

Health States Utility Value in COVID-19

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Abstract

Background: The main aim of the study was extract the health utility value of coronavirus 2019 (COVID-19) disease.

Methods: In a cross-sectional study in Iran, 320 randomly selected treated patients from COVID-19 is studied. To collect the required data, we applied a questionnaire that included socio-demographic factors, clinical characteristics, and questions on the patients' Health-Related Quality of Life (HRQoL). Time trade-off (TTO) approach is used to measure the lost HRQoL attributed to COVID-19. Besides, we applied a two-limit Tobit regression model to determine the effects of the socio-demographic factors on the patients' health utility and used the visual analogue scale approach to estimate the perceived total current health status.

Results: The overall mean (SE) and median (IQR) of the health utility values were 0.863 (0.01) and 0.909 (0.21), respectively. This values for those who were willing to trade time in exchange for perfect health estimated at 0.793 (0.01) and 0.848 (0.17), respectively. The lowest amount of utility value were belonged to the elderly (mean (SE) = 0.742 (0.04); median (IQR) = 0.765 (0.42)) and those lived in rural (mean (SE)) = 0.804 (0.03); median (IQR) = 0.877 (0.30)). The univariate analysis shows that age, location living, and household size factors have a statistically significant effect on the health utility. The regression model's findings indicate that the participants' age and hospitalization status were the key determinants of COVID-19 health utility value.

Conclusion: COVID-19 is associated with a substantial and measurable diminution in HRQoL. This diminution in HRQoL can be directly compared with that induced by systemic health states.

Background

Novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome virus coronavirus 2 (SARS-CoV-2) was first identified in the world in Wuhan, China in December 2019. About three months later, the outbreak of the virus was declared by the World Health Organization (WHO) as a global health crisis and a pandemic[1, 2]. COVID-19 is an acute respiratory syndrome with common symptoms including fever, cough, shortness of breath, muscle aches, tiredness, sore throat, headache, and loss of smell and taste. Although, this disease is mild in most people and can be treated with no special treatment, in some people it can lead to serious illness and even death[3, 4]. The mortality rate and severity of the disease vary with age, underlying medical conditions such as cardiovascular disease, diabetes, cancer, and chronic respiratory disease and other health conditions[5–7]. Evidence suggests that COVID-19 has a negative effect on the physical and mental health and health-related quality of life of COVID-19 patients [8–10]

Severe acute respiratory infections annually lead to illness, death, and hospitalization of millions of people worldwide, and are one of the main reasons for the referral and hospitalization of the elderly and children[11]. By July 08, 2020, SARS CoV had infected approximately 12 million people worldwide and

killed over 540,000[12]. The rapid spread of COVID-19 worldwide has placed a heavy burden on health systems and many countries are facing a shortage of hospital equipment and facilities, such as intensive care beds and ventilation. And the number of hospitalized patients of COVID-19 has exceeded the standard capacity of hospitals[13–15]. Despite the urgent need for appropriate evidence for key decision-making, information about COVID-19 in the world is still limited. Appropriate epidemiological information is needed for appropriate policy-making and to control COVID-19 disease[16]. One of this information is the utility value of the disease. Without knowing the utility value of the disease, it is not possible to calculate the burden of the disease and conduct economic evaluation studies of preventive and therapeutic interventions[17]. Utility value for a disease indirectly indicates a patient's Health-Related Quality of Life (HRQoL) level[18, 19]. Depending on the severity of the disease, age, and the underlying medical conditions, COVID-19 disease imposes various physical and mental limitations on the patients[4, 10, 20].

The aim of this study was to calculate the disease utility of for different degrees of Covid-19 disease in different socio-economic subgroups. The findings of the study can be used in economic evaluation studies and also calculating the burden of Covid-19 disease in different geographic levels.

Methods

Study design and participants

This cross-sectional multicenter study included treated patients from COVID-19 disease was conducted at three affiliated hospitals in provinces of Kurdistan, West Azerbaijan, and Hamadan in western and northwestern Iran between May 21, 2020, and June 18, 2020. The participants included 320 randomly selected individuals who have discharged from the hospitals over the past two weeks. To avoid overestimating the disutility value for COVID-19 and to be able to extract people's logical and real judgments about the effects of the disease on the HRQoL, we studied the newly treated patients.

Diagnosis of COVID-19 has been made by trained laboratory staff using real-time reverse transcriptase polymerase-chain-reaction (RT PCR) assay for nasal pharyngeal swab specimens based on World Health Organization interim guidance[21]. No exclusion criteria were applied in this study, and only the laboratory-confirmed cases were included in the analysis. For patients under the age of 18 and those who unable to speak, the interview was conducted with the most literate member of his/her family as a proxy, who was over 15 years old.

Data collection

To collect the required data, we applied a questionnaire that included sociodemographic factors, clinical characteristics, and questions on the patients' HRQoL. The telephone interviews were conducted by three trained nurses who worked in dedicated hospital wards to patients with COVID-19. Sociodemographic variables included age, gender, living location (urban/ rural), education level (illiterate/ non-university/ university), having a job (yes/ no), marital status (single/ married), household dimension, standardized

monthly household expenditure (monthly household expenditure is divided by square root of household size), and having basic health insurance (yes/ no). This part of the questionnaire was completed self-reportedly.

Clinical characteristics cover information on having an underlying disease (yes/ no), the patient's hospitalization condition during the disease (quarantine at home/ hospitalized at general wards/ hospitalized at Intensive Care Unit (ICU) without intubation/ and hospitalized at ICU with intubation), hospitalized days, arterial blood hemoglobin oxygen saturation (SpO₂), and level of lung involvement (non or minor/ poor/ moderate/ severe). SpO₂ was measured by pulse oximeter and given as a percentage in which normal reading is considered above 95%. The overall extent of pulmonary involvement was determined objectively by the radiologists based on chest computed tomography severity score (CT-SS). The clinical information is extracted from the patients' hospital records.

Measurement of utility value

The third part of the questionnaire comprises Time Trade-off (TTO) questions to measuring the COVID-19 utility value that we used before in a similar study[22]. We first asked the participants to imagine themselves in an untreated condition of COVID-19 disease. Then, the respondent was asked how many months (X) of remained life they would give up to avoid the effects and complications of COVID-19 disease and live rest of life in perfect health. In all cases, in the first question, the amount of X was considered as 72 months (six years). This initial time was selected enough large to avoid framing effect. If the respondent agrees/ disagrees with this baseline point, interviewer increased/ decreased the X number to such an extent that the respondent subjectively becomes indifferent between their current health states in the remaining life-years (Y) and perfect health state in a shorter time and the participant considers equal value for both conditions. Dividing x by y (x/y) defines the COVID-19 disease disutility, and result of the expression of $1 - (x/y)$ presents its utility for each respondent. To measuring Y amount, we applied the Iranian life table 2016, which defines the gender-age standardized life expectancy[23]. The possible range for the TTO value is between zero for those who unwilling to lose any time of their life (non-traders) and one for persons who willing to lose all their remaining time of life to avoid the disease.

Besides, we used the visual analogue scale (VAS) approach to measuring the perceived total current health status. The respondents were asked that rate their HRQoL on a ruler, which is numbered between zero (worst HRQoL) and 10 (best HRQoL).

Statistical analysis

The descriptive results of the study were presented using statistics of number (with percentage), mean (with standard error), and mean (with interquartile range [IQR]) for all sociodemographic and clinical subgroups. Due to the utility variable has right-skewed distribution, which is confirmed by Shapiro-Wilk test, we applied non-parametric tests of Mann-Whitney and Kruskal Wallis, respectively, to statistically comparisons of observed differences of utility values for two and more than two groups. The significance

level was considered at a p-value below 0.05. The expenses were changed from Iran's national currency Rial to USD taking the average exchange rate (USD 1.00 = IRR 160000).

To determine the effects of sociodemographic and clinical factors on the amount of COVID-19 disease utility value, we applied the Two-limit Tobit regression model. Upper and lower limits were set at 1.00 and 0.00, which corresponds to utility value ranges. In this analysis, we solve the non-normal distribution of the dependent variable, utility value, by taking the logarithm transform. Those variables that had a statistically significant relationship with the level of disease utility in univariate analysis were selected as dependent factors. All statistical analyzes were performed using STATA version 15 (Stata Crop LP, College Station, TX, USA).

Results

Out of 320 invited treated patients of COVID-19 disease, 287 individuals accepted participation in the study (response rate: 89.69%). Of these, 144 (50.17%) were women, 178 (62.02%) were over 40 years old, and 264 participants (92.31%) had health insurance. Non-traders consist of about one-third (96 people) of respondents.

Table 1 presents the descriptive statistics for COVID-19 health utility value segregation by different sociodemographic subgroups. The overall mean (SE) and median (IQR) of the health utility values were 0.863 (0.01) and 0.909 (0.21), respectively. This values for traders estimated at 0.793 (0.01) and 0.848 (0.17), respectively. The lowest amount of utility value were belonged to the elderly (mean (SE) = 0.742 (0.04); median (IQR) = 0.765 (0.42)) and those lived in rural (mean (SE)) = 0.804 (0.03); median (IQR) = 0.877 (0.30)). Univariate analysis show that age, location living, and household size factors have a statistically significant effect on the disease utility.

Table 1
Utility values of Covid-19 disease among different socio-economic groups

Socio-Demographic Factors	Number (%)	Utility value		P-value
		Mean (SE)	Median (IQR)	
Total	287 (100)	0.863 (0.01)	0.909 (0.21)	
Traders	191 (66.55)	0.793 (0.01)	0.848 (0.17)	< 0.01
Non-traders	96 (33.55)	1.00 (0.00)	1.00 (0.00)	
Age groups				< 0.01
Young (< 40 yrs)	109 (37.98)	0.917 (0.01)	0.932 (0.11)	
Middle age (40–65 yrs)	115 (40.07)	0.877 (0.01)	0.886 (0.20)	
Elderly (> 65 yrs)	63 (21.95)	0.742 (0.04)	0.765 (0.42)	
Gender				0.28
Male	143 (49.83)	0.851 (0.02)	0.907 (0.23)	
Female	144 (50.17)	0.874 (0.01)	0.909 (0.17)	
Marital Status				0.15
Single	67 (23.51)	0.889 (0.02)	0.923 (0.08)	
Married	218 (76.49)	0.853 (0.01)	0.899 (0.23)	
Living location				0.03
Urban	250 (87.11)	0.871 (0.01)	0.920 (0.19)	
Rural	37 (12.89)	0.804 (0.03)	0.877 (0.30)	
Education level				0.06
Illiterate	70 (25.36)	0.821 (0.02)	0.920 (0.31)	
Non-university	136 (49.28)	0.862 (0.02)	0.899 (0.19)	
University	70 (25.36)	0.893 (0.01)	0.908 (0.15)	
Employed				0.09
Yes	125 (44.48)	0.882 (0.01)	0.904 (0.18)	
No	156 (55.52)	0.846 (0.02)	0.928 (0.24)	
Having basic insurance				0.76
Yes	264 (92.31)	0.863 (0.01)	0.909 (0.21)	
No	22 (7.69)	0.851 (0.04)	0.889 (0.18)	

Socio-Demographic Factors	Number (%)	Utility value		P-value
		Mean (SE)	Median (IQR)	
Household dimension				
< 3 persons	119 (41.46)	0.834 (0.02)	0.889 (0.24)	0.02
> 3 persons	168 (48.54)	0.882 (0.01)	0.924 (0.62)	
Standardized household's monthly cost				0.29
Lowest (< 50 USD)	193 (67.25)	0.870 (0.01)	0.909 (0.19)	
Highest (> 50 USD)	94 (32.75)	0.846 (0.02)	0.906 (0.23)	

Table 2 depicts the findings of estimated utility values of COVID-19 disease for treated patients with different clinical characteristics. Out of 287 the respondents, 107 (37.28%) had at least one underlying disease, 17 (5.92%) were hospitalized at ICU, 95 (33.10%) were hospitalized for more than four days, 217 (65.61%) had SpO2 below normal values, and 33 patients (11.5%) had moderate and severe pulmonary involvement. Factors of having an underlying disease and disease severity (in terms of hospitalization status and level of lung involvement) had a statistically significant positive effect on obtained utility values. The lowest utility values were related to intubated patients (mean (SE) = 0.629 (0.13); median (IQR) = 0.727 (0.33)), those with severe lung involvement (mean (SE) = 0.651 (0.11); median (IQR) = 0.684 (0.24)), and participants that had underlying disease (mean (SE) = 0.818 (0.02); median (IQR) = 0.886 (0.26)), respectively. The results also show that there is no statistically significant difference in currently people's perceived health status.

Table 2
Utility values of Covid-19 disease based on clinical characteristics

Socio-Demographic Factors	Number (%)	Utility value		P-value
		Mean (SE)	Median (IQR)	
Total	287 (100)	0.863 (0.01)	0.909 (0.21)	
Having underlying disease				< 0.01
Yes	107 (37.28)	0.818 (0.02)	0.886 (0.26)	
No	180 (62.72)	0.889 (0.01)	0.923 (0.08)	
Patient's condition				0.01
Quarantine at home	123 (42.86)	0.896 (0.02)	0.98 (0.13)	
General wards hospitalized	147 (51.22)	0.847 (0.01)	0.886 (0.24)	
ICU hospitalized-no-intubated	13 (4.53)	0.766 (0.06)	0.808 (0.21)	
ICU hospitalized-intubated	4 (1.39)	0.629 (0.13)	0.727 (0.33)	
Hospitalized days				
1 day	77 (26.83)	0.872 (0.02)	0.915 (0.19)	0.33
1–4 days	115 (40.07)	0.875 (0.02)	0.931 (0.17)	
Over 4 days	95 (33.10)	0.840 (0.02)	0.896 (0.25)	
Blood oxygen saturation				0.33
Normal (over 95%)	70 (24.39)	0.881 (0.01)	0.904 (0.19)	
Below normal (under 95%)	217 (75.61)	0.857 (0.01)	0.923 (0.21)	
Degree of lung involvement				< 0.01
Non/minor involved	64 (22.30)	0.927 (0.01)	0.966 (0.11)	
Poorly involved	190 (66.20)	0.844 (0.01)	0.894 (0.24)	
Moderately involved	28 (9.76)	0.859 (0.04)	0.969 (0.20)	
Sever involved	5 (1.74)	0.651 (0.11)	0.684 (0.24)	
Perceived total health status (VAS*)				0.19
> 0.7	206 (71.78)	0.869 (0.01)	0.917 (0.17)	
0.5–0.7	23 (8.01)	0.894 (0.03)	0.969 (0.23)	

*Visual Analogue Scale

Socio-Demographic Factors	Number (%)	Utility value		P-value
		Mean (SE)	Median (IQR)	
< 0.5	58 (20.21)	0.826 (0.02)	0.864 (0.26)	
*Visual Analogue Scale				

Table 3 presents the results of the two-limit Tobit regression analysis. The findings indicate that the participants' age and hospitalization status were the key determinants of COVID-19 disease utility value. As age and disease severity increases, the disease utility value statistically significantly decrease.

Table 3 Estimation results of the two-limit Tobit model of utility value for Covid-19 disease

Variables	Coefficient	t statistics	P-value	95% CI
Age	-0.004	-4.71	< 0.01	[-0.005 – -0.002]
Living location	0.059	1.46	0.14	[-0.020–0.138]
Household dimension	0.013	1.36	0.17	[-0.006–0.032]
Having underlying disease	0.016	0.48	0.63	[-0.050–0.083]
Patient's condition	0.107	4.02	< 0.01	[0.054–0.159]
Degree of lung involvement	0.036	1.27	0.20	[-0.020–0.092]
_Cons	0.485	3.23	< 0.01	[0.190–0.781]
Model statistics; Likelihood ratio = 47.33, P-value = < 0.01, Pseudo R2 = 0.302				

Discussion

This multicenter study was performed to estimate the health utility value and its clinical and socio-demographic determinants among newly treated patients from COVID-19 disease. The overall mean (median) of the disease is obtained as 0.863 (0.909). This means that patients who suffer from COVID-19 lost an average of 13.7% of their HRQoL. However, if we exclude non-traders from the analysis, the mean (median) of the disease will increase significantly to 0.793 (0.848). In other words, people who are severely affected by the disease lose an average of 20.7% of their HRQoL. The findings indicate that 33.35% of the respondents did not accept any time trade-off to get perfect health, meaning that they considered the disease's effects very insignificant and thought that there was no threat to their health. Further analysis of the data confirms this claim, as 57.29% of non-traders were quarantined at home, compared to 35.60% for traders. Besides, the overall mean of hospitalized days for non-traders and traders was 3.16 and 3.88 days, respectively.

As expected, there was a significant negative association between the severity of COVID-19 disease and the disease utility. As the highest mean utility values were observed for those patients that quarantined at home (0.896) and had minor lung infection (0.927), and the lowest mean utility values belong to the participants who intubated (0.629) and had severe lung involvement (0.651). In other words, patients who have intubated or had severe lung involvement lost 37.1% and 34.9% of their HRQoL, respectively. However, we do not observe such statistically significant associations for SpO2 levels and the number of hospital days. These results suggest that variables of the patient's hospitalization and lung health status are appropriate indicators for defining the quality of life and measuring the effects of COVID-19 disease on patients' health. However, the two-limit Tobit regression analysis results confirm only the patient's hospitalization status as representing the factor of the patient's HRQoL. Depending on the patient's hospitalization status, a statistically significant difference is seen in the average hospitalization days. This amount was 12.75, 9.31, and 3.19 days for patients admitted to the ICU with intubation and without intubation, as well as hospitalization in the general ward, respectively.

The findings showed that the severe symptoms of COVID-19 disease were significantly higher among the elderly than other age groups. As the incidence of underlying disease was 76.19% and 26.34%, the rate of moderate to high pulmonary involvement was 15.88% and 10.27%, and rate of SpO2 less than normal value were 88.89% and 71.88%, respectively among elderly and others. These observations explained the statistically significant negative association between age and utility values. As age increases, COVID-19 disease utility value dramatically falling. This value was 0.917 and 0.714 for the youth and elderly, respectively. This means that COVID-19 detriment 8.3% and 28.6% of HRQoL for these two age groups, respectively. Other studies have confirmed higher morbidity and mortality among elderly patients compared with others[24, 25]. This explanation is also correct for the variable of having underlying diseases. Respondents with underlying diseases showed statistically significantly higher severe symptoms, hospitalization rates in the ICU, and severe lung involvement than their counterpart's without underlying diseases. Therefore, both age and underlying disease factors can be introduced as confounding variables in our analysis.

COVID-19 disease in terms of a detrimental effect on HRQoL among survivors of diseases is comparable with Crohn's disease, ulcerative colitis [26], thalassemia patients that receive oral iron chelator [27], rheumatoid arthritis [28] and chronic eustachian Tube dysfunction [29]. All of these diseases lead to the loss of 15–17% of patients' HRQoL. However, it should be noted that the burden of COVID-19 disease is not comparable to the diseases mentioned above, because COVID-19, unlike others, is an acute disease and has a much higher mortality rate.

As far as we know, this study, for the first time, calculated and presented the utility value of COVID-19 disease, which has very fundamental applications in the burden of disease and economic evaluation studies. To calculate the disease burden, we must calculate the indexes of years of life lost due to premature mortality (YLL) and years lived with disability (YLD), separately[30]. Utility value for the YLL will be zero, but for YLD, we can apply the obtained overall mean (median) value for different health states in this study.

Besides, in cost-effectiveness studies on COVID-19 disease, researchers need to know the health states and associated health utility values. Based on the findings of the univariate and multivariate analysis models, it is recommended that the patient's hospitalization status (non-hospitalized, general wards hospitalized, ICU hospitalized, and intubated) be used as a reliable proxy to express the severity and grading of COVID-19 disease. Because of the disease's symptoms and complications have significant variations in different patients, the same criteria cannot be considered for all[31, 32]. Nevertheless, the patient's hospitalization status can represent all effects of COVID-19 disease. The post-hoc analysis confirmed that the mean (median) of utility values obtained for each of the four conditions has a statistically significant difference compared with its higher-grade at 0.01 significant level.

Multi-centeredness and a have a sufficient sample size in the different health states were strengths of the study. However, the findings of the study should be interpreted in light of its limitations. First, we invited the most literate persons of the family for the interview as a proxy, instead of subjects below 15 years old, which constitute 6.2% (18 persons) of the total participants. This sample selection strategy could lead to the over-estimation of the disease utility value because the mean (median) value of the disease utility was 0.966 (0.993) and 0.856 (0.904) for patients younger and older than 15 years, respectively. Second, due to the impossibility of face-to-face interviews with the participants due to the prevention of possible transmission of the disease to the interviewer, the telephone interview may have affected the responses of the participants. Third, while the respondents were newly treated from the disease, the study's clinical findings can only be generalized to the survivors. The severity of the disease among treated participants could be significantly lower than the whole patients.

Conclusion

Hospitalization status of the patients with COVID-19 is a valid factor in classification or grading the disease. These patients lost approximately an average of 13% of their HRQoL. The burden of disease caused by COVID-19 appears to be substantial.

Abbreviations

COVID-19

Coronavirus 2019; SARS-COV-2:Severe Acute Respiratory Syndrome Virus Coronavirus 2; WHO:World Health Organization; HRQoL:Health-Related Quality of Life; TTO:Time trade-off; RT PCR:Real-time reverse transcriptase polymerase-chain-reaction; ICU:Intensive Care Unit; VAS:visual analogue scale.

Declarations

Ethics approval and consent to participate

The Research Deputy of Kurdistan University of Medical Sciences approved this study (IR.MUK.REC.1399.002). Before the study, all participants gave written informed consent to participate in

the study. Also, the researchers adhered to the tenets of the Declaration of Helsinki in the implementation of all stages of the study

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflicts interests.

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Authors' contributions

BP, CA, and FZA designed the study and drafted the article. SY, AA, NS, SP, HM and GM prepared it for publication. CA, BP and FZA designed the study and reviewed the article. All authors have read and approved the manuscript.

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