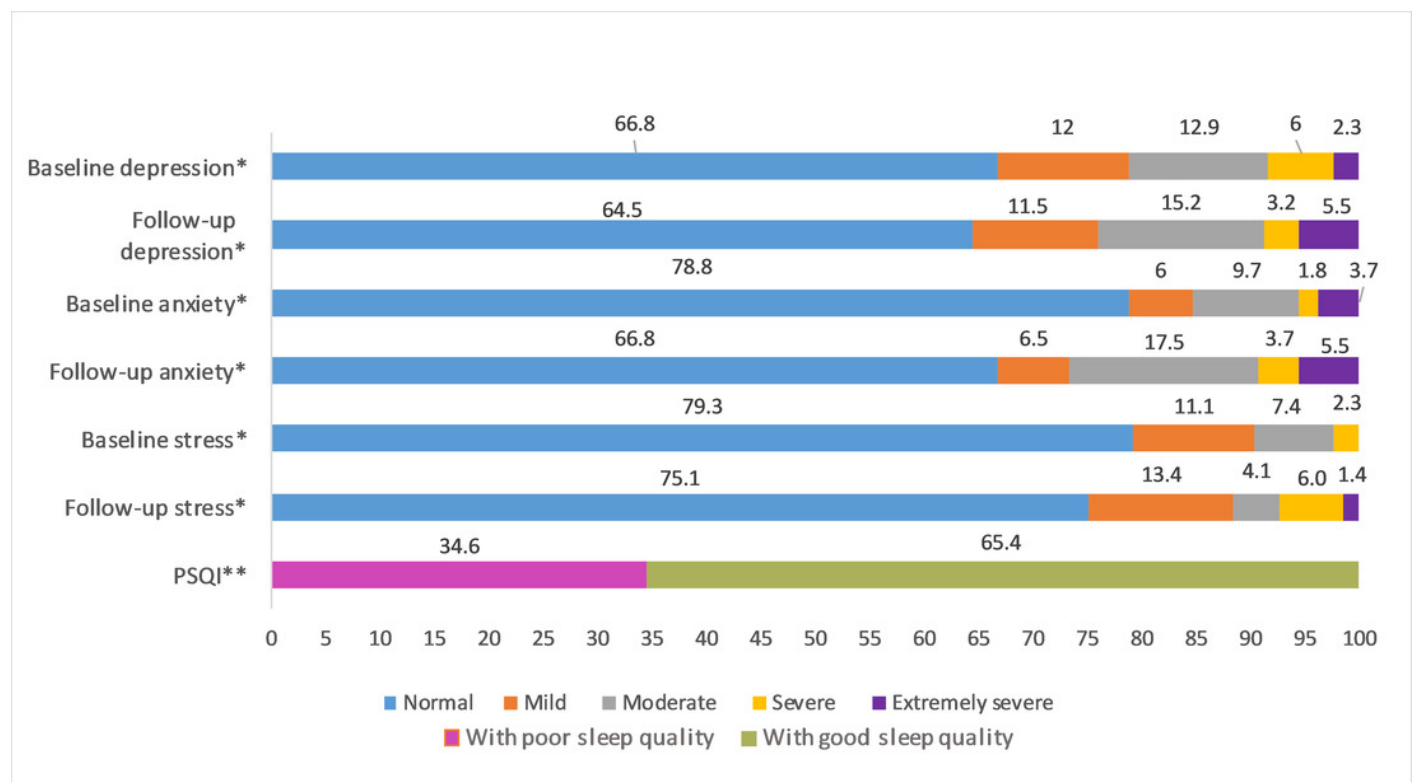
Figure 4

Forest plot showing adjusted binary logistic regression analysis of follow-up PSQI scores (cross sectional)

aOR adjusted odds ratio; odds ratio adjusted for age, gender, year of study, urban/rural residential status, family's monthly financial status; 95%CI 95% confidence interval;
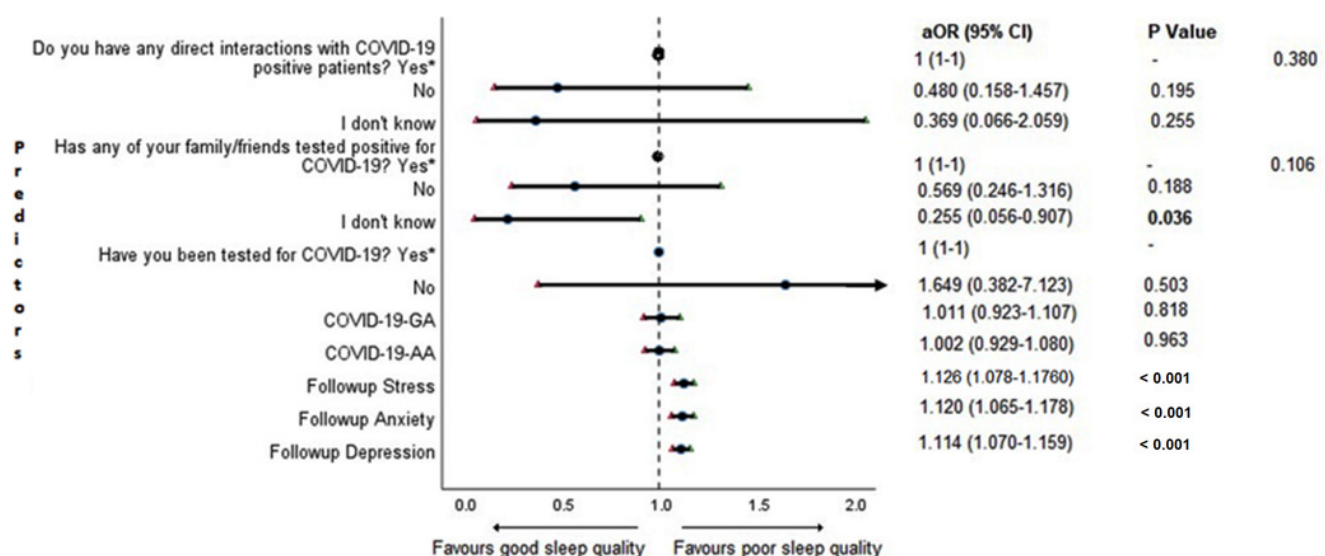
Figure 5

Forest plot showing adjusted binary logistic regression analysis of follow-up depression scores

aOR adjusted odds ratio; odds ratio adjusted for age, gender, year of study, urban/rural residential status, family's monthly financial status; 95%CI 95% confidence interval;
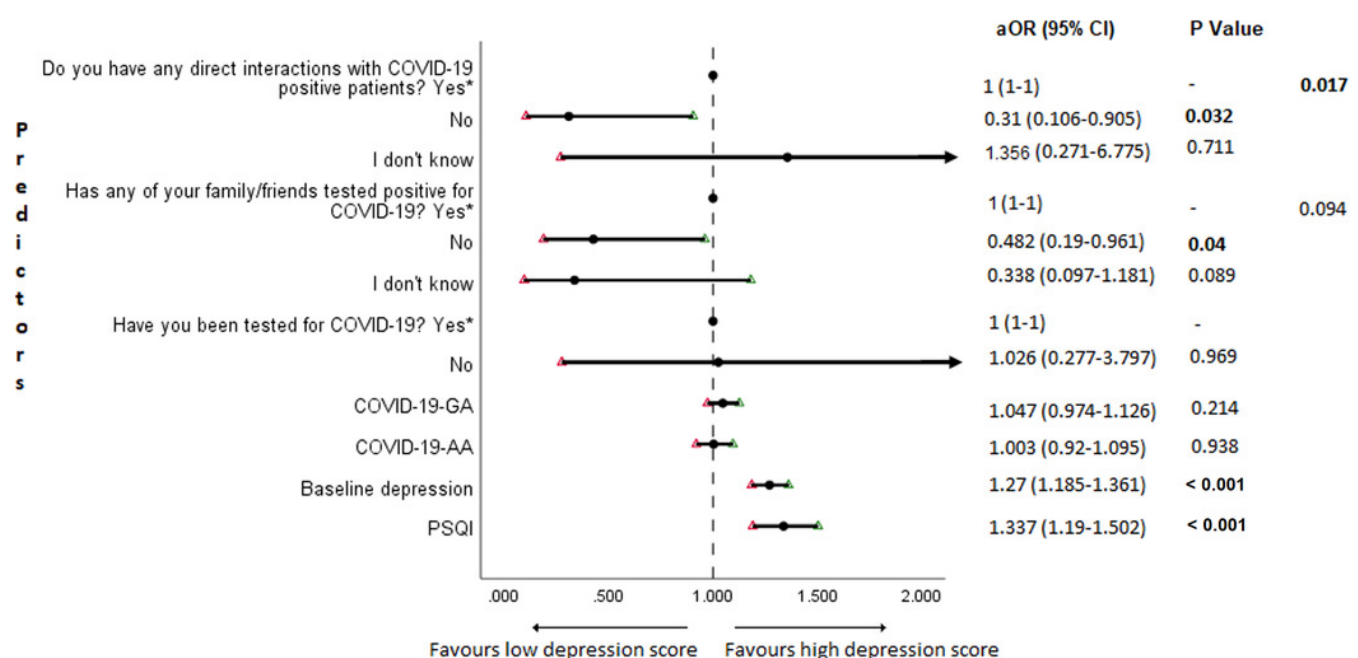
Figure 6

Forest plot showing adjusted binary logistic regression analysis of follow-up anxiety scores

aOR adjusted odds ratio; odds ratio adjusted for age, gender, year of study, urban/rural residential status, family's monthly financial status; 95%CI 95% confidence interval;
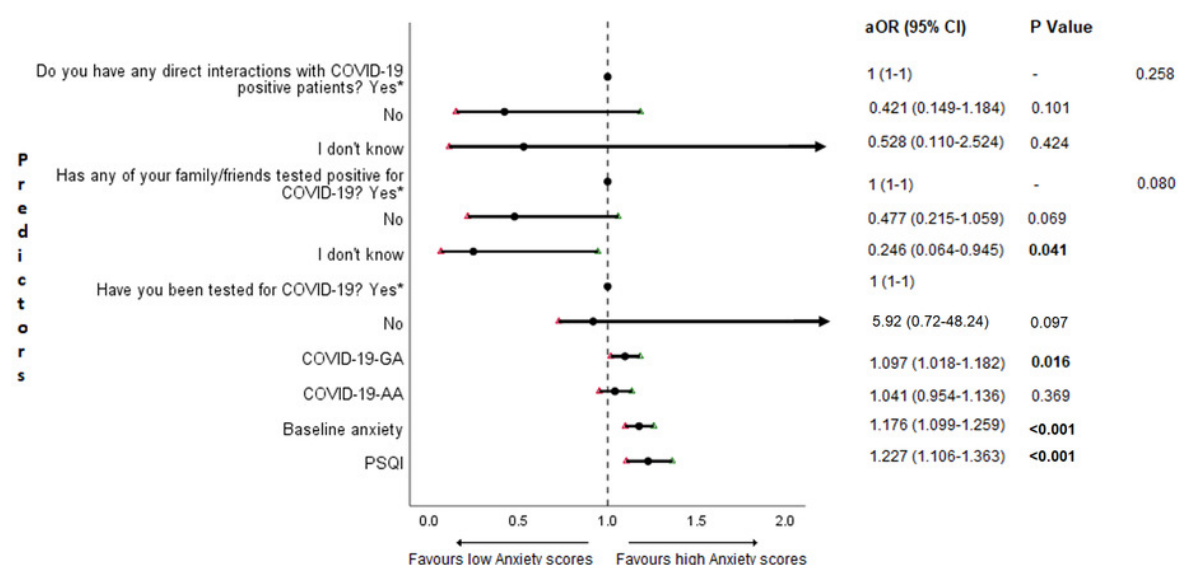
Figure 7

Forest plot showing adjusted binary logistic regression analysis of follow-up stress scores

aOR adjusted odds ratio; odds ratio adjusted for age, gender, year of study, urban/rural residential status, family's monthly financial status; 95%CI 95% confidence interval;