ORIGINAL ARTICLE:

FREQUENCY OF DEPRESSION IN PATIENTS OF CHRONIC HEPATITIS C BEFORE STARTING TREATMENT

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Abstract:

Introduction: Pre-existing psychiatric illnesses, such as mood and psychotic disorders, are 3–4 times more common and frequently undetected in HCV patients. This could be brought on by a diminished desire to use or access mental and primary health care services, actual or imagined stigma against HCV patients, or denial of their psychiatric symptoms. Comorbid depression can impact the outcome because it is linked to decreased HCV therapy adherence.

Objectives: To quantify the prevalence of depression among Hepatitis C patients not receiving treatment.

Study Design: This was a cross-sectional study.

Setting: Medical Department, Faisalabad Medical University and affiliated Allied Hospital, Faisalabad.

Study duration: 30th December 2021 to 29th June 2022.

Methods: A total of 310 patients having Hepatitis C infection, with an age range of 20 years to 60 years, were included, while the patients suffering from an additional underlying chronic medical disease like CKD, COPD, and diabetes, which can cause depression, were excluded. Demographic data, including age, gender, residence (rural or urban), education of patient (Primary, middle or higher education), marital status (single, married or separated), income of patient and duration of Hepatitis C infection were recorded. The researcher interviewed the selected patients by using Beck Depression Inventory.

Results: The study's age ranged from 20 to 60 years, with a mean age of 41.75 + 8.62. Most 163 patients (52.58%) were in the 20–40 age range. 166 (53.55%) of the 310 patients were men, and 144 (46.45%) were women, for a male-to-female ratio of 1.2:1. In our study,

the frequency of depression in patients with Hepatitis C infection not receiving any treatment was found in 187 (60.32%) patients.

Conclusion: The conclusion of the study is that the frequency of depression in patients suffering from Hepatitis C infection not receiving any treatment is very high.

Keywords: hepatitis C, depression, Beck Depression Inventory.

INTRODUCTION:

The Flaviviridae family includes the Hepatitis C virus. The genome of the HCV virion is a single-stranded positive RNA. [1] It has numerous subtypes and six genotypes. Worldwide, 175 million HCV patients are or 3% of the world's population. [2] The highest incidence rate has been discovered in Egypt (15–20%)[3], while the United Kingdom has the lowest occurrence (0.01-0.1%). [3] Hepatitis C infection is present in 25% of people with hepatocellular carcinoma and 27% of people with cirrhosis, according to estimates. [4] Hepatitis C (HCV), which has a significant morbidity and mortality rate in Pakistan, is present in more than 10 million persons in the Pakistani population. [5]

Unsterilised sharp objects or needle stick injuries, blood and blood products transfusion, and tattooing are risk factors for spreading the hepatitis C virus. The possibilities of contribution from sexual and perinatal transmission have been estimated to be close to 5%. The other modes of spread are vertical transmission and sexual transmission. [6] Previous research revealed that the use of non-disposable needles for frequent medical parenteral injections was strongly linked to HCV seropositivity and that the majority of people who tested positive for the anti-HCV did not have a history of blood transfusions.

Hepatitis C is one of the most widespread causes of chronic liver disease worldwide. [7] There are an estimated 71 million chronic hepatitis C infections worldwide. Those who get chronic hepatitis C infection run a 15%–20% chance of developing liver cirrhosis within 20 years. [8] According to the World Health Organisation, the Eastern Mediterranean and European regions, with 2.3% and 1.5% prevalence rates, respectively, are the most effective regions. [7] In Pakistan, which has a population of 190 million people, the hepatitis C virus has infected about 10 million people. [9]

Cirrhosis, hepatocellular carcinoma (HCC), and end-stage liver disease requiring liver transplantation are the most common outcomes of chronic hepatitis C. [10] A considerable global disease burden is a result of both rising mortality and morbidity from HCV-related advanced liver illnesses as well as patient-reported outcomes, such as quality of life or mental health status. [11]

Pre-existing psychiatric illnesses, such as mood and psychotic disorders, are 3–4 times more common and frequently go undetected in HCV patients. This could be brought on by a diminished desire to use or access mental and primary health care services, actual or imagined stigma against HCV patients, or denial of their psychiatric symptoms. As comorbid depression is linked to decreased adherence to HCV medication, it can impact prognosis. Between 20 and 50% of HCV patients report having depression, compared to

10% of the general population. [12]

Before beginning treatment, 264 Hepatitis C patients were enrolled in a local study [13] in Karachi. The subjects' average ages ranged from 17 to 71 and mean age was 39.82 ± 10.6121 years. 127 (48.1%) were men, and 223 (84.5%) were married. Hepatitis C was present for an average of 3.665 2.445 (0.1 to 12) years. 191 (72.3%) of the participants had depression.

The rationale of this study was to find the prevalence of depression in those patients with Hepatitis C who have not given any treatment yet (pretreatment prevalence in hepatitis C patients). Seeing the magnitude of the disease will help us find the burden of the disease and make policy for routine psychiatry evaluation in all patients of Hepatitis C infection before starting treatment. Without addressing depression, physicians cannot complete the treatment of chronic disease. Depression results in poor compliance and poor outcomes of medical treatment. Finding the frequency of depression and treating the undiagnosed depression will help improve the quality of life in patients suffering from Hepatitis C infection.

METHODS:

THE STUDY DESIGN:

It was a Descriptive, Cross-sectional study.

SETTING:

Medical Department, Faisalabad Medical University and affiliated Allied Hospital, Faisalabad.

OPERTATIONAL DEFINITION.

Hepatitis C infection: Hepatitis C infection is defined as patient having positive ELISA report anti HCV antibodies.

Depression: Depression is operationally defined as symptoms meeting the Beck's Depression Inventory. (Performa will be filled for the selected sample in urdu language).

DURATION OF THE STUDY:

30th December 2021 to 29th June 2022.

SAMPLE SIZE:

It was calculated using the WHO sample size calculator,

P = 72.3%[3]

Confidence Interval = 95%

Absolute precision required = 5%

Sample size = 310 patients

SAMPLE TECHNIQUE:

It was non-probability, consecutive sampling.

SAMPLE SELECTION:

a. Inclusion Criteria:

- Patients of both gender
- Patients aged 20 to 60 years.
- Patients were suffering from Hepatitis C infection as per the operational definition.

b. Exclusion Criteria:

- Already diagnosed cases of depression (Determined on medical record)
- Patients with underlying chronic diseases like CKD, COPD and diabetes can cause depression. (Determined by medical history).

DATA COLLECTION PROCEDURE:

After the approval from the hospital's ethical review committee, via letter No.F.4ERC/FMU/2020-21/, 310 patients with Hepatitis C infection were enrolled on OPD of the Medical Unit of Allied Hospital Faisalabad. Patients were enrolled after matching the inclusion and exclusion criteria. Written informed consent was taken from patients or guardians. Demographic data, including age, gender, residence (rural or urban), education of patient (Primary, middle, or higher education), marital status (single, married or separated), income of patient and duration of Hepatitis C infection were recorded. The researcher interviewed the selected patients by using the Beck Depression Inventory[4].

All the pieces of information were collected on specially designed proforma. Patients with depression were treated as per hospital protocols.

DATA ANALYSIS PROCEDURE:

All the data was entered in SPSS V-23. The mean and standard deviation were calculated for all quantitative variables like age, duration of disease and Beck Depression Inventory score. Frequency and percentage were calculated for all qualitative variables like gender, income status, educational level, residence status and depression.

Effect modifiers like age, gender, duration of disease, educational status, residence status, income and marital status were controlled by stratification. Post-stratification chi-square test was applied, and a P-value ≤ 0.05 was taken as significant.

RESULTS:

The age range in this study was from 20 to 60 years, with a mean age of 41.75 ± 8.62 years. Most of the patients, 163 (52.58%), were between 20 to 40 years of age, as shown in Table I.

Of 310 patients, 166 (53.55%) were male, and 144 (46.45%) were females, with a male-to-female ratio of 1.2:1, as shown in Figure I. Our study's mean disease duration was 5.84 ± 2.16 years, as shown in Table I. The distribution of patients according to place of living is shown in Table I. The distribution of patients according to education, income & marital status is shown in Table II.

In our study, the frequency of depression in patients with Hepatitis C infection not receiving any treatment was found in 187 (60.32%) patients (Figure II).

Stratification of depression concerning age groups and gender & duration of illness is shown in Table III. Tables IV shows the stratification of depression concerning the income, education & marital status. The stratification of depression for residence is shown in Table V.

Table 1: Distribution of patients according to age, duration of disease, place of living, education, income, and marital status. (N=310 each group)

Age in year	No. of patients	%	Duration of disease (years)	No. of patients	%	Place of living	No. of patients	%
20-40	163	52.58	>5	177	57.10	Rural	110	35.48
41-60	147	47.42	<5	133	42.90	urban	200	64.52
Mean ± SD = 41.75 ± 8.62 years			Mean ± SD = 5.84 ± 2.16 years					

Table 1I: Distribution of patients according, education, income, and marital status, (N=310 each group)

Education	No. of patients	%	Income status	No. of patients	%	Marital status	No. of patients	%
Primary	50	61.13	Lower	98	31.61	Unmarried	66	21.29
Middle	128	41.29	Middle	138	44.52	Married	224	72.26
Higher	132	42.58	Affording	74	23.87	Separated	20	6.45

Table III: Stratification of depression concerning age group, gender, duration off illness.

Age	Depression		Gender	Depression		Duration	Depression	
	Yes	No		Yes	No		Yes	No
20-40	99 (60.4%)	65 (39.26%)	Male	112 (67.47%)	54 (32.53%)	>5 years	100 (56.50%)	77 (43.50%)
41-60	89 (60.54%)	58 (39.46%)	Female	75 (52.08%)	69 (47.92%)	<5 years	87 (65.41%)	46 (34.59%)
p-value	**0.974**		**p-value**	**0.006**		**p-value**	**0.112**	

Table IV: Stratification of depression concerning income, education, marital status.

Income	**Depression**		**Education**	**Depression**		**Marital status**	**Depression**	
	Yes	No		Yes	No		Yes	No
Lower	62 (63.27%)	39 (35.45%)	Primary	32 (64.0%)	18 (36.0%)	Unmarried	45 (68.18%)	21 (31.82%)
Middle	82 (559.42%)	84 (42.0%)	Middle	75 (58.59%)	53 (41.41%)	Married	130 (58.04%)	94 (41.96%)
Affording	43(58.11%)	31 (41.89%)	Higher	80 (60.61%)	52 (39.39%)	Separated	12 (60.0%)	08 (40.0%)
p-value	**0.758**		**p-value**	**0.799**		**p-value**	**0.334**	

Figure I: Distribution of patients according to gender (n=310).

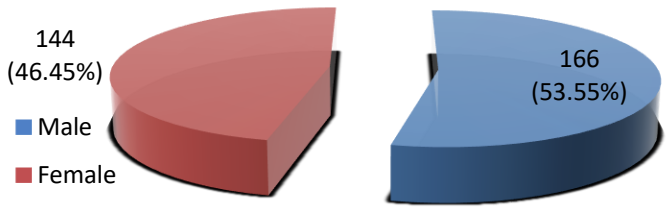

Figure II: Frequency of depression in patients of Hepatitis C infection not receiving any treatment (n=310).

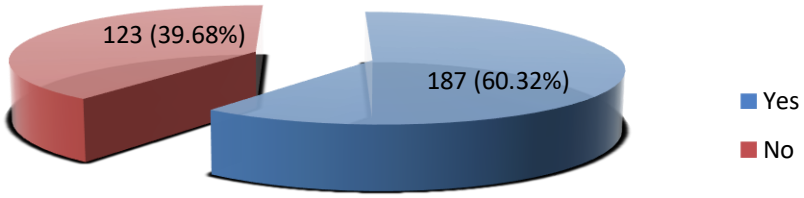

Table V: Stratification of depression concerning residence.

Residence	Depression		p-value
	Yes	No	
Rural	71 (64.55%)	39 (35.45%)	**0.259**
Urban	116 (58.0%)	84 (42.0%)	

DISCUSSION:

A frequent mental disorder and the main contributor to disability globally is depression [5]. Major depression has been linked to long-term hepatitis C (HCV) exposure and prior interferon-alpha antiviral therapy. [6,7] In over 80% of instances, HCV infection results in chronic hepatitis C (CHC), and in one in five people within 20 to 50 years of the initial condition, liver cirrhosis; of these, 5 to 10% will develop hepatocellular carcinoma or decompensated liver disease. [5] It is now known that chronic hepatitis C (CHC) is a systemic illness with a wide range of extrahepatic symptoms, such as anhedonia, lethargy, irritability, anxiety, sleeplessness, and heightened pain sensitivity. [9] There is proof that HCV directly invades the brain [10] and that the immune system has been chronically stimulated. [11] These elements may work in conjunction with several neuronal pathways, neurotransmission, and neurotrophic mechanisms to cause neuropsychiatric symptoms in CHC.[6,7]

To ascertain the prevalence of depression in Hepatitis C patients who are not receiving therapy, we did this study. The study's participants ranged in age from 20 to 60, with a mean age of 41.75 + 8.62 years. 163 (52.58%) of the patients, or the majority, were in the 20–40 age range. 166 (53.55%) of the 310 patients were men, and 144 (46.45%) were women, for a male-to-female ratio of 1.2:1. In our study, 187 patients (60.32%) with hepatitis C infection who were not receiving therapy frequently experienced depression. Before beginning treatment, 264 Hepatitis C patients from Karachi were included in a local study [3]. The subjects' average ages ranged from 17 to 71 and were 39.82 10.6121 years. 127 (48.1%) were men, and 223 (84.5%) were married. Hepatitis C was present for an average of 3.665 2.445 (0.1 to 12) years. 191 (72.3%) of the participants had depression.

In a substantial American cohort (n=4,781) with prior history of intravenous drug use (IVDU) in 51.4%, the prevalence of depression in chronic HCV-infected patients was reported to be 29.7%, which is higher than the 9% prevalence in the general population using the personal health questionnaire (PHQ-8) with a cutoff score of 10,[14]which was consistent with the findings of the other studies. [8,9] In contrast to chronic hepatitis B, chronic hepatitis C (CHC) was independently related to depression, according to data from the National Health and Nutrition Examination Survey (2005–2010, n=10,231). Major

depressive disorder occurred in 11.4% of HCV patients, with a 54.6% prevalence of depression, according to the Patient Health Questionnaire (PHQ-9). [10–14] Among Australian CHC patients (n=395), the Hospital Anxiety and Depression Scale (HADS-D 8) depression prevalence was 27%, which is 2.4 times higher than community norms and linked with single status. [15] In a nationwide survey carried out in Japan, 7.1% of patients reported having depression. Even though a substantial prevalence (51.6%) of depression by Beck depression inventory (BDI-II) was identified in 67 Chinese IVDUs, there are data on the majority of depression in CHC patients from Asian countries. [16]

One hundred thirty-five individuals with chronic hepatitis C and 76 patients with chronic hepatitis B were assessed for major depressive disorder by Mauro G. Carta et al. [17]. When compared to chronic hepatitis B and the control group, they found that major depressive disorder was more common in people with chronic hepatitis C. Ultimately, interferon therapy did not affect the association between chronic hepatitis C and major depressive disorder (based on international diagnostic criteria). This could be due to fewer therapeutic alternatives, increased social anxiety, and an unremarkable outlook for chronic hepatitis C, which together increase the prevalence of depression. [17,18]

There is a considerable range in the commonness of depression among Hepatitis C patients. Compared to the general population (6–10%), it ranges from roughly 24–70%[19]. The wide variety of prevalence estimates made by various studies may be due to the complexity of the disease itself, the racial and population makeup of the study participants, and other factors related to depression and anxiety. According to Kenny-Walsh, 376 Irish women who had contracted iatrogenic hepatitis C had a 16% prevalence of sad mood documented in their medical records. [20] In 500 patients evaluated at a tertiary referral center, a majority of 24% were diagnosed with depression, according to Lee et al. Using a standardized psychiatric interview, Dwight et al. discovered a 28% frequency in 50 individuals. [21]

Uncertain factors may be at play in the increased rate of depression among hepatitis C patients. However, it has been hypothesized that several factors may be at play, including disease characteristics, such as changes in brain metabolites as shown by dynamic brain imaging and unpredictable, inconsistent, and complex disease progression. The reasons for depression in this population have also lately been linked to affective variables, stigma perception, and the involvement of platelet 5-HT. [22] As seen in numerous studies in Pakistan, where the prevalence of depression is twice as high in female patients compared to male patients, gender differences also play a crucial role. [23-25]. However, this study's HCV patients did not exhibit this gender disparity.

CONCLUSION:

This study concluded that the frequency of depression in patients with Hepatitis C infection not receiving any treatment is very high. So, we recommend that in every patient with hepatitis C, depression should be considered, and its early recognition and management should be done to reduce the community's morbidity.

Conflict of interest

It is educational research, and there is no intervention of any kind, and researchers have no conflict of interest.

References:

1. Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C virus in Pakistan: A systematic review of prevalence, genotypes and risk factors. World J Gastroenterol [Internet]. 2009 Dec 12 [cited 2023 Aug 19];15(45):5647. Available from: /pmc/articles/PMC2789216/
2. Umer M, Iqbal M. Hepatitis C virus prevalence and genotype distribution in Pakistan: Comprehensive review of recent data. World J Gastroenterol. 2016 Jan 28;22(4):1684–700.
3. Bhutto AR, Jatt MI, Rafi S, Washdev W, Arsalan M, Ullah A. FREQUENCY OF ANXIETY AND DEPRESSION IN CHRONIC HEPATITIS C PATIENTS VISITING A TERTIARY CARE HOSPITAL AT GADAP TOWN, KARACHI. J Postgrad Med Inst [Internet]. 2019 Oct 10 [cited 2023 Aug 19];33(2). Available from: https://jpmi.org.pk/index.php/jpmi/article/view/2447
4. Carepatron [Internet]. [cited 2023 Sep 3]. Available from: https://app.carepatron.com/Onboarding?redirect=?type=admin&isBusiness=true&type=admin&isBusiness=true
5. WHO. Epidemiological update: increasing mortality calls for action 03. Glob Hepat report, 2017. 2017;7–20.
6. Oriolo G, Egmond E, Mariño Z, Cavero M, Navines R, Zamarrenho L, et al. Systematic review with meta-analysis: neuroimaging in hepatitis C chronic infection. Aliment Pharmacol Ther [Internet]. 2018 May 1 [cited 2023 Aug 19];47(9):1238–52. Available from: https://pubmed.ncbi.nlm.nih.gov/29536563/
7. Yarlott L, Heald E, Forton D. Hepatitis C virus infection, and neurological and psychiatric disorders - A review. J Adv Res [Internet]. 2017 Mar 1 [cited 2023 Aug 19];8(2):139–48. Available from: https://pubmed.ncbi.nlm.nih.gov/28149649/
8. Ashraf S, Ahmad A. Viral hepatitis in Pakistan: challenges and priorities. Asian Pac J Trop Biomed. 2015 Mar 1;5(3):190–1.
9. Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C virus in Pakistan: A systematic review of prevalence, genotypes and risk factors. World J Gastroenterol [Internet]. 2009 Dec 12 [cited 2023 Sep 3];15(45):5647. Available from: /pmc/articles/PMC2789216/
10. Lee K, Otgonsuren M, Younoszai Z, Mir HM, Younossi ZM. Association of chronic liver disease with depression: a population-based study. Psychosomatics [Internet]. 2013 Jan [cited 2023 Aug 19];54(1):52–9. Available from: https://pubmed.ncbi.nlm.nih.gov/23295007/
11. ElSerag HB, Kunik M, Richardson P, Rabeneck L. Psychiatric disorders among veterans with hepatitis C infection. Gastroenterology [Internet]. 2002 [cited 2023 Aug 19];123(2):476–82. Available from: https://pubmed.ncbi.nlm.nih.gov/12145801/
12. Fireman M, Indest DW, Blackwell A, Whitehead AJ, Hauser P. Addressing tri-morbidity (hepatitis C, psychiatric disorders, and substance use): the importance of routine mental health screening as a component of a comanagement model of care. Clin Infect Dis

[Internet]. 2005 Apr 15 [cited 2023 Aug 19];40 Suppl 5(SUPPL. 5). Available from: https://pubmed.ncbi.nlm.nih.gov/15768336/

13. Evon DM, Ramcharran D, Belle SH, Terrault NA, Fontana RJ, Fried MW. Prospective analysis of depression during peginterferon and ribavirin therapy of chronic hepatitis C: results of the Virahep-C study. Am J Gastroenterol [Internet]. 2009 Dec [cited 2023 Aug 19];104(12):2949–58. Available from: https://pubmed.ncbi.nlm.nih.gov/19789525/

14. Weinstein AA, Kallman Price J, Stepanova M, Poms LW, Fang Y, Moon J, et al. Depression in patients with nonalcoholic fatty liver disease and chronic viral hepatitis B and C. Psychosomatics [Internet]. 2011 Mar [cited 2023 Aug 19];52(2):127–32. Available from: https://pubmed.ncbi.nlm.nih.gov/21397104/

15. Stewart B, Mikocka-Walus A, Morgan J, Colman A, Phelps M, Harley H, et al. Anxiety and depression in Australian chronic hepatitis C outpatients: prevalence and predictors. Australas Psychiatry [Internet]. 2012 Dec [cited 2023 Aug 19];20(6):496–500. Available from: https://pubmed.ncbi.nlm.nih.gov/23099509/

16. Wang Z, Du J, Zhao M, Page K, Xiao Z, Mandel JS. HCV infection is independently associated with depression among methadone maintenance treatment heroin users in China. Asia Pac Psychiatry [Internet]. 2013 Sep [cited 2023 Aug 19];5(3):191. Available from: /pmc/articles/PMC4513657/

17. Carta MG, Hardoy MC, Garofalo A, Pisano E, Nonnoi V, Intilla G, et al. Association of chronic hepatitis C with major depressive disorders: irrespective of interferon-alpha therapy. Clin Pract Epidemiol Ment Health [Internet]. 2007 Oct 23 [cited 2023 Aug 19];3:22. Available from: /pmc/articles/PMC2203967/

18. Kraus MR, Schafer A, Csef H, Scheurlen M, Faller H. Emotional state, coping styles, and somatic variables in patients with chronic hepatitis C. Psychosomatics [Internet]. 2000 [cited 2023 Aug 19];41(5):377–84. Available from: https://pubmed.ncbi.nlm.nih.gov/11015623/

19. Schäfer A, Wittchen HU, Seufert J, Kraus MR. Methodological approaches in the assessment of interferon-alfa-induced depression in patients with chronic hepatitis C - a critical review. Int J Methods Psychiatr Res [Internet]. 2007 [cited 2023 Aug 19];16(4):186–201. Available from: https://pubmed.ncbi.nlm.nih.gov/18188838/

20. Kenny-Walsh E. Clinical Outcomes after Hepatitis C Infection from Contaminated Anti-D Immune Globulin. N Engl J Med [Internet]. 1999 Apr 22 [cited 2023 Aug 19];340(16):1228–33. Available from: https://pubmed.ncbi.nlm.nih.gov/10210705/

21. Lee DH, Jamal H, Regenstein FG, Perrillo RP. Morbidity of chronic hepatitis C as seen in a tertiary care medical center. Dig Dis Sci [Internet]. 1997 [cited 2023 Aug 19];42(1):186–91. Available from: https://pubmed.ncbi.nlm.nih.gov/9009136/

22. Schäfer A, Scheurlen M, Seufert J, Keicher C, Weißbrich B, Rieger P, et al. Platelet serotonin (5-HT) levels in interferon-treated patients with hepatitis C and its possible association with interferon-induced depression. J Hepatol [Internet]. 2010 [cited 2023 Aug 19];52(1):10–5. Available from: https://pubmed.ncbi.nlm.nih.gov/19897271/

23. Husain N, Creed F, Tomenson B. Depression and social stress in Pakistan. Psychol Med

[Internet]. 2000 [cited 2023 Aug 19];30(2):395–402. Available from: https://pubmed.ncbi.nlm.nih.gov/10824659/

24. Quek TTC, Tam WWS, Tran BX, Zhang M, Zhang Z, Ho CSH, et al. The global prevalence of anxiety among medical students: A meta-analysis. Int J Environ Res Public Health. 2019 Aug 1;16(15).

25. Ahmed I, Banu H, Al-Fageer R, Al-Suwaidi R. Cognitive emotions: Depression and anxiety in medical students and staff. J Crit Care. 2009;24(3):e1.

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3rd Auth	Prof Dr Ahmed Bilal	Ex-Professor, Dean of Medicine, Faisalabad Medical University.	Conception of idea, data collection	
4th Auth	Dr Yasir Yaqoob	Assistant Professor Faisalabad Medical University.	Discussion write up	
5th Auth	Dr Kamran Ahmed	PGR Medicine Faisalabad Medical University.	Discussion write up	
6th Auth	Dr Ayesha Izzat	Private Clinician	Plagiarism check. Data collection.