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Original Article

Effect of ACE2 expression inhibiting drugs on COVID-19 disease severity, outcome and length of admission in Ethiopian patients: A causal inference using marginal structural model with inverse probability weight

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Abstract

Background: *There are varying and contradicting reports and in the face of lack of evidence generated on the effect of ACE2 (Angiotensin-converting enzyme inhibitors) expression inhibiting drugs on COVID-19 Disease. The aim of this study was to assess the effect of acute or chronic ACEIs, ARBs (Angiotensin receptor blockers) and/or NSAIDs (Nonsteroidal anti-inflammatory drugs) use on COVID-19 disease severity, outcome and length of admission among patients with COVID-19 admitted to the Millennium COVID-19 Care Center in Ethiopia.*
Methods: *A retrospective cohort study was conducted among 945 patients with COVID-19 who were on follow up from July 2nd to December 25th, 2020. Data was described using frequency tables and cross tabulations. To identify the effect of ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity, disease outcome and length of admission, Marginal Structural Model (MSM) with inverse probability weighting (IPW) approach was used.*
Results: *Among the 945 patients studied, 115 (12.2%) had a history of ACEIs, ARBs and/or NSAIDs use. At admission, the majority (39.6%) had mild disease and 272 (28.8%) had severe disease. Among the study participants, 900 (95.2%) were discharged improved and the rest 45 (4.8%) died. The median length of admission was 14.0 days (IQR, 13-16). Multinomial Logistic Regression, Log Binomial Regression and Negative Binomial Regression models were fitted to assess the effect of ACEIs, ARBs and/or NSAIDs use on disease severity, outcome and length of admission respectively. In all the three outcome models, ACEIs, ARBs and/or NSAIDs use didn't show a statistically significant association with the outcomes.*
Conclusion: *Acute or chronic use of ACEIs, ARBs and/or NSAIDs showed no effect on COVID-19 disease severity, outcome and length of admission and therefore should not be withdrawn from patients who need these therapies unless new evidences proving clear contraindications emerge.*

Keywords: *COVID-19, ACEIs, ARBs and/or NSAIDs, retrospective cohort, causal inference, Ethiopia*
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Introduction:

The Coronavirus pandemic has affected the entire world causing a tremendous loss to human life and also caused a burden to the existing health care system making it difficult to provide the best care possible for a better outcome especially in the developing countries. As a result, the World Health Organization (WHO) has continuously improved patient admission, treatment, and discharge criteria to accommodate the growing number of cases with more severe disease categories that require advanced care and close monitoring. To that end, risk stratification based on disease presentation, severity, patient characteristics, existing medical conditions and drug intake history has been given great importance. Therefore, providing preventive services and strict observation for high-risk groups should be strictly applied to prevent deterioration and complication at which point the care provided might not bring favorable results. With this aim, different research studies were conducted with results showing geographical disparity and

also inconsistency even in similar setups calling for the need for more research to be conducted especially in the African setup with limited research reports on COVID-19 so far.

Among the proposed important predictors of COVID-19 disease progression and outcome is a history of taking drugs that inhibit the expression of Angiotensin-converting enzyme 2 (ACE2). This is proposed because of the pathological process of the SARS-CoV-2 virus entry into the body using ACE2. Therefore, taking these type of drugs (ACE inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and nonsteroidal anti-inflammatory drugs (NSAIDs)) increase the level of ACE2 and in turn increasing the possibility of the virus to enter the body [1-3]. Therefore, to better understand the effect of these drugs on disease progression and outcome (hospital/ ICU admission, length of hospital stay, complications, need for mechanical ventilation and mortality), different studies in different countries were conducted reporting contradicting results.

Systematic review and meta-analysis reports demonstrated that there is no increased risk of any of the disease related complication or outcome in those with ACEIs and ARBs intake history [2, 4-6]. In addition, NSAIDs were reported to have no effect on disease progression and outcome in another systematic review [7]. Similarly, studies conducted in Italy, China, Korea, Spain and the United States showed that the use of ACEIs, ARBs and NSAIDs did not affect disease progression, complication and outcome [8-13].

On the contrary, studies conducted in Turkey and Saudi Arabia reported that ACEIs and ARBs therapy were associated with higher risk of severe or critical COVID-19 disease, need of ICU care and higher incidence of in-hospital death [14, 15]. As opposed to this, studies conducted in Kuwait, China and Canada showed that use of ACEIs and ARBs is inversely associated with ICU admission and mortality implying that these drugs have a protective effect from adverse disease outcome [3, 16-19].

ACEIs, ARB s and NSAIDs are widely used drugs for the treatment of chronic conditions which are problems in developing countries, as much as it is a developed countries problem, showing an increasing trend in recent years with a larger proportion (77%) of deaths reported from low- and middle-income countries [20]. With such varying and contradicting reports and in the face of lack of evidence generated on the effect of these drugs on the disease in the African population, clinical judgement to continue or discontinue these life-saving medications should solely rely on evidence generated from the local population.

Therefore, the aim of this study was to assess the effect of acute or chronic ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity, outcome and length of admission among patients with COVID-19 admitted to the Millennium COVID-19 Care Center in Ethiopia from July 2nd to December 25th, 2020.

Methods:

Study setting, design and population

The current study was a cross-sectional study designed to determine the incidence-associated risk factors of bacterial keratitis with their antibiotic susceptibility pattern.

The follow up was made from July 2nd to December 25th, 2020. The source population was all cases of COVID-19 admitted at MCCC with a confirmed diagnosis of COVID-19 using RT-PCR, as reported by a laboratory given mandate to test such patients by the Ethiopian Federal Ministry of Health and who were on follow up from July 2nd to December 25th, 2020 [21].

All consecutively admitted patients with COVID-19 during the follow up period and who consented to participate were included in the study. With these criteria, a total of 945 patients with COVID-19 were included in the final analysis.

Operational Definitions

COVID-19 disease [22]:

Mild Disease: characterized by fever, malaise, cough, upper respiratory symptoms, and/or less common features of COVID-19 (headache, loss of taste or smell etc…)

Moderate Disease: Patients with lower respiratory symptom/s. They may have infiltrates on chest X-ray. These patients are able to maintain oxygenation on room air.

Severe COVID-19 disease: Includes patients who have developed complications. The following features can define severe illness.

- Hypoxia: SPO2 ≤ 93% on atmospheric air or PaO2:FiO2 < 300mmHg (SF ratio < 315
- Tachypnea: in respiratory distress or RR>30 breaths/minutes
- More than 50% involvement seen on chest imaging

Data Collection Procedures and Quality Assurance

Data was extracted from patients' admission, follow up and discharge medical records using a pretested electronic data abstraction tool that is adopted from the WHO CRF (case record form)

by trained data collectors [23]. Appropriate infection prevention and control measures were followed during the data collection process. Data quality was further assured through double data entry, and data cleaning through checking for inconsistencies, numerical errors and missing parameters. Where discrepancies are observed, data entered was verified with the primary data source. Once data cleaning was complete, data was exported to STATA software version 14 (College Station, TX) for analysis

Statistical Analysis

Data was summarized using frequency tables and percentages. To compare the socio-demographic and clinical characteristics between the two groups (ACEIs, ARBs and/or NSAIDs users Vs Non users), Chi-square test, Fischer's exact test and independent t-test were used.

To identify the effect of ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity (mild vs moderate vs severe), disease outcome (alive vs dead) and length of admission (in days), Marginal Structural Model (MSM) with inverse probability weighting (IPW) approach was used.

Treatment model

The treatment model that uses binary logistic regression was fitted to estimate the probability of exposure given the covariates (propensity score). The estimated probability of exposure was used to compute the inverse probability weights for each individual. The inverse of the probability of exposure was then used to weight each individual in the estimation of the marginal odds ratio. Variables to be included in the final treatment model were selected by univariate analysis at 25% level of significance and also based on the existing literature reviewed.

Outcome models

There are three outcome variables in this study; disease severity (mild vs moderate vs severe), disease outcome (alive vs dead) and length of admission (in days). All the three outcomes were predicted by including the treatment variable alone in the respective models after adjusting for inverse probability weights.

To identify the effect of treatment on COVID-19 disease severity, Multinomial Logistic Regression model was used where adjusted relative risk (ARR), P-value and 95% CI for ARR were used to test the presence of statistically significant relationship.

To identify the effect of treatment on COVID-19 disease outcome, Log Binomial Regression model was used where adjusted relative risk (ARR), P-value and 95% CI . for ARR were used to test the presence of statistically significant relationship.

To identify the effect of treatment on length of admission, Negative Binomial Regression model was used where adjusted relative risk (ARR), P-value and 95% CI for ARR were used to test the presence of statistically significant relationship. Negative binomial Poisson regression model was used instead of Standard Poisson regression model because the assumption of Standard Poisson regression model (mean equals variance) was checked and there was over dispersion depicted by comparison of mean and variance of the outcome variable and confirmed by the significance of dispersion parameter. And finally Model fitness was checked for the Negative binomial Poisson regression model using Pearson chi square and deviance tests and the model fits the data well.

In all the three models, with a p-value of ≤ 0.05, the treatment was considered as a significant predictor of disease severity.

Ethics approval and consent to participate

The study was conducted after obtaining ethical clearance from St. Paul's Hospital Millennium Medical College Institutional Review Board. Written informed consent was obtained from the participants. The study had no risk/negative consequence on those who participated in the study. Medical record numbers were used for data collection and personal identifiers were not used in the research report. Access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the project. And all methods were carried out in accordance with relevant national guidelines and regulations.

Results

Socio-demographic and clinical characteristics

The median age of the participants was 41 (IQR, 29-58) years. More than half of the participants were males (60.6%). Four hundred thirteen (43.7%) had a history of one or more preexisting co-morbid illness. The majority had hypertension (26.9%) followed by Type II diabetes mellitus (TIIDM) (18.5%) and Asthma (5.5%). The most common reported symptoms were cough (52.9%), shortness of breath (SOB) (27.1%), fatigue (24.4%) and fever (21.8%).

One hundred fifteen (12.2%) had a history of ACEIs, ARBs and/ or NSAIDs use. At admission, the majority (39.6%) had mild disease and 272 (28.8%) had severe disease.

Among the study participants, 900 (95.2%) were discharged improved and the rest 45 (4.8%) died. The median length of admission was 14.0 days

Table 1: Socio–demographic and clinical characteristics (n=945)

Variable	Frequency (%)	Variable	Frequency (%)
Age category (in years)		Runny nose	
< 30	250 (26.5)	No	875 (92.6)
30-39	177 (18.7)	Yes	70 (7.4)
40-49	170 (18.0)	Chest pain	
50-59	125 (13.2)	No	802 (84.9)
≥ 60	223 (23.6)	Yes	143 (15.1)
Sex		Myalgia	
Female	372 (39.4)	No	812 (85.9)
Male	573 (60.6)	Yes	133 (14.1)
Preexisting Co-morbid illness		Arthralgia	
No	532 (56.3)	No	812 (85.9)
Yes	413 (43.7)	Yes	133 (14.1)
Cardiac		Fatigue	
No	886 (93.8)	No	714 (75.6)
Yes	59 (6.2)	Yes	231 (24.4)
Hypertension		SOB	
No	691 (73.1)	No	689 (72.9)
Yes	254 (26.9)	Yes	256 (27.1)
Type II Diabetes Mellitus		Headache	
No	770 (81.5)	No	793 (83.9)
Yes	175 (18.5)	Yes	152 (16.1)
Asthma		ACEIs, ARBs and/or NSAIDs use	
No	893 (94.5)	No	830 (87.8)
Yes	52 (5.5)	Yes	115 (12.2)
Fever		COVID-19 Severity	
No	739 (78.2)	Mild	374 (39.6)
Yes	206 (21.8)	Moderate	299 (31.6)
Cough		Severe	272 (28.8)
No	445 (47.1)	Outcome	
Yes	500 (52.9)	Alive	900 (95.2)
Sore throat		Dead	45 (4.8)
No	827 (87.5)		
Yes	118 (12.5)		

Comparison of socio-demographic and clinical characteristics based on drug use history

Based on the chi-square or Fisher's exact test and independent t-test result, a significant difference between those who has a history of ACEIs, ARBs and/or NSAIDs use and those who don't indicated that the two groups showed a significant difference in age category, the presence of shortness of breath, disease severity, outcome and length of admission.

Accordingly, a significantly higher proportion of patients who has a history of ACEIs, ARBs and/or NSAIDs use are in the age range of 50-59 years (27.0 % Vs 11.3%, p-value<0.0001) and 60 years and older (47.0 % Vs 20.4%, p-value<0.0001) compared to those with no drug use history.

In addition, patients with a history of ACEIs, ARBs and/or NSAIDs use were found to present with shortness of breath and severe COVID-19 at a significantly higher proportion as compared with those with no

drug use history (41.7% % Vs 25.1%, p-value<0.0001 for shortness of breath and 47.0% % Vs 26.3%, p-value<0.0001 for severe COVID-19). Moreover, a significantly higher proportion of patients with a history of ACEIs, ARBs and/or NSAIDs use died of COVID-19 compared to those with no drug use history (9.6% % Vs 4.1%, p-value=0.010).

Furthermore, a statistically significant difference was observed in the length of admission, where having a history of ACEIs, ARBs and/or NSAIDs use was associated with a delayed recovery compared to those with no drug use history (14.5 days Vs 14.4 days, p-value=0.002). But this difference might not have a significant clinical implication. **(Table 2**)

Table 2: Comparison of socio-demographic and clinical characteristics based on drug use history (n=945)

Variable	ACEIs, ARBs and/or NSAIDs use		p-value
	No (n=830)	Yes (n=115)	
Age category (in years)			
< 30	246 (29.6 %)	4 (3.5 %)	<0.0001*
30-39	168 (20.2 %)	9 (7.8 %)	
40-49	153 (18.4 %)	17 (14.8 %)	
50-59	94 (11.3 %)	31 (27.0 %)	
≥ 60	169 (20.4 %)	54 (47.0 %)	
Sex			
Female	332 (40.0 %)	40 (34.8 %)	0.283
Male	498 (60.0 %)	75 (65.2 %)	
Fever			
No	642 (77.3 %)	97 (84.3 %)	0.088
Yes	188 (22.7 %)	18 (15.7 %)	
Cough			
No	385 (46.4 %)	60 (52.2 %)	0.244
Yes	445 (53.6 %)	55 (47.8 %)	
Sore throat			
No	726 (87.5 %)	101 (87.8 %)	0.914
Yes	104 (12.5 %)	14 (12.2 %)	
Runny nose			
No	767 (92.4 %)	108 (93.9 %)	0.564
Yes	63 (7.6 %)	7 (6.1 %)	
Chest pain			
No	706 (85.1 %)	96 (83.5 %)	0.657
Yes	124 (14.9 %)	19 (16.5 %)	
Myalgia			
No	712 (85.5 %)	100 (87.0 %)	0.735
Yes	118 (14.2 %)	15 (13.0 %)	
Arthralgia			
No	712 (85.8 %)	100 (87.0 %)	0.735
Yes	118 (14.2 %)	15 (13.0 %)	
Fatigue			
No	626 (75.4 %)	88 (76.5 %)	0.797
Yes	204 (24.6 %)	27 (23.5 %)	
SOB			
No	622 (74.9 %)	67 (58.3 %)	<0.0001*
Yes	208 (25.1 %)	48 (41.7 %)	
Headache			
No	695 (83.7 %)	98 (85.2 %)	0.685
Yes	135 (16.3 %)	17 (14.8 %)	
COVID-19 Severity			
Mild	344 (41.4 %)	30 (26.1 %)	<0.0001*
Moderate	268 (32.3 %)	31 (27.0 %)	
Severe	218 (26.3 %)	54 (47.0 %)	
Outcome			
Alive	796 (95.9 %)	104 (90.4 %)	0.010*
Dead	34 (4.1 %)	11 (9.6 %)	
Length of admission (in days)	14.5 (5.03)	14.4 (5.99)	0.002*

Treatment model: Logistic regression of factors affecting use of ACEIs, ARBs and/or NSAIDs

The treatment model using a binary logistic regression model was run by including variables that were significant on univariate analysis at 25% level of significance and also from variables selected to be useful based on literature review [24-32].

Table 3: Treatment model: Binary Logistic Regression model of factors affecting use of ACEIs, ARBs and/or NSAIDs (n=945)

Variables	AOR	95% CI for AOR	p-value
Age category (in years)			
< 30	1	1	
30-39	2.07	0.58, 7.32	0.261
40-49	1.69	0.49, 5.73	0.398
50-59	3.82	1.14, 12.79	0.030*
≥ 60	1.89	0.57, 6.37	0.300
Male sex (Vs Female)	1.83	1.08, 3.11	0.025*
Cardiac illness (Yes Vs No)	9.95	4.69, 21.09	<0.0001*
Hypertension (Yes Vs No)	14.87	7.89, 28.01	<0.0001*
Type II Diabetes Mellitus (Yes Vs No)	1.52	0.88, 2.64	0.137
Asthma (Yes Vs No)	1.69	0.66, 4.32	0.278
Fever (Yes Vs No)	0.69	0.33, 1.44	0.323
Cough (Yes Vs No)	0.57	0.31, 1.04	0.065
Sorethroat (Yes Vs No)	1.06	0.46, 2.43	0.895
Runny nose (Yes Vs No)	1.40	0.47, 4.18	0.543
Chest pain (Yes Vs No)	1.49	0.69, 3.25	0.313
Myalgia (Yes Vs No)	1.31	0.53, 3.22	0.558
Arthralgia (Yes Vs No)	0.62	0.23, 1.72	0.360
Fatigue (Yes Vs No)	0.53	0.25, 1.12	0.095
Shortness of breath Yes Vs No)	1.67	0.87, 3.19	0.121
Headache (Yes Vs No)	1.55	0.75, 3.24	0.239

Note: AOR, Adjusted Odds ratio; CI, Confidence interval; *statistically significant

Accordingly, age category, sex, cardiac illness, hypertension, TIIDM, asthma, fever, cough, sore throat, runny nose, chest pain, myalgia arthralgia, fatigue, shortness of breath and headache were included in the final treatment model. By fitting the final treatment model, propensity score was estimated and it was used to compute the inverse probability weights for each individual. The inverse of the probability of exposure was then used to weight each individual in the estimation of the marginal odds ratio. (**Table 3**)

Outcome Model: Effect of ACEIs, ARBs and/or NSAIDs use on disease severity, outcome and length of admission

Three outcome models; Multinomial Logistic Regression, Log Binomial Regression and Negative Binomial Regression models were fitted to assess the effect of ACEIs, ARBs and/or NSAIDs use on disease severity, outcome and length of admission respectively. To predict all the three outcomes, the treatment variable was fitted as an explanatory variable after adjusting for inverse probability weights.

The result shows that patients who were taking ACEIs, ARBs and/or NSAIDs had a slightly increased risk of progressing to severe disease and dying from COVID-19. On all the three outcome models, ACEIs, ARBs and/or NSAIDs use didn't show a statistically significant association with all the three outcomes at 5% level of significance. (**Table 4, 5 and 6**)

Table 4: Multinomial logistic regression of Effect of ACEIs, ARBs and/or NSAIDs use on disease severity (n=945)

Variable	Moderate (Vs Mild)		Severe (Vs Mild)	
	ARR (95% CI)	P-value	ARR (95% CI)	P-value
ACEIs, ARBs and/or NSAIDs				
No	1		1	
Yes	0.76 (0.25, 2.31)	0.628	1.21 (0.45, 3.27)	0.708

Note: ARR, Adjusted Relative Risk; CI, Confidence Interval; *statistically significant

Table 5: Log binomial regression of Effect of ACEIs, ARBs and/or NSAIDs use on disease outcome (n=945

Variable	Death(Vs Disharged improved) ARR (95% CI)	P-value
ACEIs, ARBs and/or NSAIDs		
No	1	
Yes	1.14 (0.27, 4.82)	0.861

Note: ARR, Adjusted Relative Risk; CI, Confidence interval; *statistically significant

Table 6: Negative binomial regression of Effect of ACEIs, ARBs and/or NSAIDs use on length of admission (n=945)

Variable	Length of admission ARR (95% CI)	P-value
ACEIs, ARBs and/or NSAIDs		
No	1	
Yes	0.99 (0.88, 1.11)	0.842

Note: ARR, Adjusted Relative Risk; CI, Confidence interval; *statistically significant

Discussion

In this study, we assessed the effect of acute or chronic ACEIs, ARBs and/or NSAIDs use on COVID-19 disease severity, outcome and length of admission among patients with COVID-19 admitted to the Millennium COVID-19 Care Center in Ethiopia from July 2nd to December 25th, 2020. To our knowledge, this is the first study conducted in the African set up. Understanding this helps (provides an input) in modifying the risk stratification, prevention and admission practices so that better patient outcome can be achieved.

One hundred fifteen (12.2%) had a history of ACEIs, ARBs and/or NSAIDs use. At admission, the majority (39.6%) had mild disease and 272 (28.8%) had severe disease. Among the study participants, 900 (95.2%) were discharged improved and the rest 45 (4.8%) died. The median length of hospital admission was 14.0 days (IQR, 13-16).

On comparison of the characteristics of the cohort based on the other exposure variables and the outcomes, a significant difference was observed in some characteristics. Accordingly, a significantly higher proportion of patients with a history of ACEIs, ARBs and/or NSAIDs were 50 years and older, had shortness of breath at admission, severe disease at presentation, had delayed recovery and died from the disease. But on further regression analysis using MSM model with IPW approach, use of ACEIs, ARBs and/or NSAIDs did not show a significant effect on disease severity, outcome and length of admission. Although there are few contradictory reports showing that these drugs have a significant effect on both directions affecting the disease outcome both negatively and positively [14-16], this finding is supported by a number of other institution and community based studies including systematic reviews conducted in non-African setup [4-13]. In addition, a WHO review based on studies conducted outside Africa also showed that there is no well-established evidence that patients on these drugs are at higher risk of poor outcome [32]. It is not known if the finding of the study has consistency across Africa as there is no similar study conducted in the continent so far.

ACEIs, ARBs and/or NSAIDs are drugs which are widely used for the treatment of chronic medical conditions. In the current study, chronic medical conditions were reported in 413 (43.7%) of the participants among which hypertension and cardiac disease, which rely mainly on these drugs for treatment and control, constitutes 313 (75.8%) of the co-morbid illnesses. In addition, at the global and national level, these conditions are found in a considerable proportion of the general population, implying that the issue of continuing or discontinuing these drugs in patients with COVID-19 will continue to be raised. These medical conditions are also found to be significant determinants of disease severity and outcome among patients with COVID -19 [24, 7]. Part of COVID-19 management is stabilizing existing co-morbid conditions so that the body can be at its best immunity for fighting the virus. Therefore, taking these medications is crucial to control the co-morbid conditions which otherwise could exacerbate and lead to progression of the disease leading to complications and death as demonstrated by findings of researches conducted in Ethiopia and other African countries [24-28, 31, 38-40].

Therefore, the use of these drugs is crucial as part of the management of patients with COVID-19

with co-morbid conditions without affecting the COVID -19 disease severity, outcome and length of admission [2, 4-6] or even with the possibility of leading to improved outcome as indicated by recent reports [1-3, 17-19].

The following strengths and limitations should be considered when interpreting the study findings. Its strength is that, it is the only study conducted in the country and one of the few in Africa. In addition, the study is conducted in Ethiopia's largest COVID-19 Center, which also serves as a national referral center, and thus is representative of patients across the country. The other strength is the use of causal inference model to answer the research question which can give us a more accurate inference about the causal relationship between the exposure and outcome. It does, however, have the following limitations: behavioral factors, laboratory and radiologic parameters were not included in the study because information on these variables were not consistently available for every participant.

Conclusion

Based on the finding of this study, acute or chronic use of ACEIs, ARBs and/or NSAIDs showed no effect on COVID-19 disease severity, outcome and length of admission. As a result, unless new evidences proving clear contraindications emerge, we recommend that clinical decision in favor of continuing these drugs for the greater benefit of controlling the co-morbid conditions of patients of any COVID-19 severity would benefit the patient more.

List of Abbreviations

ACE2……Angiotensin-converting enzyme 2
ACEIs……Angiotensin-converting enzyme inhibitors
ARBs……. Angiotensin receptor blockers
ARR…….....Adjusted relative risk
CI…….Confidence Interval
COVID-19…...Coronavirus Disease 2019
IPW……..Inverse probability weighting
IQR……. Interquartile range
NSAIDs……...Nonsteroidal anti-inflammatory drugs
MSM……Marginal Structural Model
OR ……...Odds Ratio
RT-PCR…… Real Time Polymerase Chain Reaction
SARS-COV-2……Severe Acute Respiratory Syndrome Coronavirus 2
TIIDM……Type II Diabetes Mellitus
WHO……. World Health Organization

Consent for publication

Not applicable

Availability of data and materials:

All relevant data are available upon reasonable request from Tigist W. Leulseged, tigdolly@gmail.com.

Competing interests

The authors declare that they have no known competing interests.

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Authors' Contribution:

TWL conceived and designed the study, revised data extraction sheet, performed statistical analysis, and drafted the initial manuscript. ISH, WCZ, EHM, LKN, YGT, MGE, NAB, FEM, ZAT, NTK, HND and DAA contributed to the conception, obtained patient data, reviewed the manuscript and approved the final version.

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