

Pre-infection global psychosocial status on SARS CoV-2 disease outcome

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Abstract

The present pandemic situation due to Covid-19 disease has raised a severe threat on human health both physically and mentally. Globally, 794,435 persons were died from a total 22,767,009. We assumed that existed psychosocial-conditions in the pre-infection-period have a great role in disease pathogenesis-severity. This might have geographically/regionally influenced different parameters of the disease. The present aim was to delineate the impact of pre-infection or post-infection psychosocial impact on Covid-19 outcome. Existing global mental-status (depression-anxiety, economic-status, quality-of-life/QOL, Global-Health-Security/GHS, tobacco-smoking and suicide-mortality were verified with their possible correlation with the total-infection/death-rate/case-fatality-rate(CFR) analyzed in >170 countries. The data was collected from World-Health-Organization/World-Bank/United-Nations, and the Johns-Hopkins-Center for Health-Security. The SPSS/version-16.0 was utilized for student's t test, multivariate-ANOVA, [Correlation](#) and Prediction for numerical-outcomes, [Linear-regression](#). Pearson's-chi-square-test was performed in the current study. Psychological wellbeing like happiness-GSH-QOL, mental-impairments like depression-anxiety have been variably-positively correlated with total-confirmed-infection-cases, total-death and CFR ($p < 0.05$ - $p < 0.001$). Happiness has been positively associated with QOL/GSH/anxiety-depressive-disorder. Higher CFR has been noticed more in the developed countries. Virus-host interactions may have some variability depending on the race-ethnicity-and individual's-body-compositions. Because, this study has been done >170 countries, the present outcome is important. The positive correlation between happiness-QOL index with the apparent adverse outcome of Covid-19 and the correlation between happiness/QOL with anxiety-depression disorder are found to be parallel. This suggests more characterizations of these psychosocial-indices are needed. The open-minded nations with non-conserved nature which eventuates to more transportation, tourist trafficking and more social association/collaborations, that might have affected more. Further studies are necessary in this regard.

Introduction

At this very moment, the pandemic situation developed by the novel corona virus SARS CoV-2 (COVID-19) that has been still uprising with an active case number of 17 106 007 with the deaths of 668 910 persons in 215 countries [1]. Beside the direct physiological effects due to infection, the psychological status or the mental health impact of both infected and uninfected individuals cannot be underestimated [2]. Nevertheless, the situation becomes complex for those who are suffering from addiction, substance abuse or other compulsive disorder. Different levels of tensions, hypertension, anxiety and depressions are heightened in the form of individual and global stress [2]. Other than direct physiological effects the main causes of psychological effects here are the uncertainties in the life; in the form of economic, job-services, social and political states and the synergistic effects of these factors are compounded due to the process of isolation, lockdown or quarantine situation. Stress is the ingredients of life practices which remained at a consistent level of exposure in pre-covid situation. This level of exposition is country-community and region specific. Different parameters designating the psychological status are regularly evaluated and indexed by the different competent authorities like WHO, World Bank and United Nations or others. We evaluated here the impact of pre-covid global psychological and socio-economic condition on the Covid19 infection outcome [3]. The Covid-19 disease has been developed atypical manifestations from fever, coughing, hypoxia and

dyspnea. These patients also manifest some symptom like delirium. Report reveals from several case studies that an atypical nature of psychotic and confusion-like symptoms might be the feature of COVID-19 patients [4]. The causes of mental health effects in the context of COVID-19 are multi-factorial outcome developed from biological, behavioral, and environmental determinants which influence the pathogenesis and severity of Covid-19 infection. This situation threatens the human basic needs and might be related to the crucial environmental factor and mental health [5].

For better and all-round protective measures the Covid patients should be taken care of by the dual supervision of a psychiatrist and an internist/infectious disease specialist. All the health workers should receive specific training, frequent medical check-ups and close psychological support [6]. This is important to mention the connection between the psychological state and the infection severity of an individual when it is noticed that several psychiatric patients being infected with COVID-19 and COVID-19 patients developed with psychiatric symptoms after treatment with antiviral drugs [7]. Ambient temperature and air quality were significantly associated with the COVID-19 pandemic [8]. Lifestyle, food-habits and body composition has been linked to the infection outcome and disease severity [9]. Economic and food safety in the different socioeconomic community determine their psychological status in the present pandemic situation [10]. Imbalance in the distribution of health beneficiaries in different communities may impair the psychological state of an individual. Fair and transparent allocation of medical resources maintaining equity in all aspect helps in the confidence build-up of a community [11]. At the very beginning of this situation, economic impacts of Wuhan 2019-nCoV have been implicated in communities of China and the world psychosocial status as well [12]. All these literatures suggest that human psychosocial state has impact on disease occurrence-severity and vice versa.

Extrinsic and intrinsic stress has been significantly associated with individual's neuro-endocrine and immunological status. An important investigation in '80s decade on a large number of students demonstrated that their immunity went down every year under the simple stress developed at the examination period. They had very low count of natural killer cells, which fight tumors and viral infections. Immunity-boosting gamma interferon and T-cells responded only very weakly which is known as lymphopenia [13]. Chronic stress has been shown to generate very low antibody titer in response to pneumococcal pneumonia vaccination events [14]. Moreover, depressive symptoms are associated with highly increased and prolonged inflammatory responses following influenza vaccination [15]. A large body of literature is available in this regard. In the current situation we hypothesize that the pre-existing psychosocial status, socioeconomic condition and global determinants of the mental health could have been related to the prevalence and severity of the infectious disease COVID-19.

In this background we delineate in our present study the correlations of existing global mental-status, economic conditions with the infections, total-death and case-fatality rate counted from >170 countries. The current study will be helpful for the understanding of the metal health effects like hypertension, depression and anxiety disorder on the on the global health and immunological adaptations and resistance/sensitivity to SARS CoV -2 infections and its severity. Good metal health might have some immuno-protective effects and thus more resistance to the infection related diseases.

Methods

Ethical consideration:

The study was approved by the competent authority and the Institutional Research Ethics Committee (OIST/IRBhu/Feb/20/02).

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

We investigate the total confirmed cases (TCC) and total deaths (TD) of COVID-19 as on the WHO Coronavirus disease (COVID-19) Situation Report– 161 day [17]. According to WHO the “data as received by WHO from national authorities by 10:00 CEST, 29 June 2020” [17]. The total estimated population as on July 2020 of the respective countries/territories/areas was collected from Department of Economic and Social Affairs Population Dynamics of United Nations [18]. The TCCM and TDM of population were calculated by the following equations.

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

TDM: [(TD of 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 measures the risk of persons dying from a certain disease within a given time period. CFR was calculated as number of deaths from a specific disease during a specific time period divided by number of cases of the disease during the same time period, usually expressed as per 100 [19].

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.

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 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 [20].

Low-income economies: GNI per capita \leq \$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 \geq \$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) [21].

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 number of doctors and hospital beds in relation to the number of inhabitants), security (deals with the security of life such as total number of incidents, the number of people killed, wounded and abducted also the terrorism statistics), 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 [22].

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 resembles the indexing of the International Health Regulations. The GHS Index was an important proposal of the Nuclear Threat Initiative and the Johns Hopkins Center for Health Security. It was developed by The Economist Intelligence Unit [23].

Anxiety disorders prevalence (ADP):

According to **WHO** "Anxiety disorders refer to a group of mental disorders characterized by feelings of anxiety and fear, including generalised anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD)" [24]. We followed the latest report of WHO for the prevalence of anxiety disorders [24].

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. Depression can lead to suicide at its most severe condition [24]. We followed the latest report of WHO for the prevalence of depressive disorders [24].

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 [25].

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 [25].

Statistical Analysis:

Statistical analysis was performed using SPSS software version 16.0. Data were presented as number (percentage) or mean±SD as appropriate. ANOVA was applied to study the mean difference of QoL, prevalence of Depressive disorders, prevalence of Anxiety disorders, GHS Index on the basis of severity of CFR. Pearson's chi square test was used to determine significant differences between the different grades of CFR and categories of income economics of the countries. Pearson product moment correlation and linear regression analysis were performed. The *p* value <0.05 was considered statistically significant.

Results

The mean CFR of COVID-19 from the 215 countries/territories/areas as reported by WHO was 3.32±3.83. The most affected country was Yemen with CFR 27.01 while there were 29 countries/territories/areas where CFR=0 as no case of deaths due to COVID-19 was reported from these countries/territories/areas (table 1). The most affected countries in total confirm cases per million of population and total deaths per million of population were Qatar (32770.23) and San Marino (1237.55) respectively. While least affected countries in respect to total confirm cases per million of population was Papua New Guinea (1.23).

Relationship between different psychological wellbeing indicators with COVID-19 infection outcome is presented in table 1. It indicated that World Happiness, Depressive Disorders prevalence, Anxiety Disorders prevalence, Quality of Life, Global Health Security Index were positively associated with total confirm cases per million of population. This study clearly indicated that those countries/territories/areas having the higher level of depressive disorders prevalence and anxiety disorders prevalence have the tendency of infected with COVID-19. This may prove that the depressive disorders and anxiety disorders inhibit the immunity system. While the association between these psychological parameters with total death per million of population further confirmed that the immunity system of the people living in these countries/territories/areas were severely affected.

Intra-relationship between different health and psychological wellbeing indicators is presented in table 2. This study may be suggested that in the countries/territories/areas, where high score of World Happiness,

Quality of Life and Global Health Security Index are persist there are simultaneously poor psychological health (Depressive Disorders prevalence and Anxiety Disorders prevalence and Suicide mortality rate per 100,000) is noted. The materialistic indicators of happiness and quality of life may be the cause behind it. Another cause may be the ever increasing demand of the people that may not possible to fulfill that is responsible for depression and ultimately lead them into severe depression and suicidal attitude. While 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. It was also noted that 14 (6.51%) of the countries/territories/areas were most severely affected (table 2).

The study clearly noted that the prevalence of anxiety disorders was statistically ($F=3.039$; $P<0.05$) increased in a linear manner with the severity CFR, however the prevalence of depressive disorders increased with the severity CFR though statistical significance ($F=2.304$; $P=0.06$) was not noted. Impact of income economics of the countries on the case fatality rate is presented in Fig 1. Ironically, this study noted that highest percentage of most severe case of CFR i.e., CFR >9.00 were observed in the countries with high income economics (12.99%) and while the countries with upper middle income economics and low income economics had shown that 2.00% and 3.57% of them having CFR >9.00. This further indicated that immunity system of the people living in the countries with high income economics were in critical condition.

Effect of Quality of Life, World Happiness and Global Health Security Index on the CFR is presented in Fig 2. This study indicated that the countries in the high income economics are enjoying better quality of life and happiness. These two indicators probably act as immune-booster and make the people with less affected with diseases and if affected then having being protected in the primary level. But, in this study it was clearly noted that high rate of case fatality rate was observed in the countries with high income economics, this may be suggested that the materialistic indicators used for the calculation of Quality of Life and World Happiness is not sufficient. Moreover, it may hardly represent the psycho-patho-physiological condition or health and wellbeing of ultimate happiness of the people.

Regression analysis of the different indicators of Quality of Life and the parameters of COVID-19 is presented in Fig. 3. The Quality of Life is composed of seven different factors including Stability, Rights, Health, Security, Climate, Costs and Popularity. Among these factors this study clearly indicated that popularity of the countries was most important indicator associated with total confirm cases per million of population, total deaths per million of population and case fatality rate of COVID-19.

Discussion

This present study showed that DDP and ADP were associated with TCCM and TDM. This is further established the close relationship between psychological disorders and immune system. In a recent study Segerstrom and Miller 2004, suggested that long or even short term of any kind of stress significantly impairs the functions of immune-competent cells and modulators and ultimate the protective capacity against pathogens are drastically diminished [26]. In a study on rat model found that the cellular and humoral immunity of the mice was adversely affected by the high anxiety and restraint stress [27]. Jaremka

et al. 2013, in their study among married couples found that the participants with higher attachment anxiety produced more cortisol and had fewer numbers of CD3(+) T cells, CD45(+) T cells, CD3(+)CD4(+) helper T cells, and CD3(+)CD8(+) cytotoxic T cells than participants with lower attachment anxiety [28]. This may be the cause behind the countries/territories/areas had more prevalence of anxiety disorders resulting in higher number of COVID-19. In a condition of diminished immune system and without having the specific medicine to fight against this disease situation become out of control. It ultimately results in lower chances of survival with other co-morbidities like cardiac and renal insufficiencies. This is supported in this study by showing the positive relationship between ADP with TDM and CFR. Similarly, the clinical depression was associated with several large alterations in cellular immunity including lowered proliferative response of lymphocytes to mitogens, lowered natural killer cell activity, and alterations in numbers of several white blood cell populations [29]. Thus the depressive disorders drastically affect the immunity system and the present study supported this.

Surprisingly this study indicated that positive health indicators of a country like QoL were positively correlated with TCCM and TDM (Table 1). Nevertheless, we noticed that rights, health, costs and popularity were among the seven subject area or sub-sectors that were considered while calculating QoL were significantly increased with the severity of CFR (Table 3). The regression analysis suggested that among these seven subject area or sub-sectors, popularity was strongly associated with TCCM, TDM and CFR. The probable explanation may be the calculating process of the popularity of a country. While evaluating a country's popularity, the general migration rate and the number of foreign tourists were considered as indicators [22]. Therefore, the countries/territories/areas with high number of foreign travelers had the high chance of being seriously affected with pandemic diseases.

Corona virus disease (COVID-19) has been declared as a manageable pandemic by the World Health Organization (WHO). Beside its nature to predominantly develop respiratory illness; it can also affect brain and other organs like heart, liver and kidneys. Moreover, neuropsychiatric manifestations are common during viral pandemics but are not effectively addressed [27]. A large body of evidence suggests the close relationship of stress and immune system. Reviews on a large body of experimental studies suggest that long or even short term of stress exposure significantly impairs the functions of immune competent cells. In addition, different immuno-competent modulators and protective signaling molecules are drastically diminished against a pathogenic threat [28]. This may be correlated with our present findings. Laboratory investigations on human stress exposure showed severe manifestations weakening of neuroendocrine and immune system. For stress of any significant duration - from a few days to a few months or years resembling the real life situations clearly showed significant impairment of immunity and physical/mental stability [28,29].

Report reveals that in the initial phase of the COVID-19 outbreak in China, around 60% 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 psychological interventions can be utilized to improve the mental health of vulnerable groups during the COVID-19 epidemic. In some cases sex-dimorphic association has been noticed. In female, some specific physical symptoms (e.g., myalgia, dizziness, coryza) were noticed. Notwithstanding, a poor self-rated health status were significantly

associated with a greater psychological impact of the outbreak and higher levels of stress, anxiety, and depression ($p < 0.05$) [31]. We have discussed in the introduction section about the existing ill mental-health could be detrimental to the infection sensitivity. After the occurrence of the Covid outbreak there are possibilities of uninfected persons to be more sensitive to infection as a result of their traumatized condition on the report regarding the severity of the pandemic nature of the infection. Several observations suggest that present outbreak might lead to additional health problems such as stress, anxiety, depressive symptoms and insomnia. Several influencing factors like economy, prevention strategies and decision-making from policy makers, health organizations and medical centers can control over strategies of COVID-19 management. So an more organized endeavor may control the mental health and morbidity at global level [32,33].

Survey based study with large sample size revealed psychological stress in all groups of the community. A more realistic approach of study from the participants of the first infection-affected area of hospitals in Wuhan showed more convincing mental-health states. Of all participants of health care workers especially nurses, women reported health and mental burden and those were undergone diagnosis management and treatment [34,35]. The present situation has affected different frontiers of lives and induced many psychiatric conditions in large number of individuals. Some of those mental-health problems are panic, anxiety, depression, post-traumatic stress disorders, suspiciousness, infodemia, cacophony, xenophobia, racisms, etc. [36]. In these situation educational interventions are urgently needed to reach to affected individuals especially health care workers worldwide [37, 38]. The present disease outcome is not only related to the viral exposure and its load but also related to the physiological/immunological states, inflammatory responses, vascular health and other comorbidity factors of the individuals. These factors of an individual might be associated to his/her mental health and interactions to the society. On the other hand post infection condition of an individual might interfere to his/her psychological condition and ultimate disease outcome. Notwithstanding, uninfected persons having knowledge with large number of infections around him/her may have impaired psychological states hence increased sensitivity to a new infection.

In conclusion, major portions of the affected people, associates to them, younger people, people experiencing the thought of outbreak, and healthcare workers are at high risk of mental illness. Continuous monitoring of the psychological consequences for outbreaks should become routine efforts worldwide [39]. Very well characterized psychosocial determinants are developed in the current pandemic situation like; contamination fears, fears economic-job-service crisis, xenophobia, compulsive disorder, substance abuse and other traumatic stress symptoms [40]. Both pre-infection and post infection traumatic situations have great role in the present pandemic conditions. So, special care should be taken for the proper management of the affected and the sensitive persons.

Declarations

Conflict of Interests: None

Data availability: All data are available upon request

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Tables

Table 1: Relationship between different psychological wellbeing indicators with COVID-19 infection outcome

Parameters	N	TCCM	TDM	CFR
Happiness	142	0.414***	0.439***	0.212*
DDP	174	0.306***	0.293***	0.121
ADP	174	0.208**	0.325***	0.231**
QoL	166	0.295***	0.366***	0.115
GHS Index	181	0.196**	0.365***	0.286***
SMRL	175	0.021	0.165*	0.126
TSP	138	0.014	0.140	0.096
Significance level at *P<0.05, **P<0.01 and ***P<0.001				

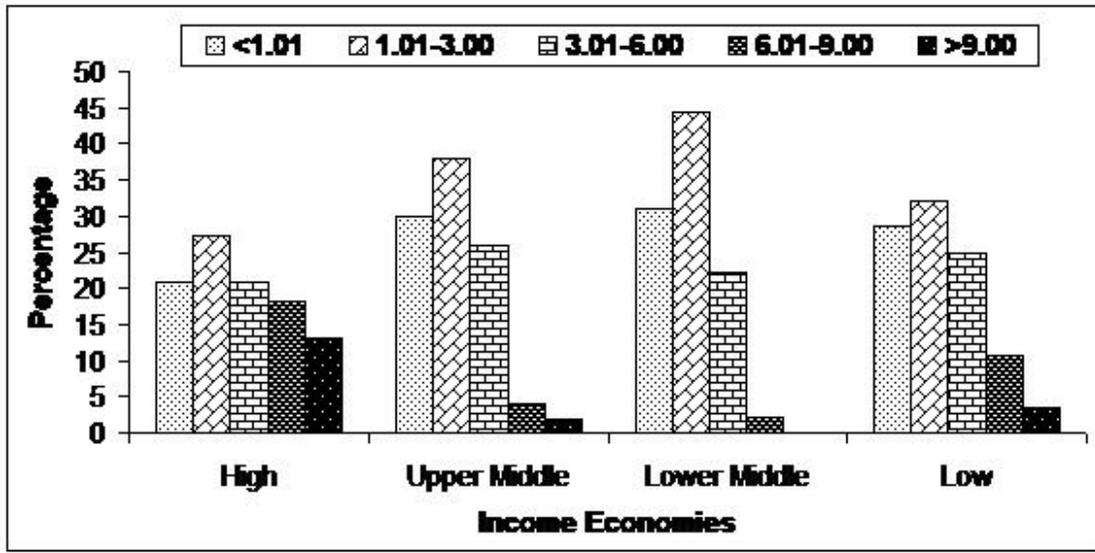
Table 2: Intra-relationship between different health and psychological wellbeing indicators

Parameters	DDP	ADP	QoL	GHS Index	SMRpL	TSP
Happiness	0.490*** (141)	0.529*** (141)	0.708*** (138)	0.676*** (142)	0.305*** (142)	0.180* (120)
DDP		0.503*** (174)	0.628*** (162)	0.469*** (174)	0.402*** (174)	0.238** (137)
ADP			0.426*** (162)	0.355*** (174)	0.044 (174)	0.030 (137)
QoL				0.702*** (163)	0.365*** (163)	0.347*** (132)
GHS Index					0.407*** (175)	0.260** (138)
SMRL						0.306*** (137)
Number of countries/territories/areas are given in parenthesis						
Significance level at *P<0.05, **P<0.01 and ***P<0.001						

Table 3. Impact of case fatality rate of the countries on the Quality of Life (Score), Anxiety Disorders (Prevalence), Depressive Disorders (Prevalence), and Global Health Security Index (Score)

Parameters	Case Fatality Rate					Sig.
	<1.01	1.01-3.00	3.01-6.00	6.01-9.00	>9.00	
QoL (Stability)	58.18±18.69	52.67±23.20	54.15±24.67	63.73±23.71	61.33±22.34	NS
QoL (Rights)	35.53±23.78	42.64±29.65	45.12±33.35	56.07±37.93	66.67±33.32	<0.05
QoL (Health)	38.48±24.39	44.62±30.13	51.34±32.92	56.80±30.37	71.89±28.35	<0.05
QoL (Security)	83.43±15.27	73.56±26.92	75.93±26.18	75.87±21.17	76.22±26.29	NS
QoL (Climate)	55.18±16.28	57.41±19.76	50.49±18.94	41.60±22.28	52.67±23.28	0.052
QoL (Costs)	51.75±14.30	46.98±13.76	47.78±17.51	40.00±16.72	37.33±12.57	<0.05
QoL (Popularity)	31.65±23.65	33.28±21.51	43.29±24.45	39.53±23.79	66.22±30.59	<0.001
QoL (Total)	51.75±10.91	51.41±14.72	53.34±16.28	54.47±17.68	61.67±15.39	NS
DDP	4.26±0.59	4.53±0.55	4.61±0.78	4.55±0.66	4.72±0.51	0.06
ADP	3.68±1.03	3.99±1.27	4.19±1.37	4.67±1.28	4.84±1.06	<0.05
GHS Index	36.22±8.72	40.94±13.27	43.91±15.13	43.65±17.99	56.55±18.83	<0.001

Figures



	High	Upper Middle	Lower Middle	Low
<1.01	20.78	30.00	31.11	28.57
1.01-3.00	27.27	38.00	44.44	32.14
3.01-6.00	20.78	26.00	22.22	25.00
6.01-9.00	18.18	4.00	2.22	10.71
>9.00	12.99	2.00	0.00	3.57

Figure 1

Impact of income economics of the countries on the case fatality rate. $\chi^2=24.953$; $P<0.05$. Data (Not for table)

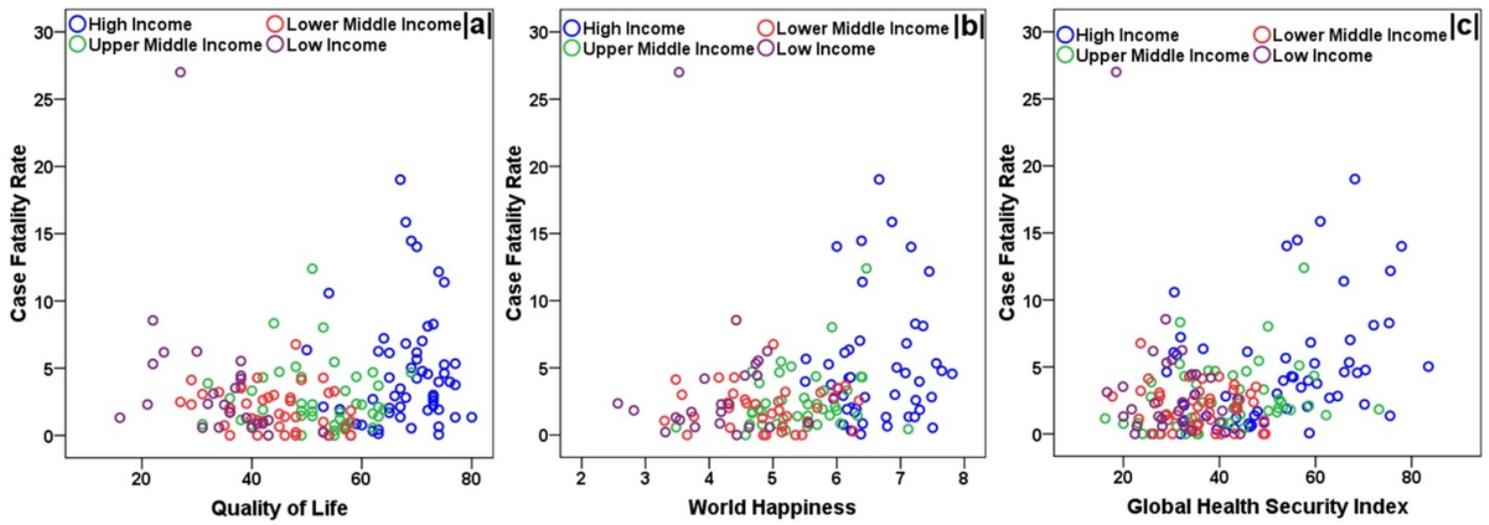
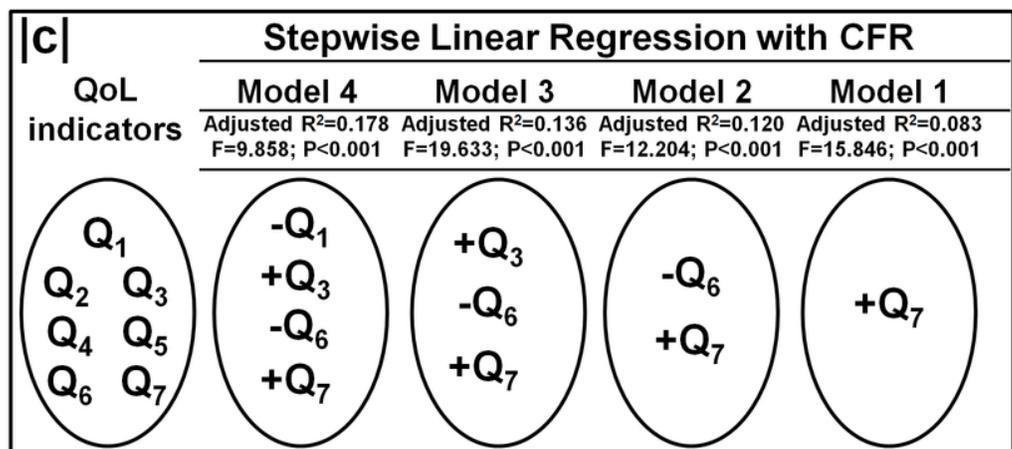
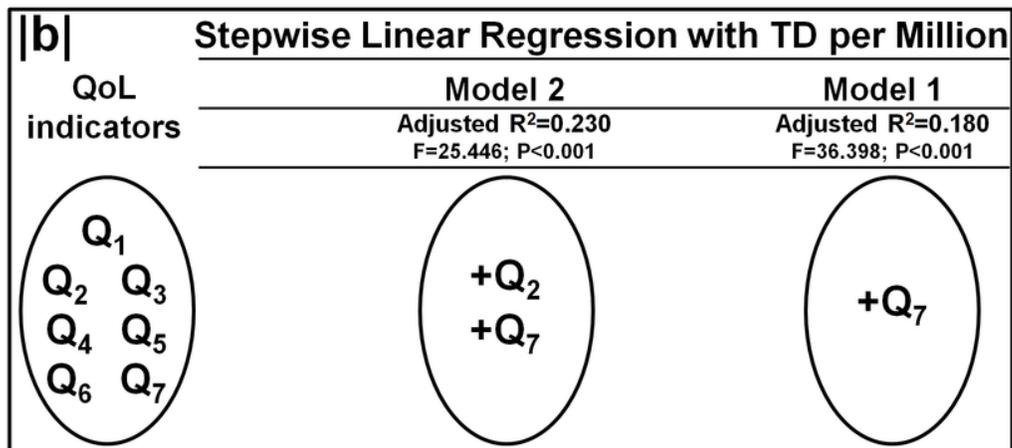
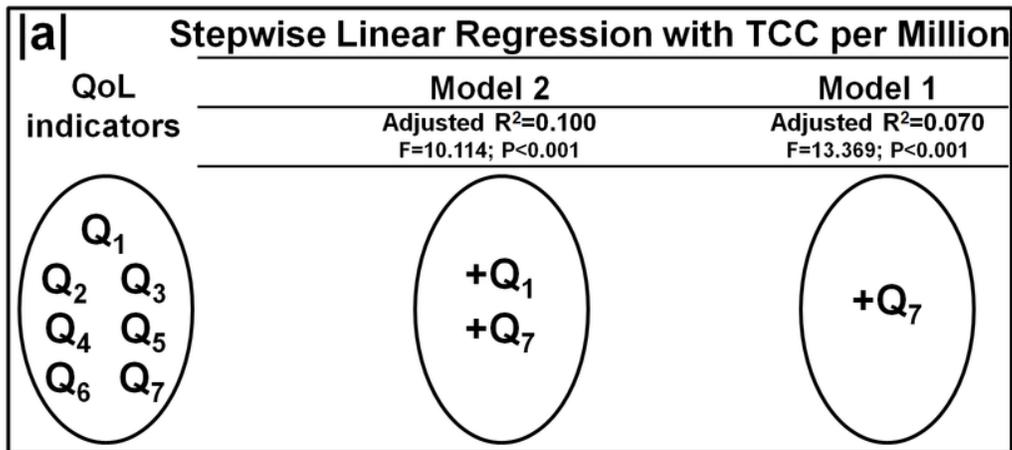


Figure 2

Effect of Quality of Life, World Happiness and Global Health Security Index on the CFR.



Q1: QoL (Stability); Q2: QoL (Rights); Q3: QoL(Health); Q4: QoL(Security); Q5: QoL(Climate); Q6: QoL(Costs); Q7: QoL(Popularity)

Figure 3

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