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## IMPACT OF COVID-19 RELATED STRESSORS ON MENTAL HEALTH IN JUNIOR MEDICAL STUDENTS

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### Abstract

**Introduction:** Concern for mental health consequences in general population worldwide has been apparent since the start of the actual pandemic.

**Aim of the study** was to assess the impact of COVID-19 related stressors on mental health in junior medical students during December 2020 COVID-19 related lockdown.

**Material and methods:** The investigation included 275 second-year medical students aged 19-28 years, from the Faculty of Medicine, Ss. Cyril and Methodius University in Skopje during December 2020. Self-administered questionnaire containing standardized instruments for assessment of parameters of psychological distress (BAI, BDI and PSS) were used. COVID-19 related attitudes questionnaire for assessment of status of COVID-19 testing and infection, self-perceived levels of concerns related to academics [COVID-19-AA (academic apprehensions)] and those related to the self and family/friends [COVID-19-GA (general apprehensions)] were included.

**Results:** The prevalence of anxiety, depression and stress was 74.9%, 43.3% and 78.9%, respectively. Almost 29% of students reported high anxiety, 6.2% had severe depression and 21.45% reported high levels of perceived stress. There was a significant positive correlation between COVID-19 GA score and BAI, BDI  $\mu$  PSS scores (p<0.05). Correlations between the COVID-19 AA scores and scores on BAI, BDI and PSS scales were also statistically significant (p=0.0000). Academic apprehension was found a predictive factor for high anxiety, depression and high stress ( $R^2 = .12$ , F(1,273) = 38.79, p < .001.  $\beta = 1.12$ , p < .001).

**Conclusion:** General and academic apprehension related to COVID-19 have negative effects on mental wellbeing in second year medical students.

Keywords: COVID-19, medical students, mental health

## Introduction

Higher rates of anxiety, depression and high levels of perceived stress along with evident growing concern for mental health consequences related to COVID-19 in general population, college population (non-medical and medical) and health workers worldwide have been frequently reported since the pandemic outbreaks in the beginning of 2020. Salari *et al.*, (2020), reported a prevalence of anxiety of 31.9% and a prevalence of depression of 33.7% among general population during the COVID-19 pandemic in a recent meta-analysis [1]. In other studies, the prevalence of anxiety, depression and stress during COVID-19

pandemic was shown to be higher in women than in men [2-4]. COVID-19 pandemic was found to have impact on anxiety levels among university students, with increased levels of anxiety in non-medical students and decreased ones in medical students after introduction of online learning [5].

Medical students are recognized as an at-risk group for developing anxiety disorders with significantly larger rates than general population, even under normal circumstances. Quek et al., (2019), estimated the global prevalence rate of anxiety among medical students to be of 33.8% based on their meta-analysis study before the pandemic outbreak [6]. The second and the third year are the most challenging in medical faculties curricula all over the world. Academic burden along with financial and personal problems have been identified as riskfactors associated with high anxiety and depression in second year medical students [7]. During COVID-19 pandemic, a drastic change in medical education happened abruptly. Traditional face-to face courses and patient bed-side teaching were ordered to be replaced with distant online learning from home. This triggered immediate, forced, prolonged and ongoing shift in medical students' lives and their learning strategies and techniques towards excessive sedentary behaviors and decreased levels of physical activity, while academic challenges of the curricula did not change. During the early stage of the pandemic, several studies from different parts of the world (Europe, USA, Asia) reported a very high prevalence of anxiety (over 60%), and depression (over 40%) in undergraduate medical students [8-10]. Guo et al, 2021, also reported the highest stress (66.1%) in second-through fourth-year medical students. They found that students with preexisting mental health conditions had significantly higher stress and anxiety scores, and higher percentage of stress attributed to COVID-19 [9]. Safa et al, 2020, reported 65.9% prevalence of different levels of anxiety and 49.9% prevalence of varying degrees of depressive symptoms in medical students in Bangladesh, with 3.3% of the participants who had suffered from severe depressive symptoms during the early stage of the pandemic. They reported that the students, who were severely tensed of getting infected by the virus, were at a higher risk of suffering from anxiety (3.5-fold) and depressive (2.7-fold) symptoms in comparison with no/minimally stressed students [10].

In contrast, Lasheras *et al.*, (2020), reported in their meta-analysis study that the prevalence of anxiety in medical students was similar to that prior to the pandemic (28.9%). It was negatively correlated with several specific COVID-related stressors such as knowledge and cognitions on COVID-19 transmission, treatment, prognosis and prevention [11]. Saraswathi *et al.*, (2020), also reported negative effects of COVID-19 pandemic on mental health of undergraduate medical students with increased prevalence of anxiety and levels of stress and unaltered prevalence of depression [12]. It is possible that observed variation in results may be due to cultural differences, differences in socio-demographic background of participants, differences in the health-care system, and the tools used for measurement in these studies.

The aim of this study was to assess the impact of COVID-19 related stressors on the levels of anxiety, depression and perceived stress in second year (junior) medical students during the second COVID-19 related restrictive public health measures in December 2020.

#### Materials and methods

The study was performed at the Faculty of Medicine, Institute of Physiology, Student Counseling Service, Ss. Cyril and Methodius University in Skopje, during December 2019 and December 2020. It was part of a scientific research project entitled: "The relationship between the parameters of body composition, the level of physical activity and the levels of anxiety and depression in medical students", which was approved by the Ethics Committee of the Faculty

of Medicine, under administrative number 03-3152/11 in 2018. During December 2019 - baseline, a cohort of 350 first-year students, aged 18-27 years received questionnaires containing biographic information and Macedonian versions of the following self-rating psychological instruments: the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Perceived Stress Scale (PSS). The response rate was 94% (329 students agreed to participate and returned their responses). One year later in December 2020 (follow-up) the same cohort (second-year medical students) received by e-mail COVID-19 related attitudes questionnaire in addition to the same questionnaires that were used previously. The response rate was 78.5%. Two hundred seventy five students (55 males and 220 females) gave informed consent to participate and completed and returned the questionnaires via e-mail. The average age of students was  $20.4\pm1$  years and the gender structure of the sample during follow-up was consisted of 20% male and 80% female participants.

#### Methods

Beck Anxiety Inventory consists of 21 questions related to various behavioral, emotional, cognitive and physiological symptoms of anxiety [13]. The intensity of perceived anxiety for every question is scored from 0 to 3, with 0 representing the least serious and 3 the most serious symptoms. The sum scores of BAI from 0-7 were ranked as "normal anxiety level" (LA); 8-25 as "moderate" (MA); and 26-63 as" high anxiety" (HA).

The degree of depressive symptoms was measured by the 21-item-revised form of Beck Depression Inventory [14]. The BDI statements for each question are ranked from 0 to 3, with 0 representing the absence of symptoms and 3 the most serious symptoms. The sum scores of BDI < 10 indicate "absence of depressive symptoms" (No), BDI scores from 11-20 indicate "mild depressive symptoms" (Mild), while BDI scores from 21-30 indicate "moderate depressive symptoms" (Moderate). BDI scores higher than 30 indicate "clinically manifested depressive episode" (Severe).

The Perceived Stress Scale consists of ten questions; scoring is by 5-point Likert scale (0 = Never, 1 = Rarely, 2 = Sometimes, 3 = Fairly often, and 4 = Always) [15]. Individual scores on the PSS can range from 0 to 40. with higher scores indicating higher perceived stress. Sum scores range from 0 to 13 indicating "low-stress level" (LS), scores range from 14 to 26 indicates "moderate stress level" (MS), scores range from 27 to 40 indicates "high-stress level" (HS) [16].

A Macedonian version of a self-administered COVID-19 Related Attitudes Questionnaire, which had been constructed and used earlier by Sarawashi *et al.*, 2020 (12), was used for the assessment of self-perceived worries and attitudes towards COVID-19. It included 12 questions, out of which items 1-3 focused on the subjects' status of COVID-19 testing and their or their close family member contraction of the disease (Yes/No). Question 4 focused on the loss of close family member due to COVID related complications (Yes/No). The sums of scores on three individual items (number 6, 7, and 8) ranking from 3 to 15 were named COVID-19-related general apprehensions (COVID-19-GA), with higher scores denoting higher general apprehension. Similarly, sums of scores on four individual items (questions 9, 10, 11 and 12) ranging from 4 to 20 were COVID-19-related academic apprehensions (COVID-19-AA) in accordance with Sarawashi *et al.* (12).

Students who reported high scores on psychological instruments received feedback (by e-mail) with an advice how to reduce their anxiety levels and depression. Ten students with depression and high anxiety visited the Counseling service in person and received one hour of counseling per person with an advice for prolonged therapy and management of situation.

For statistical evaluation of the data, SPSS 16 software (SPSS Inc., Chicago, IL) was used.

The results are represented by mean values and their standard deviations as measures of central tendency; the analysis was performed with the Student t test, Pearson coefficient of correlation, chi-square test and linear regression. The level of significance was p < 0.05.

#### Results

### Parameters of anxiety, depression and perceived stress

Table 1 shows the prevalence of different levels of anxiety, depression and perceived stress and the mean values of BAI, BDI and PSS scores at baseline and during the follow up in our sample of preclinical medical students. During baseline (2019), the prevalence of anxiety in first year students was 76.9%, prevalence of depression was 36.2% and the prevalence of high stress was 87.2%. The prevalence of anxiety, depression and high stress during follow-up was 74.9%, 43.3% and 78.9%, respectively. The prevalence of anxiety (chi square =0.4477; df=5; N=604; p=0.7994) and depression (chi square =5.8311; df=5; N=604; p=0.05417) was not statistically different between samples during baseline and follow-up.

The prevalence of manifested depression (BDI scores > 20) among students during follow-up was 15.6% compared to 9.4% during baseline (chi square = 5.38; df=3; N= 604; p= 0.0203). The prevalence of stress was significantly lower during follow-up compared to baseline (chi square = 8.8724; df=5; N=604; p=0.01184).

Mean scores of BDI were significantly higher during follow-up compared to baseline values (p=0.0079) (Table 1).

Variable		Baseline N=329 N (%)	(mean ± SD) (min – max)	Follow-up N=275 n (%)	(mean ± SD) (min – max)		
BAI	LA	76 (23.1)	$(18.0 \pm 12.1)$	69 (25.09)	$(185 \pm 133)$		
	MA	160 (48.6)	$(10.9 \pm 12.1)$	127 (46.18)	$(10.3 \pm 13.3)$		
	HA	93 (28.3)	(0 - 34)	79 (28.73)	(0 - 01)		
BDI	No	208 (63.8)		156 (56.73)			
	Mild	87 (26.7)	$(9.9 \pm 8.1)$	76 (27.64)	$(11.8 \pm 9.2)$ *		
	Moderate	24 (7.4)	(0 - 39)	26 (9.45)	(0 - 52)		
	Severe	7 (2.1)		17 (6.18)			
PSS	LS	42 (12.8)	$(20.4 \pm 6.8)$	58 (21.09)	(20.1 + 7.6)		
	MS	222 (67.5)	$(20.4 \pm 0.8)$	158 (57.45)	$(20.1 \pm 7.0)$		
	HS	65 (19.7)	(0 - 57)	59 (21.45)	(0 - 37)		
*p=0.0079							

**Table 1.** Prevalence of different levels of anxiety, depression and stress in junior medical students during baseline and follow-up

## **COVID-19 Related Stressors**

Table 2 shows the distribution of responses to questions included in the Macedonian version of COVID-19 Related Attitudes Questionnaire. The questionnaire internal consistency Cronbach's alpha coefficient was 0.782. According to obtained answers, 20% (50 students) underwent COVID-19 PCR test, while 14.2% (39 students) recovered from COVID-19. Almost 35% of the students (96) had a family member who had recovered from the disease, while 12.4% (34) lost a close relative due to COVID-19 complications.

Students were very concerned for their family members lives, i.e. 60% (165) reported that they were extremely worried that their close relatives could get ill and could die from COVID-19. Out of all students, 22.5% (62 students) reported extreme worry related to social distancing from family members and friends because of the actual pandemic.

The distribution of answers to questions related to perceived fear of negative effects of COVID-19 associated lockdown and online education on academic success in second year medical students showed that 39.3% (108) were extremely afraid that the COVID-19 pandemic would prevent them from acquiring the necessary practical and clinical skills (Table 2).

**Table 2.** Distribution of responses to questions included in the Macedonian version of COVID-19 Related

 Attitudes Questionnaire

No	Variable		No			
INU	variable	n(%)	n(%)			
1	Have you been tested for COVID-19?	55	220			
I Have	Thave you been tested for COVID-17:	20	80			
2	Have you contracted with COVID-19?	39	236			
-		14.18	85.82			
3	Has any of your family members been infected and	96	179			
5	recovered from COVID-19?	34.91	65.09			
4	Have you lost a family member due to COVID-19 related	34	241			
•	complications?		87.64			
		1	2	3	4	5
		n(%)	n(%)	n(%)	n(%)	n(%)
5 F	How likely are you to contract COVID-19?		70	127	37	21
U		7.27	25.45	46.18	13.45	7.64
6	I worry whether I will survive if I get COVID 19	117	78	48	19	13
Ũ		42.54	28.36	17.45	6.91	4.73
7	I worry about poor relationship between family members,	26	55	71	61	62
•	friends and me because of COVID-19 pandemic	9.45	20	25.82	22.18	22.54
8 I an	I am concerned about my family members contracting and	9	6	35	60	165
Ū	surviving COVID-19		2.18	12.73	21.82	60
<sub>Q</sub> I	I fear that the COVID-19 outbreak hinders my acquisition	32	36	51	75	8
,	of theoretical knowledge	11.64	13.09	18.54	27.27	2.9
10	I fear that the COVID-19 outbreak affects my acquisition of	13	17	62	75	108
10	practical and clinical skills	4.73	6.18	22.54	27.27	39.27
11	I fear that COVID-19 pandemic would affect my grades in	24	37	63	81	70
11	the end of year examination	8.73	13.45	22.91	29.45	25.45
12	I fear that COVID-19 pandemic would affect my future	44	52	81	51	47
14	<sup>12</sup> prospects in medical carrier		18.91	29.45	18.54	17.09

1= Not at all, 2= A little, 3= Moderately, 4=Very, 5= Extremely

The prevalence of anxiety among students who had lost close relative due to COVID-19 complications was insignificantly higher compared to students without such loss (82.35% (28) *vs.* 74.4% (177), p=0.3). The prevalence of depressive symptoms among students who suffered family loss due to COVID-19 complications was insignificantly higher than the one among students without such loss 55.9% (19) *vs.* 42%(100), p=0.13). Only 8.8% (3) of all students who suffered family loss due to COVID-19 complications and 22.4% (53) students without such loss reported that they did not perceive any stress during last month (p=0.068).

## Correlation between COVID-19 related attitudes questionnaire and BAI, BDI and PSS

Analyzed correlations between the score regarding the statement "I worry whether I will survive if I get COVID-19" and the scores on BAI, BDI and PSS scales were statistically significant (p=0.0097, p=0.047 and p=0.012, respectively). The values of Spearman coefficient of R=0.155, R=0.119 and R=0.151, respectively for the correlation between the analyzed statement and BAI, BDI and PSS scores were positive, i.e. direct.

Statistical analysis confirmed significant differences between students with different levels of anxiety (low, moderate and high anxiety), depending on the scores regarding the statement "I worry whether I will survive if I get COVID-19" (p=0.03). Between groups differences after post-hoc analysis confirmed the difference between the group with low anxiety and the group with high anxiety (p=0.0395), as a result of a significantly higher score of worry for survival from COVID-19 in participants with high anxiety levels.

For p=0.034, the overall statistically significant difference in the scores regarding the statement "I worry whether I will survive if I get COVID-19" between students without depression and those with minor, moderate and severe depression was confirmed. This overall significance was due to a significantly higher "worry" score within the group of students with moderate depression compared to students without depression (p=0.041). Severe depression was manifested in 6.9% (8) of students who did not worry "at all" about survival from COVID-19, followed by 3.85% (3) of students who were "a little worried" and 6.25% (3) of students who were "moderately" worried. Twenty three percent (3) of the "extremely" worried students showed severe depression (Table 3).

"I worry whether I will survive if I get COVID-19"						
Scale		n	$mean \pm SD$	p-level		
BAI	LA	68	$1.79 \pm 1.03$	H = 6.08  p = 0.03		
	MA	127	$1.96 \pm 1.02$	H=0.98 p=0.03		
	HA	79	$2.35\pm1.35$	LA <b>vs.</b> HA p=0.0393		
	No	155	$1.88 \pm 1.04$			
BDI	Mild	76	$2.12 \pm 1.19$	H=8.66 p=0.034		
	Moderate	26	$2.54 \pm 1.14$	No depression vs. Moderate		
	Severe	17	$2.24 \pm 1.52$			
	LS	57	$1.82\pm1.05$			
PSS	MS	157	$2.06\pm1.13$	H=2.64 p=0.27 ns		
	HS	59	$2.17 \pm 1.25$	-		

**Table 3.** Mean values and standard deviations of response scores related to fear of death in different groups of students

Analyzed correlations between the sum scores obtained for COVID-19 GA and the scores on BAI, BDI and PSS scales were statistically significant (p=0.0001, p=0.0001 and p=0.0001, respectively). The values of Spearman coefficient of R=0.271, R=0.237  $\mu$  R=0.278, respectively for the correlation between COVID-19 GA and BAI, BDI  $\mu$  PSS scores were positive, i.e. direct and led to the conclusion that with the increment of the score on COVID-19 GA there was an increase in the values of anxiety, depression and perceived stress. Greater worry related to self and family/friends survival from COVID-19 was correlated with higher levels of anxiety, depression and perceived stress, and vice versa.

Also, correlations between the sum scores obtained for COVID-19 AA and the scores on BAI, BDI and PSS scales were statistically significant (p=0.0000, p=0.0000 and p=0.0000, respectively). The values of Spearman coefficient of R=0.347, R=0.377 and R=0.423, respectively for the correlation between COVID-19 AA and BAI, BDI and PSS scores were positive. Greater worry related to academics was correlated with higher levels of anxiety, depression and perceived stress, and vice versa.

Table 4 shows mean values and standard deviations of COVID-19 GA scores and COVID-19 AA scores obtained in second year medical students during follow-up dependent on different levels of anxiety, depression and stress. As it can be seen, students with low anxiety showed lower general apprehension compared to students with moderate and high anxiety. For p=0.00001 and F=9.28857 (ANOVA), there was a statistically significant difference between groups with different levels of depression. Between groups post-hoc analysis showed that the highest general apprehension was evident in students with moderate depression. For p<0.00001

and F=12.76489 (ANOVA), there was a statistically significant difference between groups with different levels of perceived stress regarding the mean scores obtained for COVID-19 GA. Students with low stress showed lower general apprehension compared to students with moderate and high stress levels.

As it can be seen from Table 4, for p < 0.00001 and F(ANOVA) = 22.4718, students with high anxiety showed the highest academic apprehension compared to students from groups with low and moderate anxiety. Post-hoc analysis between groups showed that there were significant differences between all groups (p<0.05).

perceived stress General apprehension Scale mean ± SD p-level n  $8.4 \pm 2.9$ BAI LA 68 MA 127  $9.75 \pm 2.5$ F=11.90585 p=0.000011 HA 79  $10.4 \pm 2.4$  $9.1 \pm 2.7$ BDI 155 No Mild 76  $9.9 \pm 2.4$ F=9.28857 p=0.00001 Moderate 26  $11.3 \pm 2.1$  $10.3\pm2.5$ Severe 17 PSS LS 57  $8.1 \pm 2.9$ 157  $9.8 \pm 2.5$ F=12.7648 p<00001 MS  $10.4\pm3.4$ HS 59 Academic apprehension Scale mean ± SD p-level

 $11.5 \pm 4.4$ 

 $13.9 \pm 3.9$ 

 $15.8 \pm 3.2$ 

 $12.6 \pm 2.7$ 

 $15.1 \pm 3.5$ 

 $15.8 \pm 3.4$ 

 $17 \pm 2.7$ 

 $10.8 \pm 4.3$ 

 $14.2 \pm 3.7$ 

 $15,7 \pm 3.4$ 

F=22.4718 p<0.00001

F=13.06561 p<0.00001

F=26.68996

p<0.00001

n

68 127

79

155

76

26

17

57

157

59

BAI

BDI

PSS

LA

MA

HA

No

LS

MS

HS

Mild

Moderate

Severe

Table 4. Mean values and standard deviations of COVID-19 GA and COVID-19 AA scores obtained in students with different levels of anxiety, depression and

The mean COVID-19 AA scores obtained in students without depression were signifycantly lower compared to groups of students who manifested different intensity of depressive symptoms (F(ANOVA) = 13.06561, p<0.00001).

Students with high levels of perceived stress showed significantly higher mean values of COVID-19 AA scores compared to students with low and moderate stress (F(ANOVA)) =26.68996, p<0.00001. Post-hoc analysis between groups showed that there were significant differences between all groups (p<0.05) (Table 4).

Using linear regression analysis academic apprehension (AA) was found to be predictive factor for high anxiety, depression and high stress [ $\hat{Y} = 2.9757 + 1.1241X$  AA predicted BAI,  $R^2 = .12$ , F (1.273)=38.79, p<.001.  $\beta = 1.12$ , p<.001), AA predicted BDI,  $\hat{\mathbf{Y}} =$ **0.2476+0.8341X**  $R^2 = .14$ , F (1.273)=45.95, p<.001.  $\beta = .83$ , p<.001 and  $\hat{Y} = 9.1539 + 0.7933X$ AA predicted PSS,  $R^2$ =.19, F (1.273)=63.72, p<.001.  $\beta$ =.79, p<.001].

#### Discussion

To our best knowledge, results obtained in our study represent the first results about the connection between specific COVID-related stressors and the levels of anxiety, depression and perceived stress in medical students in our country. During autumn 2020, restrictive public health measures due to COVID-19 second medical year students showed a very high prevalence of anxiety (74.9%), depression (43.3%) and perceived stress (78.9%). The prevalence of depressive symptoms among students was insignificantly higher compared to baseline (before the pandemic) (p=0.005417). The prevalence of manifested depression (BDI>20) was significantly higher during follow-up compared to baseline (p=0.0203). The intensity of depressive symptoms was significantly higher during the pandemic. The percentage of students who perceived moderate to severe levels of stress was significantly lower compared to baseline (p<0.05).

Our results are in accordance with the findings of Guo et al., 2021, who reported prevalence of anxiety in 66.1% of undergraduate medical students, as well as with the findings of Safa et al., 2020, who reported 65.9% prevalence of different levels of anxiety and 49.9% prevalence of varying degrees of depressive symptoms in medical students in Bangladesh, with 3.3% of the participants who had suffered from severe depressive symptoms during the early stage of the pandemic [9,10]. However, Lasheras et al., (2020), based on their metaanalysis study, reported that the prevalence of anxiety in medical students during COVID-19 pandemic was similar to that prior to the pandemic (28.9%), but it correlated with several specific COVID-related stressors [11]. Studies of anxiety employ different instruments to measure anxiety. Nakhostin Ansari et al., (2020), also used BAI in their study during COVID-19 pandemic and reported 38.1% prevalence of mild to severe anxiety in students who were in clerkship (first two years of study) compared to almost 75% in our sample. Furthermore, they reported 16.7% prevalence of moderate to severe anxiety, while in our sample the prevalence of severe anxiety was 28.3% during baseline and 28.7% during follow-up [17]. In our earlier study, the prevalence of high anxiety in first and second year medical students in our country measured with BAI was 20% and 15%, compared to 28.3% and almost 29%, respectively in this study [7]. First year students in this study were tested before the pandemic outbreak.

The prevalence of manifested depression was significantly higher during follow-up compared to baseline. The prevalence of depression among medical students before COVID-19 pandemic was persistently higher compared to general population, with global prevalence of 27.2% reported by Rotenstein *et al.* [18]. During COVID-19 pandemic, it was 43.3% compared to 36% at baseline. Academic stressor of "the second year", i.e. high academic workload represented by numerous basic courses, accompanied by the fast pace in taking exams and high number of theoretical and practical classes and peer pressure were determined earlier to be a risk factor for depression in medical students in our country [7].

Almost 79% of students in our study perceived moderate to high stress during COVID-19 pandemic lockdown, compared to almost 90% at baseline, before the pandemic. These data are in accordance with the results from different studies that report high prevalence of high levels of perceived stress among university students in Middle East and Asia within a range of 50 to 92%, with the highest prevalence in medical students [16].

Twelve percent of students reported that they had lost a close family member due to COVID-19 related complications. There was no significant difference between them and the students without such loss regarding the prevalence of anxiety, depression and perceived stress. Data on which family member was lost (sibling, parent or grandparent) was not obtained in our study. The mortality rate from COVID-19 complications in our country is very high; there-fore a possible explanation for this finding could be a postponed grief reaction due to general defense and adaptation mechanisms such as denial and rationalization. On the other hand,

60% of all participants were extremely worried about their family members health outcomes connected to COVID-19. More than a half of the students who reported that they were extremely worried about possible death from COVID-19 had high anxiety, and one third of them had manifested depression. Greater worry related to self and family/friends survival from COVID-19 and greater worry related to academics were correlated with higher levels of anxiety, depression and perceived stress. COVID-19 AA score reflected concerns regarding academic obstacles due to the pandemic, such as fear that the situation would have negative effect on students' ability to study the material for partial tests and final exams, to acquire the necessary practical and clinical skills, that it would negatively affect their grades on final exams and that the pandemic would have negative effects even on their future carrier as medical doctors. The odds ratio for manifested depression in students with the highest academic apprehension scores was 4.2 times higher compared to students with lower AA scores (CI: 2.43-7.25 p<0.05). Students with low anxiety, no depression and low level levels of perceived stress showed significantly lower scores on general apprehension and significantly lower scores on academic apprehension compared to students with different levels of present psychological distress.

Within student counseling services, students with high levels of anxiety, depression and stress should be submitted to psychiatric evaluation and afterwards they should carefully be monitored and treated with different modalities of psychotherapy combined with carefully monitored pharmacotherapy, if necessary. Such high levels of anxiety and stress are often accompanied with frequent panic attacks and different types of social anxiety (fear of exams, fear of public speaking), with negative effects on academic performance. If these levels of anxiety persist during longer period of time, they could progress in clinically manifested anxiety disorder and depression [19]. One of the limitations of our prospective study is the lack of data for the cohort during the early stage of the pandemic (during spring 2020 lockdown) to compare with the data from autumn lockdown. These data should be used in order to identify individuals prone to psychological disorders among healthcare professionals. The prevalence of high anxiety, depression and high levels of stress accompanied by high general and academic apprehension related to COVID-19 in medical students, who are future healthcare workers and seem to be a valuable support to health system during COVID-19 pandemic, is very important. These data should be used to plan strategies and appropriate psychological interventions with an aim to improve individual mental health and to build resilience for the needs of management of future similar public health issues.

### Conclusion

The prevalence of anxiety, depression and high levels of stress in junior medical students was very high and was accompanied by great worry for self, family/friends health related to COVID-19 and with great worry regarding negative academic outcomes due to COVID-19 pandemic. Continuous pastoral and psychological support as a mandatory part of medical education is necessary, especially during major health crisis. Introduction of innovative learning modalities tailored to pandemic reality in order to ensure constant and stabile acquisition of practical and clinical skills and knowledge (such as telemedicine) for medical students is necessary.

Conflict of interest statement. None declared.

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