

## Research Article

# A Cross-Sectional Study Exploring Mental Health among Patients Suffering from Dengue in Pakistani Tertiary Care Hospitals

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Received 2 December 2022; Revised 20 September 2023; Accepted 21 September 2023; Published 8 November 2023

Academic Editor: Lut Tamam

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**Background.** Dengue, known as “Tropical flu,” is a widespread disease that has recently become endemic in many Asian countries. Dengue disease still lacks research in many aspects, specifically the impact of patient factors and disease prognosis on mental health. This is a cross-sectional study that evaluated the impact of different patient factors on depression, stress, and anxiety in patients with acute dengue infection. **Methods.** An interview-based data were collected through a questionnaire containing patient sociodemographic parameters, clinical parameters, and DASS 21 questions. Independent sample *T*-test, one-way ANOVA test, and post hoc test were performed to determine the degree of association of psychological manifestations with clinical signs and symptoms considering a level of significance of  $p < 0.05$ . **Results.** The patients from 39 years to 49 years of age had a higher association with stress, depression, and anxiety. The participants at primary and matriculation level education had a higher association with dengue-associated anxiety. Among the three levels of fever, i.e., mild ( $<102^{\circ}\text{F}$ ), moderate ( $102\text{--}103^{\circ}\text{F}$ ), and severe ( $>103^{\circ}\text{F}$ ), the participants suffering from severe fever experienced more anxiety and so was those with intense pain and stress. **Conclusions.** According to the DASS-21 tool, patients with severe pain and high-degree fever during dengue had significant stress and anxiety symptoms, respectively, than the patients with mild or moderate pain and fever. Middle-aged patients with low literacy levels were also found to have significant associations with stress, anxiety, and depression. To our knowledge, this is one of the first studies in Pakistan that in-depth explored the impact of patient factors’ variability on psychological illnesses related to dengue. These findings may warrant practitioners to integrate timely psychological screening and care for dengue patients.

## 1. Introduction

According to CDC, “Classic dengue fever, or “break-bone fever,” is characterized by an acute onset of high fever 3–14 days after the bite of an infected mosquito” [1, 2]. The global burden of dengue has been increasing at an alarming rate for a decade. In the last two decades, 70% of the burden of this disease is in Asia [3]. According to the November 2021 report, there are more than 25,000 cases reported in Pakistan. In this tropical region, dengue has become endemic [4].

Acute dengue fever is characterized by a disease in grown-up children and adults [5]. There is a rapid onset of symptoms such as high fever followed by retroorbital pain, nausea and vomiting, frontal headache, joint pain, rash, weakness, and

body aches [6, 7]. The initial temperature of dengue can be recorded as  $102^{\circ}\text{F}$  to  $105^{\circ}\text{F}$ , and it may last from two to seven days [8]. There is also relative bradycardia. In addition, severe pruritus followed by desquamation on the soles of the feet and palms of the hands is also seen in such patients [9, 10].

In addition to the physical symptoms, dengue can also impact mental well-being and the associated quality of life of the patient. It has been reported that depression, stress, and anxiety are comorbidities in various diseases like hypertension, blood pressure, diabetes, etc. [11]. Our goal is to determine the level of these emotional manifestations in dengue patients. Depression is a common mental disorder affecting more than 264 million people worldwide, and it is characterized by persistent sadness and a lack of interest or

pleasure in previously rewarding or enjoyable activities [12]. As per the American Psychological Association, “Anxiety is an emotion characterized by feelings of tension, worried thoughts, and physical changes like increased blood pressure” [13]. The term “stress,” as it is now used, was defined by Hans Selye in 1936, as “the nonspecific response of the body to any demand for change” [14]. These three psychological presentations are commonly present in so many people, yet these are not given due attention.

Previous studies found a correlation between dengue fever with anxiety, depression, and stress [15–19]. Our study evaluated the degree of association of dengue signs and symptoms and patient sociodemographic factors with the depression, anxiety, and stress levels of patients in Lahore, Punjab, Pakistan. None of the studies has quantified the association of all these variables with depression, anxiety, and stress. In this study, the mean depression score of each group of a variable was compared with the other variables, and the significant difference was evaluated using post hoc analysis. The findings helped us evaluate the impact of each group on a variable. No previous study to date has addressed or explored all these aspects in depth.

*1.1. Literature Review.* A study conducted in 2021 examined the different psychological manifestations of dengue fever and identified the most common psychiatric manifestation of dengue fever [15]. In this study, 60 to 90 percent of patients had anxiety and depression during the acute phase, and in the convalescent stage, 5 to 15 percent of patients were found to be depressive. At three months of follow-up, only 5% of patients had prevalent symptoms. In another study, 62 and 59 percent fulfilled the criteria for anxiety and depression during acute infection [16]. Women had more severe depressive symptoms than men [16]. The severity of depression, anxiety, and stress correlated negatively with the self-efficacy scores during the acute phase [16]. A case-control study including children observed the prevalence of depression (13.3 percent) and anxiety symptoms (34.2 percent) during acute dengue infection to be significantly higher than matched controls. Furthermore, around 25% of the admitted children were found to have agitation, visual hallucinations, aggression, and irritability. Delayed psychiatric manifestations of dengue fever were found to be chief depression and anxiety. The rates of depression were 15% after 6-24 months’ follow-up. There are many reports of manic presentation cases, catatonia, 24–31 acute polymorphic psychosis, 32–39 prolonged depression, and one case on rapid cognitive decline [16]. A case-control study was conducted in Sri Lanka which reported a higher mean value of DASS-21 mean scores for anxiety, stress, and depression in dengue patients as compared to the control group [17]. Another study observed the correlation of anxiety and depression with symptom severity [18]. The severity of fever, myalgia, retro/periorbital pain, headache, and arthralgia positively correlated with depression and anxiety scores [18]. Self-efficacy was also found to be correlated with depression, stress, and anxiety. It was explored and found negative in a study held in Pakistan [19].

Our quantitative cross-sectional study is directed toward finding the impact of different ages, gender, level of education, severity of symptoms, WBC count, and platelet count on depression, anxiety, and stress in dengue patients. In third-world countries like Pakistan, highly varied education levels, income, and employment status can be significant factors contributing to high mean DASS-21 scores. Identifying these factors might lead to optimizing the care provided to dengue patients and open a pathway of research in this lesser clinically focussed area.

## 2. Methods

*2.1. Aim and Study Design.* We employed a cross-sectional study design for our study. We conducted a community and hospital-based cross-sectional study linking factors such as patient demographics and symptom severity (fever, TLC, platelet count) to assess the relationship between dengue, fever, and its psychological manifestations. To find this degree of association, we administered a DASS-21 (Depression, Anxiety, and Stress Scale 21) to patients who were sick with dengue infection in 2021.

*2.2. Description of the Study Site.* Various study sites were explored in Lahore, Punjab, Pakistan, to find the desired patients in the year 2021 dengue-prone season, i.e., September 2021 to December 2021. Hospitals included were Services Hospital, Sir Ganga Ram Hospital, Lahore General Hospital, and Mayo Hospital. We also took data from different colonies door-to-door and different universities in Lahore including Punjab University, GCU, UVAS, and Lahore College for Women University.

*2.3. Inclusion Criteria.* Data was collected mainly from bed-ridden and outpatients who were still suffering from dengue fever or had contracted dengue within the past three months.

*2.4. Exclusion Criteria.* People who had comorbidities like hypertension and diabetes were excluded. As hypertension and diabetes are the causative agents of stress, therefore, we only recruit dengue patients so that we get a refined response. Moreover, patients who needed critical care were eliminated from the study.

*2.5. Sample Size Determination.* We calculated a sample size of 270 dengue patients for our study using the Raosoft sample size calculator with a 90% confidence interval and 10% margin of error. The size of the sample does not change for a population greater than 50,000 according to Raosoft sample size calculator.

*2.6. Statistical Analysis.* The data was analysed by the SPSS 20.0 (Statistical Package for Social Sciences; Version 20.0). The results were expressed as sample number ( $N$ ), mean scores, mean difference, and a significant  $p$  value of 0.05 keeping the confidence interval 95%. Independent sample  $T$ -tests and one-way ANOVA and post hoc analysis were performed to examine the degree of association of depression, anxiety, and stress scores with patient factors like

TABLE 1: Association of the gender of dengue patients with Depression, Anxiety, and Stress Scale 21.

	Gender	N	Mean $\pm$ SD <sup>a+</sup>	<i>t</i> value <sup>a</sup>	Degree of freedom <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	Confidence interval (CI 95%)
Stress	Male	112.00	10.59 $\pm$ 4.21	0.57	208.00	0.57	0.34 (-0.84-1.53)
	Female	98.00	10.24 $\pm$ 4.51	0.57	199.70	0.57	0.34 (-0.85-1.54)
Anxiety	Male	112.00	10.80 $\pm$ 4.33	0.89	208.00	0.38	0.54 (-0.66-1.73)
	Female	98.00	10.27 $\pm$ 4.44	0.89	202.94	0.38	0.54 (-0.66-1.74)
Depression	Male	112.00	10.64 $\pm$ 4.37	0.76	208.00	0.45	0.49 (-0.79-1.77)
	Female	98.00	10.15 $\pm$ 5.01	0.75	193.93	0.45	0.49 (-0.80-1.78)

<sup>a</sup>SD = standard deviation; <sup>b</sup>CI = confidence interval; N = number of responses for the specific variable. Note: independent *t*-test was applied to find the association between the gender of dengue patients and depression, anxiety, and stress.

demographics (age, gender, literacy, and time of onset of disease) and sign and symptom severity (degree of fever, intensity of pain, total leukocyte, and platelet count).

### 3. Results

Out of a total of 210 patients who were interviewed, 112 (56%) were males, and 98(44%) were females. There was no statistically significant difference in anxiety, depression, and stress levels among patients in terms of gender (refer to Table 1).

In accordance with Table 2, patients ranging from 18 to 50 plus years of age were included. There was a significant difference in stress levels between the age groups 18-28 and 39-49, with stress levels more in the 39-49 age group when compared to the 18-28 age group (*p* value = 0.02 with confidence interval 95%, mean difference = 2.32). Similarly, the 39-49 age group had more stress than the 50 plus age group (*p* value = 0.04 with a confidence interval of 95% and mean difference = 3.00). Regarding anxiety, the 39-49 age group had a significant difference in dengue fever-associated anxiety than the 18-28 years age group (*p* value = 0.05 with confidence interval 95%, and mean difference = 2.03). Age group 39-49 had a statistically significant difference in dengue fever-associated depression compared to the age 50 plus group (*p* value = 0.04 with confidence interval 95% and mean difference = 3.20).

According to Table 3, dengue fever-associated anxiety was more in patients with primary-level education than that in university-educated patients (*p* value = 0.03 with a confidence interval of 95% and mean difference = 4.24). A statistically significant difference existed in the anxiety level of patients with only religious education than that of university-educated patients (*p* value of 0.01 with a confidence interval of 95% and mean difference = 4.36). Matric level of educated patients had significant anxiety than the patients having some university education (*p* value = 0.03 with a confidence interval of 95% and mean difference = 1.82).

In accordance with Table 4, there existed no statistically significant difference in stress, anxiety, or depression levels among patient groups who suffered from dengue three months back and one month back from the group of patients who were suffering from dengue fever at the time of the interview.

Patients with severe pain had a significant difference in their stress levels than those with mild or no pain in accordance as in Table 5 (*p* value = 0.05 with confidence interval 95% and mean difference = 2.37).

Patients with severe fever for most of the days had a statistically significant difference in their anxiety levels than the patients who had mild fever for most of the days during the infection period (*p* value = 0.04 with a confidence interval of 95% and mean difference = 2.25). Similarly, depression level was also significantly different between both of these groups (*p* value = 0.05 with a confidence interval of 95% and mean difference = 2.3) (see Table 6).

According to Table 7, there was no significant difference in the stress, anxiety, or depression levels in patient groups having a white blood cell count less than or equal to 4500 and more than 4500 per ml of blood.

Table 8 dictates that there was no significant association with stress, anxiety, or depression levels in patient groups having platelet counts of more than 300,000 and less than 300,000 per ml of blood.

### 4. Discussion

Dengue is a common disease in subtropical and tropical regions of the world like Pakistan, Sri Lanka, Bangladesh, and India [20]. In 2021, a sudden spike in the cases of dengue infection was observed across Pakistan, particularly in Punjab [21]. Several case studies support the fact that dengue fever has an impact on a patient's psychology [15–19]. Not much attention has been paid to further exploring this area. Therefore, the main aim of our study was to determine whether variability in demographic and clinical factors was equally associated with this correlation or not. So, we designed a cross-sectional study on patient factors associated with anxiety, stress, and depression in dengue patients.

The DASS-21 scales assess depression, anxiety, and stress, with the depression scale assessing dysphoria, hopelessness, devaluation of life, self-deprecation, and a lack of interest in life. The anxiety scale evaluates autonomic stimulation, effects on skeletal muscles, personal experience, and situational anxiety whereas stress scale is an indicative of nonspecific reaction to a situation. It evaluates issues with relaxation, nervousness, and a tendency to become easily disturbed or irritated, irritable or too sensitive, and impatient [22]. The scores for the relevant questions are added

TABLE 2: Association of the age of dengue patients with Depression, Anxiety, and Stress Scale 21.

	Age	Mean score $\pm$ SD <sup>b</sup>	Mean difference <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	95% confidence interval		
					Lower	Upper	
Stress	18-28	29-38		-1.62	0.11	-3.46	0.23
		39-49	9.55 $\pm$ 4.39	-2.32	0.02	-4.36	-0.27
		50 plus		0.68	0.91	-1.94	3.31
	29-38	18-28		1.62	0.11	-0.23	3.46
		39-49	11.16 $\pm$ 4.12	-0.70	0.84	-2.87	1.47
		50 plus		2.30	0.13	-0.43	5.03
	39-49	18-28		2.32	0.02	0.27	4.36
		29-38	11.86 $\pm$ 3.83	0.70	0.84	-1.47	2.87
		50 plus		3.00	0.04	0.14	5.86
	50 plus	18-28		-0.68	0.907	-3.31	1.94
		29-38	8.86 $\pm$ 4.70	-2.30	0.13	-5.03	0.43
		39-49		-3.00	0.04	-5.86	-1.40
Anxiety	18-28	29-38		-1.68	0.09	-3.56	0.19
		39-49	9.64 $\pm$ 4.34	-2.03	0.05	-4.11	0.04
		50 plus		0.18	0.99	-2.48	2.86
	29-38	18-28		1.68	0.09	-0.19	3.56
		39-49	11.33 $\pm$ 4.00	-0.35	0.97	-2.56	1.85
		50 plus		1.87	0.30	-0.90	4.65
	39-49	18-28		2.039	0.05	-0.04	4.11
		39-49	11.68 $\pm$ 4.48	0.35	0.97	-1.85	2.56
		50 plus		2.22	0.19	-0.69	5.14
	50 plus	18-28		-0.18	0.99	-2.86	2.48
		29-38	9.45 $\pm$ 4.63	-1.87	0.30	-4.65	0.90
		39-49		-2.22	0.19	-5.14	0.69
Depression	18-28	29-38		-1.40	0.26	-3.40	0.60
		39-49	9.76 $\pm$ 4.76	-1.85	0.13	-4.06	0.36
		50 plus		1.35	0.60	-1.49	4.20
	29-38	39-49		1.40	0.26	-0.60	3.40
		50 plus	11.16 $\pm$ 4.29	-0.45	0.96	-2.80	1.90
		18-28		2.75	0.07	-0.20	5.71
	39-49	18-28		1.85	0.13	-0.36	4.06
		29-38	11.61 $\pm$ 4.20	0.45	0.96	-1.90	2.80
		50 plus		3.20	0.04	0.10	6.30
	50 plus	18-28		-1.35	0.60	-4.20	1.49
		29-38	8.41 $\pm$ 5.38	-2.75	0.07	-5.71	0.20
		39-49		-3.20	0.04	-6.30	-0.10

<sup>a</sup>t-test. <sup>b</sup>ANOVA. SD = standard deviation. Note: t-test and ANOVA were applied to find the association between the age of dengue patients and depression, anxiety, and stress in them.

up to determine the scores for depression, anxiety, and stress. The dimensional rather than categorical conceptualization of psychological pathology is the foundation of the DASS-21. The premise upon which the DASS-21 was developed (and which was supported by the research results) is that the variations in depression, anxiety, and stress experienced by normal people and clinical populations are, in essence, differences of degree. Hence, the DASS-21 has no direct effects on how patients are assigned to specific diag-

nostic categories proposed by classification schemes like the DSM and ICD.

Dengue is not a recently discovered disease. It is reported that the first case was found in the 1920s. It is a mosquito-borne viral infection. The occurrence is highly found in cities and towns. Dengue fever is also called classical dengue fever. Acute onset of this disease ranges from 3 to 14 days. The global burden of dengue is augmented at an alarming rate. The rate of dengue is considered to skyrocket during the

TABLE 3: Association of the education level of dengue patients with Depression, Anxiety, and Stress Scale 21.

		Education level of patients			95% confidence interval of the difference		
		Mean score $\pm$ standard deviation <sup>b</sup>	Mean difference	Sig. ( <i>p</i> value) <sup>a</sup>	Lower	Upper	
Stress	Illiterate	Primary		-2.9	0.54	-7.84	1.89
		Matric		-1.28	0.95	-5.06	2.50
		Secondary	9.75 $\pm$ 3.98	-1.25	0.96	-5.05	2.55
		University		0.4	1.00	-2.91	3.77
		Religious		-4.08	0.14	-8.83	0.66
		Others		-4.25	0.53	-11.19	2.69
	Primary	Illiterate		2.98	0.54	-1.89	7.84
		Matric		1.70	0.91	-2.63	602.00
		Secondary	12.73 $\pm$ 3.66	1.73	0.90	-2.61	6.07
		University		3.40	0.40	-0.54	7.35
		Religious		-1.11	1.00	-6.29	4.08
		Others		-1.27	1.00	-8.53	5.98
	Matric	Illiterate		1.28	0.95	-2.50	5.06
		Primary		-1.70	0.91	-6.02	2.63
		Secondary	11.03 $\pm$ 4.37	0.03	1.00	-3.05	3.11
		University		1.71	0.39	-0.78	4.19
		Religious		-2.80	0.42	-6.99	1.38
		Others		-2.97	0.83	-9.55	3.61
	Secondary	Illiterate		1.25	0.96	-2.55	5.05
		Primary		-1.73	0.90	-6.07	2.61
		Matric	11.00 $\pm$ 3.35	-0.03	1.00	-3.11	3.05
		University		1.68	0.43	-0.84	4.19
		Religious		-2.83	0.41	-7.04	1.37
		Others		-3.00	0.82	-9.59	3.59
	University	Illiterate		-3.83	1.00	-3.77	2.91
		Primary		-1.71	0.14	-7.35	0.54
		Matric	9.32 $\pm$ 4.54	-1.68	0.39	-4.19	0.78
		Secondary		-4.51	0.43	-4.19	0.84
Religious			-4.68	0.01	-8.30	-0.72	
Others				0.30	-11.01	1.66	
Religious	Illiterate		4.08	0.14	-0.66	8.83	
	Primary		1.11	1.00	-4.08	6.29	
	Matric	13.83 $\pm$ 2.55	2.80	0.42	-1.38	6.99	
	Secondary		2.83	0.41	-1.37	7.04	
	University		4.51	0.01	0.72	8.30	
	Others		-0.17	1.00	-7.34	7.01	
Others	Illiterate		4.25	0.53	-2.69	11.19	
	Primary		1.27	1.00	-5.98	8.53	
	Matric		2.97	0.83	-3.61	9.55	
	Secondary		3.00	0.82	-3.59	9.59	
	University		4.68	0.30	-1.66	11.01	
	Religious		0.17	1.00	-7.01	7.34	

TABLE 3: Continued.

		Education level of patients			95% confidence interval of the difference		
		Mean score $\pm$ standard deviation <sup>b</sup>	Mean difference	Sig. ( <i>p</i> value) <sup>a</sup>	Lower	Upper	
Anxiety	Illiterate	Primary		-3.39	0.38	-8.28	1.51
		Matric		-0.96	0.99	-4.77	2.85
		Secondary	10.25 $\pm$ 2.72	-0.53	1.00	-4.36	3.30
		University		-0.86	0.99	-2.50	4.22
		Religious		-3.50	0.31	-2.28	1.28
		Others		-3.75	0.68	-10.74	3.24
	Primary	Primary		3.39	0.38	-1.51	8.28
		Matric		2.42	0.65	-1.93	6.78
		Secondary	13.6 $\pm$ 4.99	-2.86	0.45	-1.52	7.23
		University		4.24	0.03	-0.28	8.21
		Religious		-0.11	1.00	-5.33	5.11
		Others		-0.36	1.00	-7.66	6.94
	Matric	Illiterate		0.96	0.99	-2.85	4.77
		Primary		-2.42	0.65	-6.78	1.93
		Secondary	11.21 $\pm$ 3.64	0.43	0.45	-2.67	3.53
		University		1.82	0.03	-0.68	4.32
		Religious		-2.54	1.00	-6.75	1.68
		Others		-2.79	1.00	-9.41	3.83
	Secondary	Illiterate		0.53	1.00	-3.30	4.36
		Primary		-2.86	0.45	-7.23	1.52
		Matric	10.78 $\pm$ 3.87	-0.43	1.00	-3.53	2.67
		University		1.39	0.66	-1.14	3.92
		Religious		-2.97	0.36	-7.20	1.26
		Others		-3.22	0.78	-9.85	3.41
	University	Illiterate		-0.86	0.99	-4.22	2.50
		Primary		-4.24	0.03	-8.21	-0.28
		Matric	9.39 $\pm$ 4.58	-1.82	0.32	-4.32	0.68
		Secondary		-1.39	0.66	-3.92	1.14
Religious			-4.36	0.01	-8.17	-0.54	
Others			-4.61	0.33	-10.98	1.77	
Religious	Illiterate		3.50	0.31	-1.28	8.28	
	Primary		0.11	1.00	-5.11	5.33	
	Matric	13.75 $\pm$ 3.84	2.54	0.55	-1.68	6.75	
	Secondary		2.97	0.36	-1.26	7.20	
	University		4.36	0.01	0.54	8.17	
	Others		-0.25	1.00	-7.47	6.97	
Others	Illiterate		3.75	0.68	-3.24	10.74	
	Primary		0.36	1.00	-6.94	7.66	
	Matric	14.00 $\pm$ 4.08	2.79	0.87	-3.83	9.41	
	Secondary		3.22	0.78	-3.41	9.85	
	University		4.61	0.33	-1.77	10.98	
	Others		0.25	1.00	-9.97	7.47	

TABLE 3: Continued.

		Education level of patients			95% confidence interval of the difference		
		Mean score $\pm$ standard deviation <sup>b</sup>	Mean difference	Sig. ( <i>p</i> value) <sup>a</sup>	Lower	Upper	
Depression	Illiterate	Primary		-4.37	0.16	-9.53	0.79
		Matric		-2.61	0.46	-6.62	1.40
		Secondary	8.81 $\pm$ 3.89	-2.53	0.50	-6.56	1.50
		University		-0.31	1.00	-3.85	3.24
		Religious		-5.52	0.21	-10.55	-0.49
		Others		-5.19	0.36	-12.55	2.18
	Primary	Primary		4.37	0.16	-0.79	9.53
		Matric		1.76	0.91	-2.83	6.34
		Secondary	13.18 $\pm$ 5.34	1.84	0.90	-2.77	6.44
		University		4.06	0.06	-0.12	8.24
		Religious		-1.15	1.00	-6.65	4.35
		Others		-0.82	1.00	-8.51	6.87
	Matric	Illiterate		2.61	0.46	-1.40	6.62
		Primary		-1.76	0.91	-6.34	2.83
		Secondary	11.42 $\pm$ 4.81	0.08	1.00	-3.19	3.35
		University		2.31	0.13	-0.33	4.94
		Religious		2.91	0.45	-7.35	1.53
		Others		-2.58	0.93	9.55	4.40
	Secondary	Illiterate		2.53	503.00	1.50	6.56
		Primary		-1.84	0.90	-6.44	2.77
		Matric	11.34 $\pm$ 3.74	0.80	1.00	-3.35	3.19
		University		2.23	1.71	-0.44	4.89
		Religious		-2.99	0.42	-7.45	1.47
		Others		-2.66	0.92	-9.64	4.33
University	Illiterate		0.31	1.00	-3.24	3.85	
	Primary		-4.06	0.63	-8.24	0.12	
	Matric	9.12 $\pm$ 4.47	-2.31	0.13	-4.94	0.33	
	Secondary		-2.23	0.17	-4.89	0.44	
	Religious		-5.22	0.00	-9.24	-1.20	
	Others		-4.88	0.32	-11.60	1.83	
Religious	Illiterate		5.52	0.21	0.49	10.55	
	Primary		1.15	1.00	-4.35	6.65	
	Matric	14.33 $\pm$ 4.05	2.91	0.45	-1.53	7.35	
	Secondary		2.99	0.42	-1.47	7.45	
	University		5.22	0.00	1.20	9.24	
	Others		0.33	1.00	-7.27	7.94	
Others	Illiterate		5.19	0.36	-2.18	12.55	
	Primary		0.82	1.00	-6.87	8.51	
	Matric	14.00 $\pm$ 5.29	2.58	0.93	-4.40	9.55	
	Secondary		2.57	0.92	-4.33	9.64	
	University		4.88	0.32	-1.83	11.60	
	Religious		-0.33	1.00	-7.94	7.27	

<sup>a</sup>*t*-test. <sup>b</sup>ANOVA. SD = standard deviation. Note: *t*-test and ANOVA were applied to find the association between the education level of dengue patients and depression, anxiety, and stress in them.

TABLE 4: Association of the disease status of the patient at the time of data collection with Depression, Anxiety, and Stress Scale 21.

	Disease onset and time status		Mean score $\pm$ SD <sup>b</sup>	Mean difference <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	95% confidence interval	
						Lower	Upper
Stress	Still suffering	One month ago	10.95 $\pm$ 4.15	0.77	0.48	0.79	2.33
		Within 3 months		1.55	0.54	-1.92	5.02
	One month ago	Still suffering	10.18 $\pm$ 4.26	-0.77	0.48	-2.33	0.79
		Within 3 months		0.78	0.84	-2.55	4.12
	Within 3 months	Still suffering	9.40 $\pm$ 5.28	-1.55	0.54	-5.02	1.92
		One month ago		-0.78	0.84	-4.12	2.55
Anxiety	Still suffering	One month ago	11.29 $\pm$ 3.94	1.04	0.27	-0.54	2.61
		Within 3 months		2.49	0.22	-1.01	5.99
	One month ago	Still suffering	10.26 $\pm$ 4.50	-1.04	0.27	-2.61	0.54
		Within 3 months		-1.46	0.56	-1.91	4.82
	Within 3 months	Still suffering	8.80 $\pm$ 4.71	-2.49	0.22	-5.99	1.01
		One month ago		-1.46	0.56	-4.82	1.91
Depression	Still suffering	One month ago	11.00 $\pm$ 4.55	-0.86	0.45	-0.83	2.55
		Within 3 months		1.30	0.69	-2.46	5.06
	One month ago	Still suffering	10.14 $\pm$ 4.63	-0.86	0.45	-2.55	2.83
		Within 3 months		0.43	0.95	-3.17	4.05
	Within three months	Still suffering	9.70 $\pm$ 6.00	-1.30	0.69	-5.06	2.46
		One month ago		-0.43	0.95	-4.05	3.17

<sup>a</sup>t-test. <sup>b</sup>ANOVA. SD = standard deviation. Note: t-test and ANOVA were applied to find the association between time and onset status disease of dengue patients and depression, anxiety, and stress in them.

monsoon as well as summer. The severity of this disease is seen in almost 96 million of the 136 million reported cases worldwide. In November 2021, the number of cases reported in Pakistan exceeded 25,000. Dengue has become endemic in our country. Based on symptom severity, there are three types of dengue fever. The first one is acute dengue fever. The initial temperature of this type ranges from 102 degrees to 105 degrees. The duration of infection lasts from two days to seven days. There is also intense pruritus and desquamation of disease. Other symptoms of acute dengue fever include bradycardia. The second type, DHF, is less prevalent but more severe, affecting the age under 15 years. However, adults are at equal risk of acquiring this stage. Platelet counts less than 100,000/mm<sup>3</sup> lead to thrombocytopenia. Despite its limited cases, the DHF classification has proved to be useful for evolving important findings on disease pathogenesis. If the patient with DHF experiences low blood pressure, then the patient has acquired DSS concurrently. The threatening signs of progression to severe dengue are present in the delayed stage of febrile phase around the time of effervescence. This phase includes severe abdominal pain, difficulty breathing, fluid accumulation, continuous vomiting, mucosal bleeding, lethargy/restlessness, liver enlargement, postural hypotension, and progressive increase in haematocrit, a condition in which there is a sudden upsurge in RBCs.

Depression, stress, and anxiety are prevailing in Pakistan. A large population faces many serious challenges as well as difficulties in their daily lives due to these mental disorders, consequently affecting their quality of life. According to the study, the prevalence of depression and anxiety in Pakistan

is reported to be in the range of 30% to 50%. This is higher among the adults when the sample size was 2401. In women, the point of prevalence of anxiety and depression was also reported as 45.5% [13]. Among male participants, there were 21.7% suffered from depression and anxiety.

Stress, depression, and anxiety depend upon many factors. There are many studies present that relate dengue infection to stress, anxiety, and depression. In DASS 21, The score of each scale for a patient is multiplied by 2 to obtain the final score. For the depression scale, score 0-9 indicates normal, 10-13 mild, 14-20 moderate, 21-27 severe, and extremely severe degree for the score 28 or above. The 0-7 score for a respondent indicates normal, 8-9 mild, 10-14 moderate, 15-19 severe, and extremely severe degree of anxiety for the score 20 or above. For the stress scale, 0-14 indicates normal, 15-18 mild, 19-25 moderate, 26-33 severe, and an extremely severe degree for score 34 or above. In a previous study, a significant association was determined with the severity of symptoms of DF (headache, fever, myalgia, arthralgia, and retroorbital pain), anxiety, and depression [18]. The depression and anxiety scores were more in patients with an average platelet count less than 30,000. Meanwhile, in our study, no such significant association in stress, anxiety, or depression levels was found with variability in average platelet count or average WBC count. Apart from this, patients with severe fever for most of the days had a statistically significant difference in their anxiety levels than the patients who had mild fever for most of the days during the infection period ( $p$  value = 0.04 and mean difference = 2.25). Similarly, the depression level was also significantly different



TABLE 5: Association of pain intensity in dengue patients with Depression, Anxiety, and Stress Scale 21.

Level of pain			Mean $\pm$ SD <sup>b</sup>	Mean difference <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	95% confidence interval	
						Lower	Upper
Stress	Mild or no pain	Moderate	8.40 $\pm$ 3.97	-1.34	0.39	-3.77	1.08
		Severe		-2.37	0.05	-4.70	-0.04
	Moderate	Mild or no pain	10.28 $\pm$ 4.28	1.34	0.39	-1.08	3.77
		Severe		-1.03	0.30	-2.66	0.60
	Severe	Mild or no pain	10.79 $\pm$ 4.31	2.37	0.05	0.04	4.70
		Moderate		1.03	0.30	-0.60	2.66
Anxiety	Mild or no pain	Moderate	8.32 $\pm$ 4.31	-2.09	0.31	-5.45	1.27
		Severe		-1.84	0.15	-4.17	0.49
	Moderate	Mild or no pain	10.06 $\pm$ 3.32	2.09	0.31	-1.27	5.45
		Severe		0.25	0.98	-2.45	2.94
	Severe	Mild or no pain	10.95 $\pm$ 4.46	1.84	0.15	-0.49	4.17
		Moderate		-0.25	0.98	-2.94	2.45
Depression	Mild or no pain	Moderate	8.80 $\pm$ 4.74	0.77	0.48	-0.79	2.33
		Severe		1.55	0.54	-1.92	5.02
	Moderate	Mild or no pain	10.89 $\pm$ 4.06	-0.77	0.48	-2.33	0.79
		Severe		0.78	0.84	-2.55	4.12
	Severe	Mild or no pain	10.64 $\pm$ 4.63	-1.55	0.54	-5.02	1.92
		Moderate		-0.78	0.84	-4.12	2.55

<sup>a</sup>t-test. <sup>b</sup>ANOVA. SD = standard deviation. Note: t-test and ANOVA were applied to find the association between the level of pain in dengue patients and depression, anxiety, and stress in them.

TABLE 6: Association of average fever in dengue patients with Depression, Anxiety, and Stress Scale 21.

Average fever			Mean $\pm$ SD <sup>b</sup>	Mean difference <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	95% confidence interval	
						Lower	Upper
Stress	Mild	Moderate	8.96 $\pm$ 4.44	-1.37	0.32	-3.62	0.88
		Severe		-2.05	0.07	-4.21	0.11
	Moderate	Mild	10.33 $\pm$ 4.46	1.37	0.32	-0.88	3.62
		Severe		-0.68	0.54	-2.19	0.84
	Severe	Mild	10.91 $\pm$ 4.17	2.05	0.07	-0.11	4.21
		Moderate		0.68	0.54	-0.84	2.19
Anxiety	Mild	Moderate	9.11 $\pm$ 4.26	-0.94	0.59	-3.21	1.32
		Severe		-2.25	0.04	-4.43	-0.08
	Moderate	Mild	10.05 $\pm$ 4.28	0.94	0.59	-1.32	3.21
		Severe		-1.31	0.11	-2.83	0.21
	Severe	Mild	11.26 $\pm$ 4.39	2.25	0.04	0.08	4.43
		Moderate		1.31	0.11	-0.21	2.83
Depression	Mild	Moderate	8.78 $\pm$ 4.71	-1.13	0.39	-3.77	1.08
		Severe		-2.37	0.05	-4.70	-0.04
	Moderate	Mild	10.12 $\pm$ 4.63	1.34	0.39	-1.08	3.77
		Severe		-1.03	0.30	-2.66	0.60
	Severe	Mild	11.05 $\pm$ 4.62	2.37	0.05	0.04	4.70
		Moderate		1.03	0.30	-0.60	2.66

<sup>a</sup>t-test. <sup>b</sup>ANOVA. SD = standard deviation. Note: t-test and ANOVA were applied to find the association between the average fever of dengue patients and depression, anxiety, and stress in them.

TABLE 7: Association of average white blood cell count with Depression, Anxiety, and Stress Scale 21.

	Average WBC count	N	Mean $\pm$ SD <sup>b</sup>	t value <sup>a</sup>	Degree of freedom <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	Mean difference (CI 95%)
Stress	Less than or equal to 4500	107.00	10.36 $\pm$ 4.47	-0.62	205.00	0.54	-0.37 (-1.54-0.81)
	More than 4500	100.00	10.73 $\pm$ 4.05	-0.62	204.80	0.54	-0.37 (-1.53-0.80)
Anxiety	Less than or equal to 4500	107.00	10.53 $\pm$ 4.59	-0.35	205.00	0.73	-0.21 (-1.39-0.98)
	More than 4500	100.00	10.74 $\pm$ 4.00	-0.34	204.01	0.73	-0.21 (-1.39-0.97)
Depression	Less than or equal to 4500	107.00	10.46 $\pm$ 4.54	-0.61	205.00	0.87	-0.10 (-1.36-1.16)
	More than 4500	100	10.56 $\pm$ 4.65	-0.16	203.28	0.87	-0.10 (-1.36-1.16)

<sup>a</sup>t-test. <sup>b</sup>ANOVA. SD = standard deviation; N = number of responses for the specific variable. Note: t-test and ANOVA were applied to find the association between the average white blood cell count of dengue patients and depression, anxiety, and stress in them.

TABLE 8: Association of average platelet count with Depression, Anxiety, and Stress Scale 21.

	Average platelet count	N	Mean $\pm$ SD <sup>b</sup>	t value <sup>a</sup>	Degree of freedom <sup>a</sup>	Level of significance (2 tailed) <sup>a</sup>	Mean difference (CI 95%)
Stress	More than 300,000	136.00	10.75 $\pm$ 4.174	1.07	204.00	0.29	0.68 (-0.57-1.93)
	Less than 300,000	70.00	10.07 $\pm$ 4.553	1.04	129.22	0.30	0.68 (-0.61-1.97)
Anxiety	More than 300,000	136.00	10.91 $\pm$ 4.242	1.35	204.00	0.18	0.86 (-0.40-2.11)
	Less than 300,000	70.00	10.06 $\pm$ 4.459	1.33	133.45	0.19	0.86 (-0.42-2.13)
Depression	More than 300,000	136.00	10.74 $\pm$ 4.456	1.11	204.00	0.27	0.75 (-0.58-2.08)
	Less than 300,000	70.00	9.99 $\pm$ 4.868	1.08	129.08	0.28	0.75 (-0.63-2.13)

<sup>a</sup>t-test. <sup>b</sup>ANOVA. SD = standard deviation. Note: t-test and ANOVA were applied to find the association between the average platelet count of dengue patients and depression, anxiety, and stress in them.

between both of these groups ( $p$  value = 0.05 and mean difference = 2.37). This can be due to the cytokine rise in infection-associated fever.

The severity of pain also seems to affect stress levels in dengue patients. Patients with severe pain had a significant difference in their stress levels than those with mild or no pain ( $p$  value = 0.05). These findings can be explained by the fact that pain and fever often cause a person to feel irritated and hopeless, making them susceptible to feeling anxious and stressed. It is supported by evidence that during a viral infection, the activation of the peripheral immune system disrupts the communication between the immune system and brain, leading to some behavioural and cognitive changes. During infection, proinflammatory cytokines like TNF-alpha and cytokines 44 and 6 are released, which may also explain the symptoms of stress, depression, and anxiety [18].

We found an observable pattern of significant differences in anxiety, depression, and stress levels in patients aged 39-49 compared to the age group 18-28 and 50 plus years. There were similar findings in the research conducted in the Philippines [23]. Advancement in age can cause a person to be more prone to a flood of misinformation and fixed perceptions about his disease. It may be the reason for the increased anxiety level. Prolonged inactivity, hospitalization, etc. hinder normal day-to-day activities, and absence from job or workplace leads to stress. The older people may have seen a larger community suffering from the same disease in even the worst scenarios. Feeling like these situations increases depression in older

patients. These facts are evident in our study as the highest degree of association of stress, anxiety, and depression with age was found in the age group 39-49 ( $N = 44$ ). Dengue fever-associated anxiety was more in patients of primary level and matric level education than that in university-educated patients ( $p$  value = 0.03 with a confidence interval of 95%). This can be attributed to the lack of understanding of the subjects of the disease due to a supposed lack of education, which could have led them to feel dystopian about this whole situation.

Multiple cases of mental instability associated with the acute and convalescent phase of dengue infection have been observed. The whole mechanism behind this occurrence is poorly understood, but there has been evidence that a cytokine upheaval occurs during this infection [24]. This may lead to anomalous behaviour which includes irritability, mood swings, feeling uncertain, self-doubts, and a feeling of imminent doom and sadness. Not only do these affect a person's mental state, but also physical health is affected by it. For instance, we observed that many subjects complained of having a dry mouth, palpitations, and tachypnoea, which could be caused by anxiety or stress, and being optimistic about the future was difficult for them while suffering from this disease. It was also evident from proposed etiopathogenesis that epigenetic mechanisms were involved in it. For instance, overexpression of the HDAC enzyme could be the reason behind it [15]. For treatment, the patient must refer to a psychiatrist for proper evaluation, and if needed, the patient should be administered prescribed mood stabilizers

and antipsychotics. If left untreated, these may exacerbate to a frightening level and compromise the physical well-being of the patient too.

**4.1. Clinical Implications.** The study encourages practitioners to clinically evaluate the psychological manifestations of dengue patients. This should be added in clinical practice. Furthermore, these practices are often left neglected and least clinically focused in low- and middle-income countries. In dengue season, various public sector healthcare centres set up dengue counters for dengue infection screening. We recommend policymakers to also devise ways to psychologically evaluate each patient soon after the initial screening is done. Timely psychological support should be provided to infectious disease patients as it will profoundly improve their quality of life.

**4.2. Strength and Limitations.** This is one of the first studies that in-depth elaborated the impact of different socio-demographic parameters and the extent of clinical symptoms on stress, anxiety, and depression in the Asian dengue population. To pave paths for future studies in this area, we discuss the various strengths and limitations of our study. Our major part of the data was from tertiary hospitals, i.e., from patients of low- or middle-income families. Future studies may include participants acquiring treatment from private hospitals as well to see whether public hospital setting care and income are impacting the relationship between anxiety and depressive symptoms and dengue infection. The sample size was not adequate. We were able to collect data from 210 patients before the end of the dengue endemic, in 2021. Thirdly, further qualitative evaluation by a psychiatrist could evaluate the patient responses. These aspects can be worked upon in future studies to open more avenues in this area and optimize patient care.

## 5. Conclusions

The degree of association of stress, depression, and anxiety in the Asian population was found with that of dengue symptoms and sociodemographic parameters. Dengue-associated stress and anxiety depend upon many factors, but a significant association was found in fever, pain, level of education, and age. The promising results generated from statistical inference were that the difference in patient factors and disease prognosis, i.e., age, level of education, intense pain, and high-degree fever, had a significant association with stress, depression, and anxiety at various levels. It is evident from our study that different level of disease prognosis in patients with dengue infection has an important impact on mental health and can cause psychological disorders. It is needed to be evaluated clinically to optimize patient care and provide timely psychological support.

## Abbreviations

DASS-21: Depression, Anxiety, and Stress Scale 21.

## Data Availability

The data will be made available by making a reasonable request to the first author.

## Ethical Approval

The study protocol was approved by the Research Ethics Committee of the University of Veterinary and Animal Sciences, Lahore. This was an observational study and did not contain any therapeutic intervention. This study also did not involve any animals for research purposes. Patients were informed about their right to withdraw from the study any time during the interview. The participants were assured about the confidentiality of their responses and data. Interview-based data were collected from dengue patients in various public hospitals, universities, and communities.

## Consent

The written informed consent to publish the obtained information was obtained from all participants. The patients were informed about the objective and nature of the study, and their consent was taken before filling in the data.

## Conflicts of Interest

The authors declare that they have no competing interests.

## Authors' Contributions

FA conducted the design of the study, collection of data, analysis of data, interpretation of statistical analyses, filling in tables, writing of abstract, ethical approval, methods, results' interpretation, discussion, conclusions, clinical implications, and strengths and limitations. FJ conducted the questionnaire, data collection, abstract, statistical analyses, background, and formatting. NC conducted the design, background, methods, data collection, and discussion. MY conducted the questionnaire, data collection, literature review, preparation and formatting of tables, and results. SF conducted the background, data collection, discussion, and reference management. AB and TK supervised the manuscript, and all authors reviewed the manuscript.

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