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BRIEF REPORT

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Psychosocial status and COVID-19 outcome are significantly associated

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Abstract

Covid-19 pandemic raised both physical and mental threat to human. Globally, 607,497,755cases of infection and 6,492,948 deaths were recorded until August, 2022. The psychosocial-conditions in pre-infection-period might influence disease. Here, we delineate the impact of socio-economic status, pre- or post- Covid-19 psychosocial and other factors (lockdown/self-isolation/diagnosis)on this disease outcome. Pre-Covid mental-status (depression-anxiety, tobacco-smoking and suicide-mortality), quality-of-life (QOL) and Global-Health-Security (GHS) were correlated with total-infection and case-fatality-rate (CFR) in > 170 countries. The database of World-Health-Organization/World-Bank/United-Nations and the Johns-Hopkins-Center for Health-Security was utilized. The Student's t test, multivariate-ANOVA, correlation and linear-regression were performed. Psychological wellbeing indicators (happiness/GSH/QOL) and mental-impairments like depression-anxiety positively correlated with infection and CFR ($p < 0.05$-$p < 0.001$). The happiness-index positively associated with QOL/GSH/anxiety and depression. Higher CFR was noticed in congested/populated territories. Canonical regression strongly suggests this result. Variable host-virus interactions associated with race/ethnicity and body-composition. Positive correlations between mental state-QOL and anxiety-depression paralleled with adverse outcome of Covid-19.

Keywords Psychosocial Health, SARS-CoV-2, Depression and anxiety, QOL, CFR

Introduction

The pandemic situation generated by the novel corona virus SARS-CoV-2 (Covid-19)is still uprising with moderately significant active case number in different countries [24]. Beside the direct physiological effects due to infection, the psychological status or the mental health impact of both infected and uninfected persons cannot be underestimated. Nevertheless, the situation becomes complex for those who are suffering from addiction, substance abuse or other compulsive disorders. Different levels of hypertension, anxiety and depression are associated with stress related disorders [5]. Life uncertainties, a lack of economic progress, and job and social insecurity are the primary causes of psychological consequences. The synergistic effects of these factors are compounded during the process of isolation, lockdown or quarantine in this pandemic situation. An important aspect of everyday living is stress. The degree of stress exposure varies by nation, society, and geographical area. Over the past two years, there has been a considerable increase in stress exposure worldwide. Different psychological parameters and their normal/cut off values are available in the databases of WHO, World Bank and United Nations or others. We evaluated here the impact of pre-Covid global psychological and socio-economic status on the Covid-19 infection outcome.

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The Covid-19 is generally manifested with the typical form of fever, coughing, hypoxia and dyspnea. Several case studies revealed that psychotic and confusion-like symptoms, delirium may be the feature in Covid-19patients [4, 20]. In this pandemic scenario, individual brain patterns, or "biotypes," are also significant for their particular presentation [12]. An internist or infectious disease expert and a psychiatrist should monitor on the Covid-19 patients for greater overall protection.

The health workers should receive specific training, frequent medical check-ups and close psychological support [3]. It is noticed that psychiatric patients are more sensitive to Covid-19and the Covid-19 patients frequently develop some psychiatric symptoms [30].Some environmental and social factors are also found to influence the rate of infection. As for example, the ambient temperature and air quality are significantly associated with the spread of Covid-19 [2]. Lifestyle, food-habits and body compositions have been linked with the infection outcome and disease severity [6]. Socioeconomic status and food safety measures in different community determine the psychological status of the individuals [19]. This suggests that inter-individual variations and regional differences have interference in disease outcome. An individual's psychological and physical well-being may be negatively impacted by an imbalance in the distribution of health benefits throughout various areas. On the other hand, equitable distributions foster the growth of a community's psycho-social ties and self-confidence [9].Anxiety and despair were brought on by an unprecedented increase in infection rates and dread of contracting the disease [1]. Taken together, it can be hypothesized that human psychosocial state has significant impact on disease occurrence-severity and vice versa is also true.

Some in depth analysis suggest that extrinsic and intrinsic stresses are associated with individual's neuroendocrine and immunological status. An important investigation in '80 s decade on a large number of students demonstrated that their immunity went down every year during the examination period. They had very low count of natural killer cells, which fight tumors and viral infections. Immunity-boosting IFN-γ and T-cells responded very weakly under a stress and this state is known as lymphopenia [8].It is known that chronic stress generates very low antibody titer in response to the pneumococcal pneumonia vaccination event (Glaser et al. 2006).It is reported that the depressive symptoms are associated with a prolonged inflammatory response in an individual following influenza vaccination [10, 17]. This suggests that anti-infective and anti-inflammatory immune mechanisms are severely impaired in stressful conditions.

In this background, the objective of the present study was to explore the impact of psychosocial status, socioeconomic condition and mental health (until Dec, 2019) on the prevalence and severity of Covid-19 from 94 to 205th day of the disease. Basically, the present work was done and data were analyzed from the first wave of Covid-19 when only the Wuhan variety and no other variety of concerns (VOCs) were in the scenario. To verify the exclusive impact of the present disease variables we selected that time period, because during that period any specific drug/therapeutic measures or the vaccination procedure was not developed.

Methods

Total confirmed cases per million of population (TCCM) and total deaths per million of population (TDM)

The impact was assessed in relation to the rate of diagnosis/ Covid testing, lockdown during this time, and the concomitant psychological condition (caused by constraints, self-isolation, and quarantine). We investigated the total confirmed cases (TCC) and total deaths (TD) from Covid-19 as documented in WHO Corona virus disease (Covid-19) Situation Report–161 day [13]. According to WHO the "data as received by WHO from national authorities by 10:00 CEST, 29 June 2020" (WHO Situation Report– 161, 2020). The total estimated population as on July 2020 of the respective countries/territories/areas was collected from the Department of Economic and Social Affairs Population Dynamics of United Nations (UN, World Population Prospects 2019). The TCCM and TDM of population were calculated by the following equations.

TCCM: [(TCC of Covid-19of a specific country/territory/area)/(Total estimated population of the same country/territory/area)] X 1 million.

TDM: [(TD from Covid-19 of a specific country/territory/area) /(Total estimated population of the same country/territory/area)] X 1 million.

Case fatality rate (CFR) of Covid-19

CFR describes the risk of persons dying from a certain disease within a given time period. CFR was calculated here as the number of deaths from Covid-19 during the experimental period divided by number of cases of the disease during the same time (Park, 23rd Ed. 2015).

CFR = (Number of deaths from a specific disease during a specific time period/Number of cases of the disease during the same time period) X 100.

CFR was divided into five categories on the severity of the affected countries viz. < 1.01, 1.01–3.00, 3.01–6.00, 6.01–9.00 and > 9.00.

As we mentioned in the introduction section, we explain that from the onset on Dec 2019, in 13–14 weeks

(approx. 90–100 days) the Covid-19 was ubiquitously outspread throughout the globe and a large number of Asian, African, American and European countries became affected. So, this time scale was helpful to us to make comparison among different geographical and socio-economical territories. And the end date (approx. 29–30 weeks) was selected based on main two reasons. During this time period, other major mutants namely Delta or D614 or Omicron did not appear, so the results what we got that is only from the pure wild type, popularly designated as Wuhan variety. Another reason is that, during this time period no vaccination or other established therapeutic strategies were developed. Application of vaccination or testing some new drugs was uneven on time scale in different territories. Quarantine, lockdown, repurposing of old drugs were globally acclaimed strategies during this period. So, to avoid the statistical bias in comparison among some uneven situations, we selected this 14th to 29th weeks time period.

Income economies

For the current 2020 fiscal year, low-income economies, lower middle-income economies, upper middle-income economies, high-income economies were determined based on Gross National Income (GNI) per capita which was calculated using World Bank Atlas method. The criteria of GNI for the income economies of the countries were given below (The World Bank, 2020a).

Low-income economies: GNI per capita ≤ $1,025.

Lower middle-income economies: GNI per capita = $1,026 – $3,995.

Upper middle-income economies: GNI per capita = $3,996 – $12,375.

High-income economies: GNI per capita ≥ $12,376.

World happiness

Happiness score of the countries/territories/areas was collected from the World Happiness Report, which was annually published by United Nations Sustainable Development Solutions Network. This score was prepared using the six variables (viz. GDP per capita, social support, healthy life expectancy, freedom, generosity, and absence of corruption) (Helliwell et al. World Happiness Report, 2020).

Quality of life (QoL) in a country

All together thirty different factors were included for calculating overall index of QoL of a country/territory/area, which were divided into seven subject area or sub-sectors such as stability (deals with economic and political stability), civil rights (deals with legal system and civil rights), health and medical services (includes different factors including average life expectancy and the treatment facilities in relation to the number of inhabitants), security, climate (deals with the geographical environment, the optimum environment assumed as maximum daily temperature of 25 °C at 55% humidity and nearly 8 rainy days per month), costs (deals with costs and expenses that includes national cost of living and average annual income) and popularity (includes general migration rate and number of foreign tourists visited in that area). The best achievable value in each division or subject area or sub-sectors was 100. The contribution of these earlier mentioned seven subject areas for the calculation of overall index of QoL were 14%, 16%, 16%, 16%, 14%, 16% and 8%, respectively (Quality of life, 2020).

The global health security (GHS) index

The GHS Index was the first accountable parameter that is the comprehensive assessment and benchmarking of health security and related capabilities across the 195 countries. This is associated with the indexing of the International Health Regulations. The GHS Index was an important proposal of the Johns Hopkins Center for Health Security. It was developed by The Economist Intelligence Unit [11].

Anxiety disorders prevalence (ADP)

According to **WHO,** "Anxiety disorders refer to a group of mental disorders characterized by feelings of anxiety and fear, including generalized anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive–compulsive disorder (OCD) and post-traumatic stress disorder (PTSD)" [28]. We followed the latest report of WHO for the prevalence of anxiety disorders [28].

Depressive disorders prevalence (DDP)

According to **WHO,** "Depressive disorders were characterized by sadness, loss of interest or pleasure, feelings of guilt or low self worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration. Depression can be long lasting or recurrent, substantially impairing an individual's ability to function at work or school or cope with daily life. In this regard, caution should be made considering the two interdependent factors like environmental and psychic so that a vicious circle is not created. Another painful situation that may mimic depression but noted as demoralization (does not fulfill criteria according to DSM-V). This situation may sometime develop resilience in some individuals (Costanza et. Al., 2021). Depression can lead to suicide at its most severe condition [28]. We followed the latest report of WHO for the prevalence of depressive disorders [28].

Prevalence of tobacco smoking (TSP)

The age-standardized prevalence of tobacco smoking among persons aged 15 years and older in different countries/territories/areas were given in the latest report of World health statistics developed by WHO in 2019 was used in this study [29].

Suicide mortality rate (SMR)

SMR per 100,000 (SMRL) in different countries/territories/areas were given in the latest report of World health statistics developed by WHO in 2019 was used in this study [29]. The important determinants which are associated with SMR are Perceived stress (PSS), availability of social provisions (SPS), Short self-report scale of loneliness (SLON) and personality assessment (BFI-S), neuroticism scale [BFIS-N], BFI-S openness scale [BFIS-O], BFI-S agreeableness scale [BFIS-A], BFI-S conscientiousness scale [BFIS-C]). The particulars of these factors were collected from the COVIDiSTRESS Global Survey dataset on psychological and behavioral consequences of the Covid-19 outbreak [23].

Lockdown period during Covid-19

The information regarding lockdown in different countries during the Covid-19 pandemic was collected from the Wikipedia literature [https://en.wikipedia.org/wiki/COVID-19_lockdowns].

Total test (TT) and total confirm cases and Total test ratio (TCC: TT) of Covid-19 cases

Country wise the total test during the investigation tenure were collected from [https://ourworldindata.org/coronavirus-testing]. The TCC: TT was calculated by dividing the number of total confirm cases on 161 days / number of total tests on the same day.

Statistical analysis

Statistical analysis was performed using SPSS/version-16.0 (special institutional version from IBMid: security code 0323373). Data were presented as number (percentage) or mean ± SE as appropriate. Data were tested by Kolmogorov–Smirnov test to verify the normal distribution pattern. Baseline variables and outcome measures were compared with Post-Hoc ANOVA test for continuous variables and the chi-square test for categorical variables. The group means were tested using Analysis of Variance (ANOVA) with Tukey post hoc test to study the mean difference of QoL, prevalence of depressive disorders, prevalence of anxiety disorders, GHS Index on the basis of the disease severity and CFR. ANOVA was used to determine the effect of TCCM on the psychological wellbeing during Covid-19 pandemic period. The Tukey post hoc test was conducted to know the mean differences of SPS, BFIS-O and BFIS-C on the severity of TCCM (viz. 100–499, 500–999 and 1000–9999). Pearson product moment correlation was performed to explore the relationship between TCCM, TDM and CFR of Covid-19 with different indicators of health and wellbeing. The stepwise linear regression analysis was done to elucidate the most important predictors of TCCM, TDM and CFR of Covid-19. Pearson's chi square test was used to determine the significant differences, if any between different grades of CFR (viz. < 1.01, 1.01–3.00, 3.01–6.00, 6.01–9.00 and > 9.00) and categories of income-economics of the countries. The p value < 0.05 was considered statistically significant.

Results

The mean CFR fromCovid-19in 215 countries, territories or areas were 3.32 ± 3.83. The most affected country was Yemen with CFR 27.01 while there were 29 countries or territories where CFR = 0 as no case of deaths due to Covid-19 was reported here. The most affected countries in relation to TCCM and TDM were Qatar (32,770.23) and San Marino (1237.55), respectively, while, the least affected country was Papua New Guinea (1.23)(data not shown).

The association of different psychological wellbeing indicators with Covid-19infection-outcome is presented in Fig. 1. It indicated that World Happiness Score, DDP, ADP, QoLGHS Index were positively associated with TCCM. This study clearly indicated that the individuals of the regions having higher prevalence of depression and anxiety disorders also have higher rate of occurrence of Covid-19 cases. This may indicate that the depressive and anxiety disorders impair the immune system.

The association of different health and psychological wellbeing indicators is presented in Fig. 2. It is noticed that depression and anxiety disorder is predominant in those regions where Happiness, QoL scores and GHS Index are high (DDP, ADP and SMRL are higher).The physical indicators of happiness and quality of life may be the cause behind it. Another cause may be the failure in fulfilling the greedy inclination of someone may ultimately develops psychological depression. Impact of the Quality of Life (Score), Anxiety Disorders (Prevalence), Depressive Disorders (Prevalence), and Global Health Security Index (Score) on Covid-19 CFR are presented in Fig. 3. When we categorize CFR into five different groups on the basis of the disease severity (viz. < 1.01, 1.01–3.00, 3.01–6.00, 6.01–9.00 and > 9.00), we noticed that the number of countries are variably affected.

The study clearly noted that the prevalence of anxiety disorders was significantly (F = 3.039; P < 0.05) increased in a linear fashion with the severity of Covid 19 (CFR), Depressive disorders are found to be associated with the

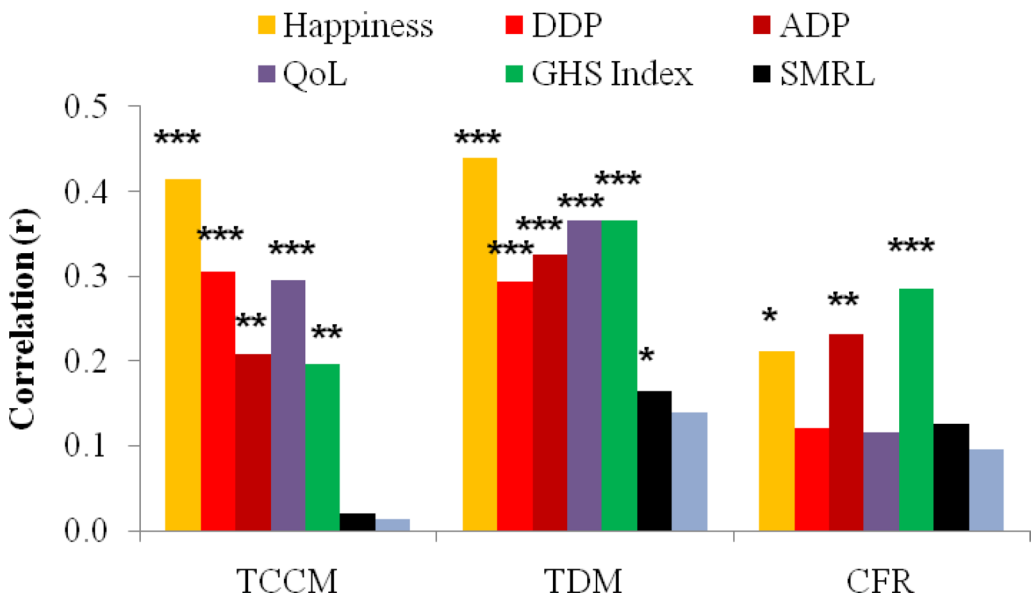


Fig. 1 Relationbetween different psychological wellbeing indicators andCOVID-19 infection outcome. It indicated that World Happiness, DDP, ADP, QoL,GHS Index were positively associated with TCCM. Significance level at *P < 0.05, **P < 0.01 and ***P < 0.001

CFR (F = 2.304; P = 0.06). Impact of income economics of the countries on the CFR is presented in Fig. 4a. The highest percentage of most severe cases of CFR (i.e., CFR > 9.00) were observed in the countries with high income economics (12.99%). And the upper middle income group and low income group have 2.00% and 3.57% of CFR > 9.00. Lifestyle issues may be associated with income economies which demonstrate an influence the Covid-19 outcome.

Effect of QoL, happiness and GHSI on the CFR in varied income economies is presented in Fig. 4b. This study indicated that the countries in the high income economics have better QoL and happiness. The high CFR was observed in the countries with high income economics, which indicate that the variables and indicators used for the evaluation of QOL and happiness are weak predictors of mental status.

Regression analysis of the different indicators of QoL and the parameters ofCovid-19 is presented in Fig. 5. The QoL is represented by seven different factors including stability, rights, health, security, climate, costs and popularity. Among these factors, it is noticed that popularity of the countries was the most important indicator of the TCCM and CFR of Covid-19. Better transportation, job and business environment, more tourist visit keep these places densely populated most of the time.

Different mental health statuses like feeling of stress, depression, consciousness and neuroticism during the Covid-19 period are analyzed with their relation to this disease. The correlation result indicated that SPS and BFIS-A were significantly associated with TTM, while PSS were significantly associated with TDM and CFR of Covid-19 (Fig. 6A). The ANOVA results focuses that the mean score of SPS, BFIS-A and BFIS-C were significantly higher with the increasing TCCM grade (viz. 100–499, 500–999 and 1000–9999). The results of the Tukey post hoc test showed that the difference of mean of SPS, BFIS-O and BFIS-C were significantly higher in the TCCM of 1000–9999 than TCCM of 100–499 (Fig. 6B). Figure 6C demonstrates that lockdown make the total death per million (TDM) and CFR more non-significant than the TD. Inversely, the corresponding correlation values decreased with CFR than that of TD (negative correlation). The WHO defined region- (Fig. 6D) and economic zone- wise (Fig. 6E) statistics, ANOVA data on total testing versus total confirmed cases are shown. The results indicated that the TTM was highest in EMR group of countries among the WHO region while high income economies have highest TTM with comparison to the countries with upper-middle, lower-middle and low-income economies. But the highest mean of TCC:TT was noted in American (AMR) countries. Figure 7 suggests the highly significant correlations (Canonical) between anxiety-depression with the total death and CFR in the COVID-19 outcome. The canonical variates analysis can express the information of association in the from cross-covariance matrices.

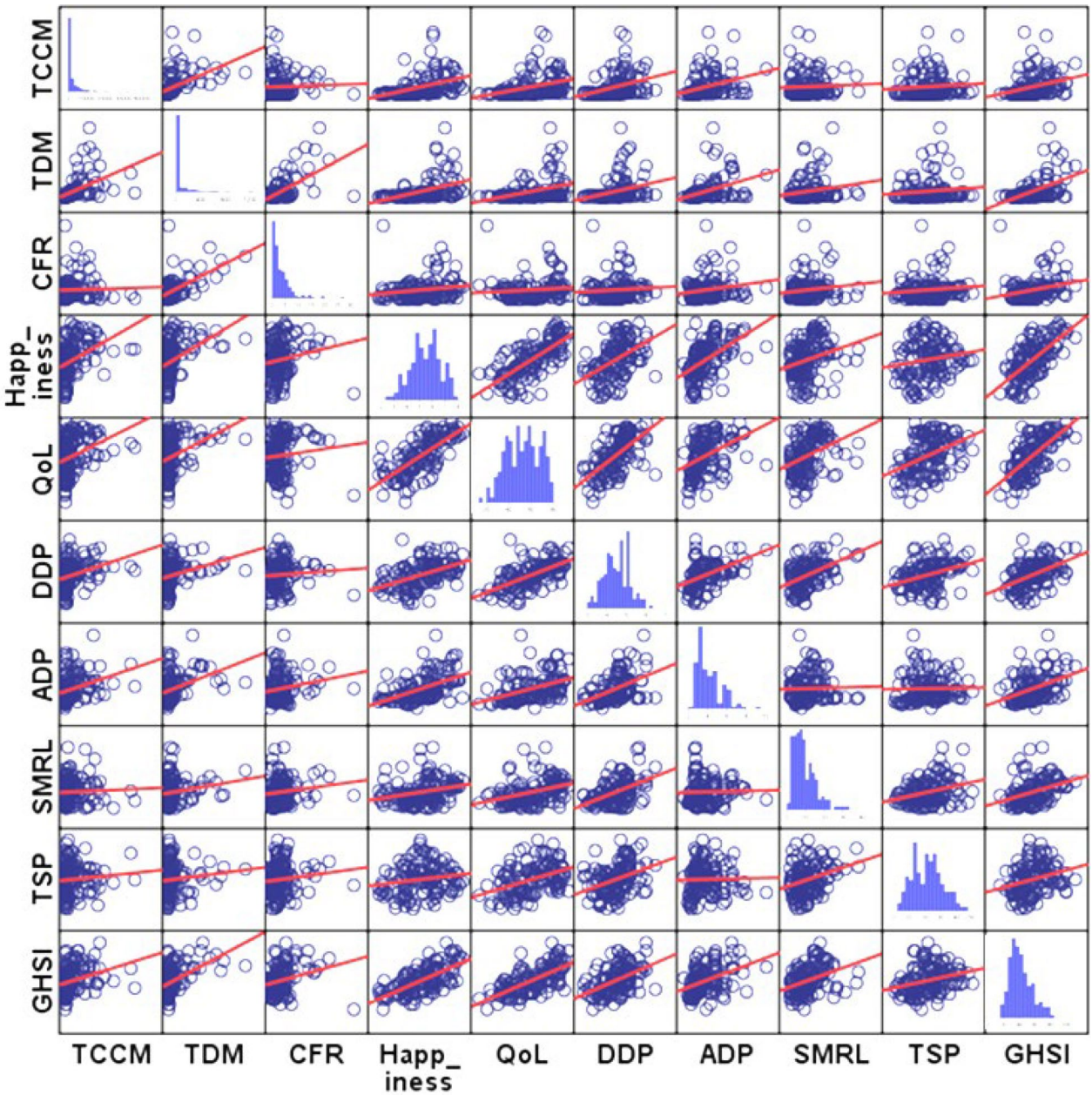


Fig. 2 Intra-relationship between different health and psychological wellbeing indicators. The depression and anxiety disorder is predominant in those territories/regions where Happiness, QoL scores and GHS Index are high (DDP, ADP and SMRL are higher)

Discussion

The present study showed that DDP and ADP were associated with TCCM and TDM. This finding supports the association between the psychological state and the efficiency of the immune system. In a recent study, Zefferino et al., 2021 suggested that stress significantly impairs the functions of the immune-competent cells and their modulators. So, the protective role of the immune system against pathogens is drastically diminished [22]. Researchers found that the cellular and humoral immunity of the rodents were affected by the stress and anxiety [14]. It is reported that the long term of anxiety produces high level of cortisol and decreases some subsets of T lymphocytes like CD45+, CD4+and helper T cells (Herbert, 1993). Taken together, both the humoral and acquired immunities are affected via neuro-endocrine impairment of the immune competent cells.

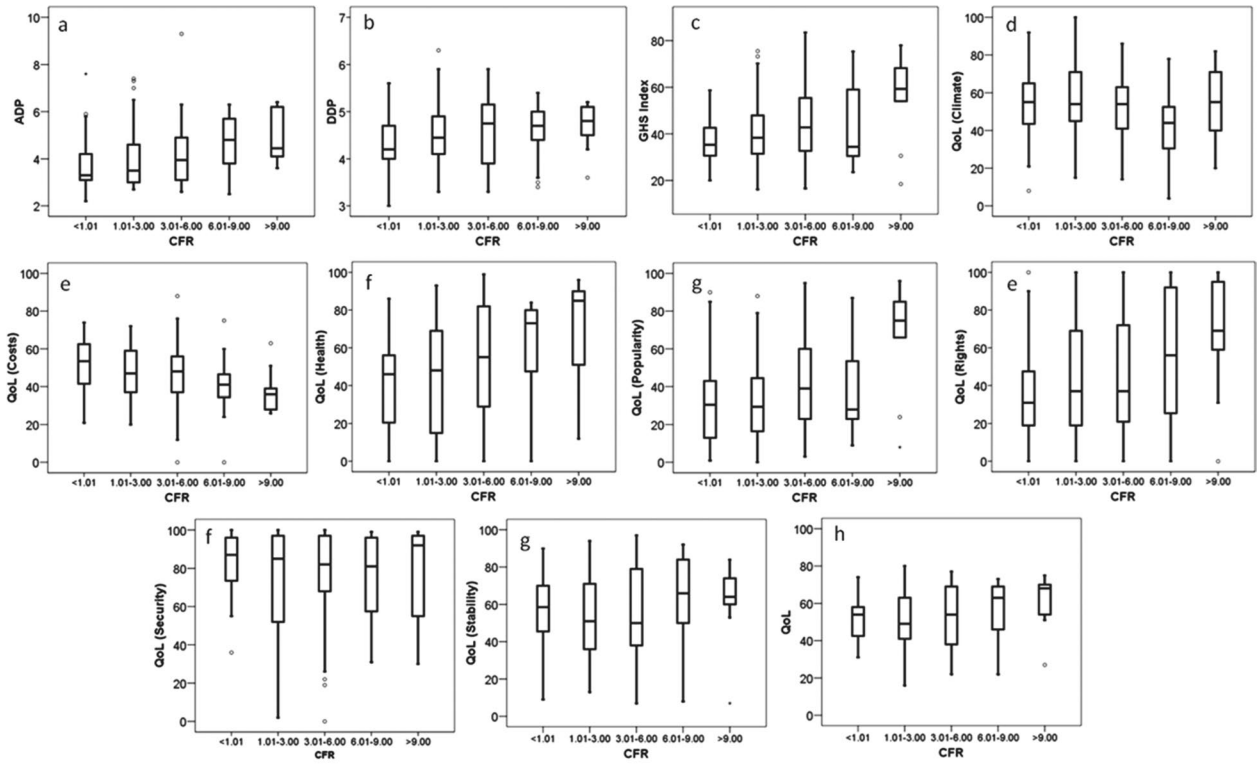


Fig. 3 Impact of case fatality rate of a country on the Quality of Life, Anxiety Disorders (Prevalence), Depressive Disorders (Prevalence), and Global Health Security Index (Score). We categorize CFR into five different groups on the basis of severity viz. < 1.01, 1.01–3.00, 3.01–6.00, 6.01–9.00 and > 9.00, it was noted that 28.84%, 32.56%, 22.33%, 9.77%, and 6.51% respectively countries/territories/areas were affected

In the present study, regions with higher prevalence of anxiety disorders are affected more with Covid-19. Moreover, lack of specific treatment, worsen the situation of an infected person with diminished immune system resulting the patient to be more sensitive to the disease. Further, the situation becomes more critical when the patient carries one or more co-morbidity factors. Interactive role of co-morbidity factors and immuno-suppression are the underlying mechanism of fatal death. This is supported from the present finding of the positive co-relation between ADP with TDM and CFR (Fig. 2). Similarly, the depression was associated with several alterations in cellular immunity which lowers the proliferative response of lymphocytes to mitogens, and the activity of natural killer cells. Overall, the populations of WBCs are also significantly diminished [25].Not only the pre-Covid mental issues, but also the developed mental trauma during the Covid-19 period honed the disintegration of immune functions resulting in higher infection rate and CFR (Fig. 6A and B).

This study indicated an important health indicator of a region like, QoL positively correlated with TCCM and TDM in the current status (Fig. 1). Nevertheless, we noticed that rights, health, costs and popularity were among the seven subject areas or sub-sectors that were considered while calculating QoL (Fig. 3).The regression analysis suggested that among these seven subjects area popularity was strongly associated with TCCM, TDM and CFR. While evaluating a country's popularity, the population density, general migration rate and the number of tourists were considered as indicators (Quality of life, 2020). Therefore, the countries or regions experiencing the issues are more sensitive to the current infection.

Covid-19 has been declared as a manageable pandemic by the World Health Organization (WHO). Beside its nature to develop respiratory illness; it can also affect brain and other organs like heart, liver and kidneys. Though, neuropsychiatric manifestations are common during viral infections they are not frequently addressed [14].A large body of evidence suggests a close association of stress and immune system. Different immuno-competent modulators and protective signaling molecules are drastically diminished against a pathogenic threat in different infectious diseases (Herbert et al. 1993).Laboratory investigations on human stress exposure showed the manifestations of severe impairment of neuro-endocrine and immune system (Herbert et al. 1993; [25]). In the last year, no specific treatment in Covid-19 raised significant

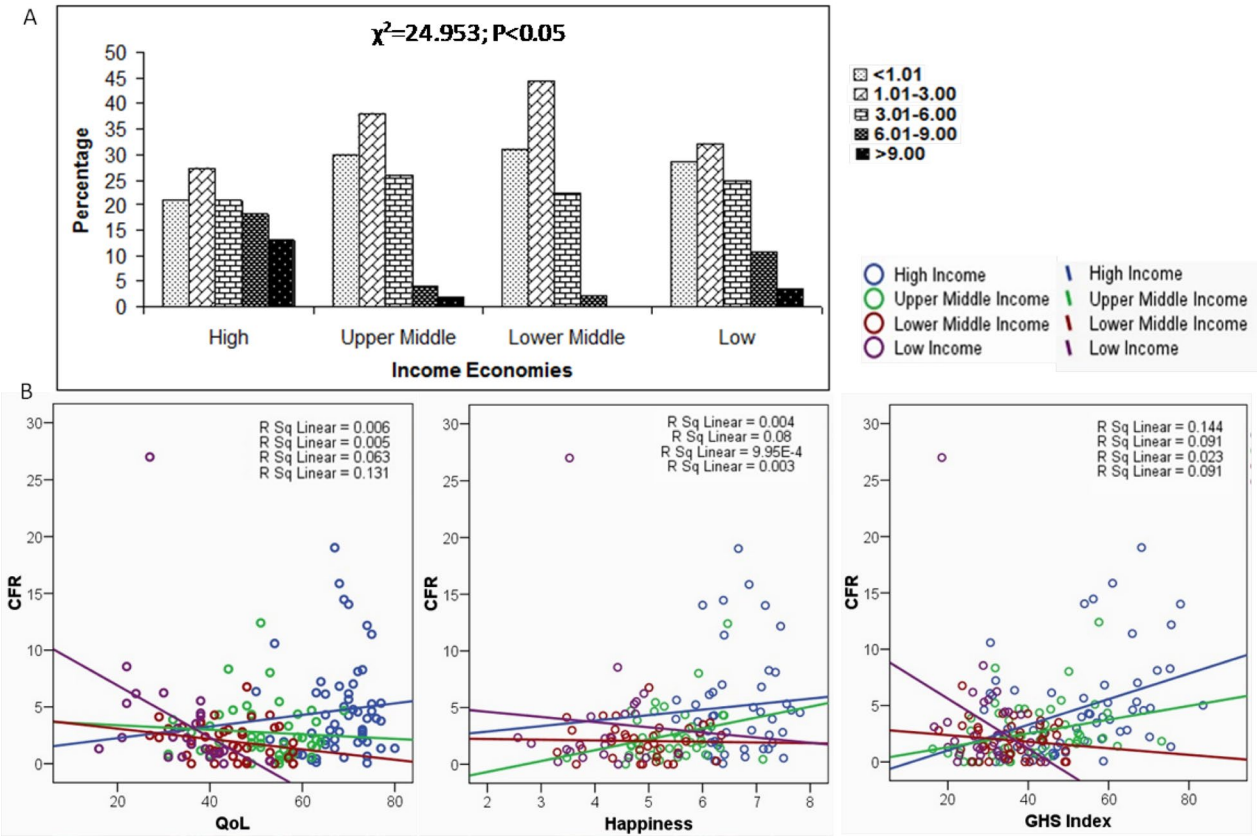


Fig. 4 Impact of income-economics of a country on itsCovid-19 case fatality rate (CFR). $\chi^2 = 24.953$; $P < 0.05$.Effects of Quality of Life (QoL), World-Happiness and Global Health Security (GHS)on the CFR in the countries/territories of varied income-economies

uncertainties and anxiety. In the current year, more specific treatment and some vaccination strategies are globally available which minimized the tension. The practical implication of the psychological concerns to Covid-19 is important. The most exposed populations—children, college students, and healthcare professionals—have shown the benefits of psychological well-being. These groups are more prone to experience signs of distress such as anxiety, depression, and post-traumatic stress disorder. Further, it is pointed that people's relationships and perceptions of empathy for others have changed as a result of social distance and security measures (Saladino et al., 2020). It is proposed that customized analysis for a single patient has been more beneficial for the better management concern of the disease. Inter-individual variability in the psycho-social status might have influenced in Covid-19 outcome. Precision psychiatry seeks to better customize healthcare to meet the needs of each patient and may present a chance to increase the accuracy of disease classification, treatment choices, and preventative initiatives. In this regard, translational and trans-diagnostic methods are very important in clinical research (Williams et. Al., 2024).

Report revealed that in the initial phase of the Covid-19 outbreak in China, approximately 60% of the respondents rated with the psychological impact as moderate-to-severe conditions. And about one-third respondents showed different degrees of anxiety disorder. It has been hypothesized that the psychological interventions can be utilized to improve the mental health of vulnerable groups of the Covid-19 patients. In some cases sex-dimorphic association has been noticed. In female, some specific physical symptoms (e.g., myalgia, dizziness, and coryza) were noticed. Specific steroids and some sex hormones may control some neuro-endocrine regulations of metabolic processes. Report reveals that a poor self-rated health status is significantly associated with a greater psychological impact of the outbreak [13]. Following the Covid-19 epidemic, there is a chance that those who are not affected may become more susceptible to infection due to their weakened immune and disturbed state. Our results suggest that post Covid / neo-normal mental health may increase the infection rate and its severity (Fig. 6). In this regard, the global strategies and Covid testing initiatives need to be considered. It is noticed

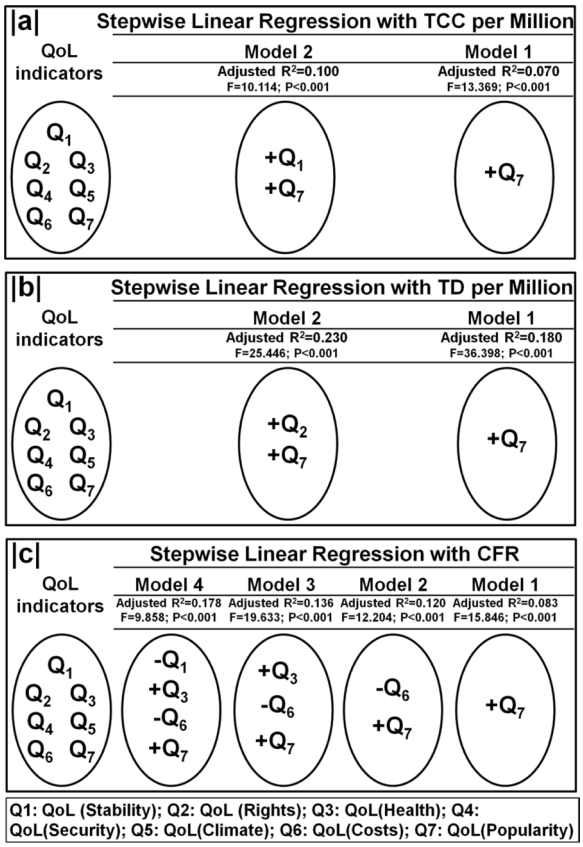


Fig. 5 Regression analysis of the different subject area or sub-sectors of Quality of Life and the parameters of COVID-19

that long term lockdown can control the infection and death rates from Covid-19 as a result of the mass isolation (Fig. 6).

As we noticed, lockdown strategies are being suggested by other investigator as possible ways to counteract the spread of COVID-19. Additionally, it was proposed that moderate-to-severe depressive symptom is substantially correlated with poor home-interior quality (Morganti et al., 2022). Our studies highlight the link between depression and Covid-19 outcome. The more number of testing uncovers a higher occurrence of infection-rate. An immediate action of individual isolation/quarantine finally restricts the rate of infection. And this is evident in several advanced countries with better infrastructural/socio-economic strength. Several observations suggest that present outbreak might lead to additional health problems such as stress, anxiety, depression and insomnia. It is discussed earlier that the determinants like economy, unemployment, confusion in Covid prevention strategies, and scarcity in health-care facilities may impact Covid-19management. So, more organized efforts may protect the mental health and morbidity due to Covid-19 [15, 18].

One survey based study with a large sample size revealed the impact of the psychological stress all groups of a community [7]. Report revealed that healthcare workers especially nurse, doctors and women were more affected with mental and health burden and those were undergone diagnosis and treatment [7, 21].Some of those mental-health problems are panic, anxiety, depression, post-traumatic stress disorders, suspicion, infodemia, cacophony, xenophobia, racisms, etc. [23]. In this situation, knowledge-based interventions are urgently needed to reach the affected individuals especially by health care workers and other professionals [16, 27]. Covid-19 outcome is not only related to the viral exposure but also it is related to the physiological/immunological states, inflammatory responses, vascular health and other co morbidity factors of an individual. These factors might be associated with the mental health and interactions to the society. On the other hand, the symptoms of the Covid-19 might interfere to an individual's psychological condition determine the final disease outcome. This is evident from our present data as presented in (Fig. 6). We examined the effects of one variant without the overlapping influence of other VOCs because this work was done during the time when just the first wave (our study period, which was the 94th to 205th date of infection) and Wuhan variety were occurring globally. During that period, no specific drugs or vaccination strategies were developed except repurposing of some old drugs. So, the impacts on the disease outcome by the presently studied psycho-social variables were more refined and less influenced by other factors. The canonical variate correlations strongly imply that psychological circumstances are associated with current disease outcomes. The present parameters of the variables are significantly associated and can be treated as strong probabilistic factors in the CCA model in influencing the disease. Conclusively, major portions of the affected people and healthcare workers are at high risk of mental illness. Depression due to socioeconomic crisis is presently become the major concern.

Nevertheless, in patients with chronic pain and destructive nature, this type of study-findings provides insight into the interactions of psychosocial thoughts and pandemic disease outcome. In this situation, the primary clinical implications pertain to supportive/psycho therapeutic therapies as well as prevention. In particular, patients can eventually break free from the bio-psychosocial vicious cycle of profound moral anguish brought on by chronic pain by concentrating on preserving the domains of interpersonal connections and personal activities.

This is important to mention some of the limitations of the present study. We have to consider that the global

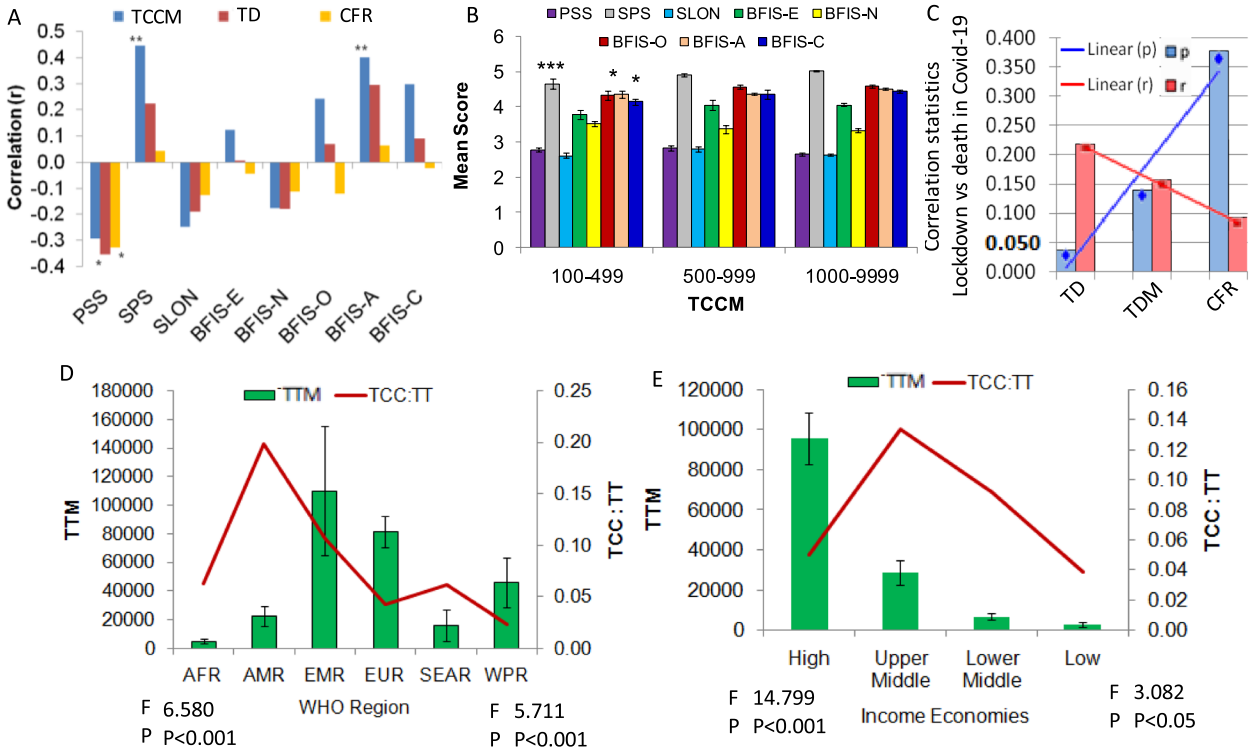
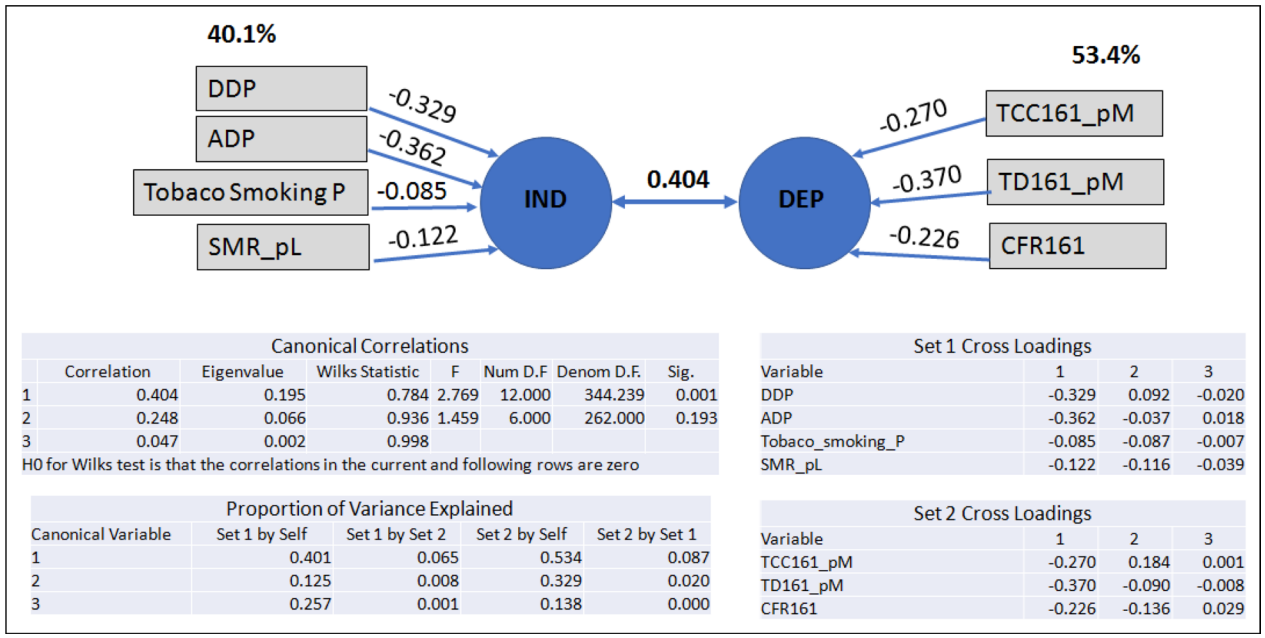


Fig. 6 During Covid period, different mental state like perception of stress, depressive and feeling of loneliness, consciousness and neuroticism etc.are analyzed with their relation to this disease outcome A. correlation and B. ANOVA statistics. Effects of lockdown on Covid-19 outcome is presented in fig. C. Result shows that lockdown make the TDM and CFR (disease severity) more non-significant than the TD. Inversely, corresponding correlation values become lower from TD to CFR (comparatively negative correlation). WHO defined region (D) and economic zone (E) wise statistics, ANOVA data are shown to find dependence between total testing and total confirmed cases. Abbreviations: TCCM: Total confirmed cases per million of population; TD: Total deaths; TDM: Total deaths per million of population; CFR: Case fatality rate; TTM: Total test per million of population; TCC:TT: Total confirm cases and Total test ratio; PSS: Perceived stress; SPS: Social Provisions Scale; SLON: Short self-report scale of loneliness; BFIS-E: Big Five Inventory (BFI-S) extraversion scale; BFIS-N: BFI-S neuroticism scale; BFIS-O: BFI-S openness scale; BFIS-A: BFI-S agreeableness scale; BFIS-C: conscientiousness scale

datasets which are dealt here comprise more than 170 countries and billion of populations. The deposited data or reported new information might have been inconsistent and can't warrant being free from unforced bias. Moreover, regional differences in geographical and socioeconomic status and finally COVID-19 reporting might have some inconsistency in the datasets used in this study. The influence of other unmeasured confounding variables also should be considered.

Well-characterized psychosocial determinants like; contamination-fears, xenophobia, compulsive-disorder, and substance-abuse should be considered in these monitoring processes [26]. Both pre-infection and post infection traumatic situations have significant role in the present pandemic conditions. The present focus should be the continuous monitoring of the psychological consequences of the Covid-19 patients. Further clarification is necessary in this regard.



Canonical Correlations

	Correlation	Eigenvalue	Wilks Statistic	F	Num D.F	Denom D.F.	Sig.
1	0.404	0.195	0.784	2.769	12.000	344.239	0.001
2	0.248	0.066	0.936	1.459	6.000	262.000	0.193
3	0.047	0.002	0.998				

H0 for Wilks test is that the correlations in the current and following rows are zero

Set 1 Cross Loadings

Variable	1	2	3
DDP	-0.329	0.092	-0.020
ADP	-0.362	-0.037	0.018
Tobaco_smoking_P	-0.085	-0.087	-0.007
SMR_pL	-0.122	-0.116	-0.039

Proportion of Variance Explained

Canonical Variable	Set 1 by Self	Set 1 by Set 2	Set 2 by Self	Set 2 by Set 1
1	0.401	0.065	0.534	0.087
2	0.125	0.008	0.329	0.020
3	0.257	0.001	0.138	0.000

Set 2 Cross Loadings

Variable	1	2	3
TCC161_pM	-0.270	0.184	0.001
TD161_pM	-0.370	-0.090	-0.008
CFR161	-0.226	-0.136	0.029

Fig. 7 Brief representation by the Canonical correlations of depression and anxiety with COVID-19 outcomes suggest highly significant association with these dependant variables

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Author contribution
Conception or design of the work: SM, Data collection: NKS, SM, Data analysis and interpretation: NKS, SM, Drafting the article: NKS, SM, Critical revision of the article: SM, All authors reviewed the manuscript. Final approval of the version to be submitted: NKS, SM.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval statement
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Research materials availability statement
All materials are available upon request

Pre-registration statement
Pre registration formalities were followed

Competing interests
The authors declare no competing interests.

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