



**ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE
POST-GRADUATE STUDY PROGRAM**

**THE EFFECT OF DIABETES MELLITUS AND CLINICAL
CHARACTERISTICS ON COVID-19 OUTCOME AMONG
HOSPITAL ADMITTED COVID 19- PATIENTS AT ALERT
HOSPITAL, ADDIS ABABA, ETHIOPIA**

BY: ABRAHAM TEKOLA GEBREMEDHIN

NOVEMBER /2022



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COVID-19 OUTCOME AMONG HOSPITAL ADMITTED COVID 19- PATIENTS AT
ALERT HOSPITAL, ADDIS ABABA, ETHIOPIA: A RETROSPECTIVE CHART
REVIEW STUDY**

**A RESEARCH THESIS TO BE SUBMITTED TO DEPARTMENT OF PUBLIC
HEALTH FOR THE PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE
MASTER'S DEGREE IN PUBLIC HEALTH TRACK TO EPIDEMIOLOGY; AT ST
PAUL HOSPITAL MILLENNIUMMEDICAL COLLEGE
ADDIS ABABA, ETHIOPIA**

BY: ABRAHAM TEKOLA GEBREMEDHIN (B.SC. PUBLIC HEALTH)

ADVISORS:

- 1. MR. KNIFE HAILE (MPH)**
- 2. MR. GETACHEW TILAHUN (MPH)**

NOVEMBER /2022

Acknowledgement

First and foremost, I would like to Praise and thank God, the Almighty who provides me health to do all activities; He gave me the spirit to write this research thesis and helped me to see this day. Then, I would like to provide my heartfelt thanks to my advisor, Mr., Kinfu H. (MPH), and Mr. Getachew T. (MPH) who provide constructive and supportive feedbacks while writing my final thesis. Besides of this I would like to thank St Paul Hospital millennium medical college and Armauer Hansen research institutes and I also thanks all lecturer and management team for their guidance and unreserved support while staying here. I would like to deeply express my gratefulness to the department of public health for providing me with the opportunity to enroll in this program. Moreover, I say thanks again to all who contribute their positive idea for the completion of this thesis and who gave technical support.

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Abbreviations

List of abbreviations**Descriptions of Abbreviations**

ACE2	Angiotensin-converting Enzyme 2
AHRI	Armauer Hansen Research Institute
AKI	Acute Kidney Injury
ALERT	All African Leprosy rehabilitation training Center
ALT	Alanine transferase
AMI	Acute Myocardial Infarction
ANC	absolute neutrophil count
aPTT	activated partial thromboplastin time
ARDS	Acute Respiratory Syndrome
AST	Aspartate Transferase
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CI	Confidence Interval
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CPK	Creatinine Phosphokinase
CRP	C-reactive protein
CT	Computed Tomography
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
ESC	Electrolyte sedimentation rate
ESC	European Society of Cardiology
ETB	Ethiopian Birr

HD	Hemodialysis
HR	Hazard ratio
ICU	Intensive care units
IL	Interleukins
LC	loss of consciousness
LDH	Lactate Dehydrogenase
LOS	Length of stay
MERS	Middle East Respiratory syndrome
NLR	Neutrophil to lymphocyte Ratio
NEWS	National Early Warning System
PMNC	Peripheral Mono Nuclear cell
RNA	Ribonucleic Acid
SARS	Severe Acute Respiratory syndrome
SD	Standard deviation
UK	United Kingdom
USA	United States of America
WBC	White Blood Cell Count
WHO	World Health Organization

Abstract

In late 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) was discovered in Wuhan, China and with the virus's rapid global spread, clinicians are increasingly confronted with challenges regarding the potential impact of preexisting conditions such as hypertension, cardiovascular disease, cancer, asthma, HIV, tuberculosis, and diabetes mellitus (DM) on the course and outcome of COVID-19. The purpose of this study is to assess the effects of diabetes on the outcomes of COVID-19 among hospitalized patients.

Methods: A retrospective chart review study on COVID-19-diagnosed patients admitted to ALERT Hospital was conducted from June 2022 to August 31, 2022. This study included 133 confirmed COVID-19 patients over the age of 18, and charts were chosen using systematic random sampling. Data were collected retrospectively from the patient's chart. Finally, SPSS version 25.0 software was used to analyze the data. The bivariate and multivariate logistic regression models were used to assess the relationship between the dependent and independent variables, and p-values less than 0.05 were considered statistically significant.

Result: A total of 133 participant charts were included in the study. The overall mortality rate was 22.6%, and the rate in the presence of diabetes was 34.9%. (p-value 0.021). At admission, diabetic patients had a higher proportion of fever, LC, and inability to walk (p-value 0.04) than non-DM patients. Diabetic patients had higher WBC, HbA1C, RBS, CRP, TBL, and creatinine levels than non-DM COVID-19 patients (p-value 0.05). Mortality outcome for diabetes (OR 1.9 [95% CI (0.7-4.8)], hypertension (OR 2.4 [95% CI 0.9--6.0]), cardiovascular disease (CVD), and asthma (OR 5.6 [95% CI 0.9-33.4]). ICU admission for diabetes (OR 2.3 [95% CI (1.1-4.8)]). The mean HbA1C in non-survivor COVID-19 patients was higher (p-value 0.021) than in survivors.

Conclusion: DM was not associated with mortality from COVID-19. Cardiovascular disease and uncontrolled hemoglobin A1C were the most common risk factors for mortality from COVID-19. DM increases ICU admission from COVID-19. Atypical clinical findings and co-existing comorbidities, such as CVD and DM should receive special attention by policymakers and medical professionals.

Key words: COVID-19; Diabetes mellitus; Survival; Retrospectives; Comorbidities; Outcome

Introduction

Back ground

The Coronaviridae family has become the foremost micro-organism triggering increasing disease outbreaks. It is a vast family of single-stranded RNA viruses (+ssRNA) that can be isolated from totally different animal species. [1] The route of transmission for “COVID-19” is made directly between humans through droplets and respiratory secretions and indirectly through contact with contaminated surfaces and can also be transmitted by asymptomatic and symptomatic individuals.

The main symptoms of “COVID-19” disease may be asymptomatic and typical symptoms include fever, dry cough, shortness of breath, muscle pain, and arthritis. Gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and diarrhea have been reported and neurologically related symptoms, particularly anosmia, hyposmia, and dysgeusia, have also been reported. Physical examination may find fever in over 44% of patients (and could be documented in over 88% of patients after admission), increased respiratory rate, acute respiratory disease, and maybe decreased consciousness, agitation, confusion, and tiredness. [2, 4]

Diabetes is a metabolic disease that occurs due to inflammation in a complex immunological process. Insulin resistance due to insulin signaling inhibition results in a series of immune responses that exacerbate the inflammatory state, which leads to hyperglycemia.[8, 9]. The results of the 1960s COVID-related pandemic are influenced by DM, which has also recently been linked to the Middle East respiratory syndrome (MERS-CoV) outbreak of 2012 and the severe acute respiratory syndrome (SARS) outbreak of 2003.[14] The recently identified coronavirus which is a severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) pandemic virus, which causes pneumonia, originated in Wuhan, China, in late 2019 and is spreading rapidly to other countries.[3].

Diabetes mellitus is associated with the pro-inflammatory state and the attenuation of the innate immune response. Individuals with diabetes have been linked to increased susceptibility to and adverse outcomes associated with infections, especially influenza and pneumonia. Metabolic disorders may impair the functions of macro- phages and lymphocytes and thereby lead to low immune function, which predisposes people to disease complications.[12]

Statement of problem

Diabetes mellitus is one of the World Health Organization's four prioritized non-communicable diseases [2]. Diabetes has been identified as a significant risk factor for a number of infections, post-infection sequelae, and mortality from severe infections. Diabetes is a growing global health concern in patients with Coronavirus Disease 2019 (COVID-19) infection, the prevalence of diabetes mellitus has varied between nations, ranging from 5-20% in China to 17% in Lombardy and Italy to 33% in the USA.[3] New research indicates a link between comorbid diabetes and illness progression and death in patients with "COVID-19" and earlier SARS-related pandemics [4, 5]. Due to changes in the immune system, DM increases the risk of infections because of alterations in the immune response.[1] Diabetes mellitus has emerged as a significant risk factor for severe immune response failure.[6] Some studies show that diabetes has a negative effect on infection, while others show that it has a neutral effect even after controlling for confounding variables.[7–9] Previous research has found a link between HbA1c and the risk of being admitted to the hospital for infections in general, and respiratory infections in particular.[10]

According to studies, hyperglycemia may be a major contributing factor to a poorer prognosis of "COVID-19," and has been proposed as a risk factor for predicting ICU admission and negative outcomes in "COVID-19" patients.[11] In terms of predictors, preliminary data from 191 SARS-CoV2 infected patients in Wuhan revealed that advanced age and the presence of pre-existing conditions such as hypertension, cardiovascular disease, and diabetes mellitus (DM), as well as elevated inflammatory markers, are the most common.[12] According to a study conducted in the United States, the mortality rate in 184 patients with diabetes and uncontrolled hyperglycemia was 28.8%, compared to 6.2% in 386 patients without diabetes or hyperglycemia.[13]

On March 11, 2020, the World Health Organization (WHO) proclaimed "COVID-19" a global pandemic. As a result, social containment strategies have been implemented globally and hospital systems have been redesigned to handle an increase in the number of critically ill people.[16] Despite the "COVID-19" prevention strategy being in place, until December 26, 2021, there were 11% more new cases globally than the week before, but there were about the same number of new deaths as there had been the week before.[17] This translates to more than 44 000 extra deaths and just under 5 million new cases. Over 278 million cases and about 5.4 million deaths had been documented globally as of December 26, 2021.[17]

According to the WHO weekly epidemiological update of the "COVID-19" report, Africa ranks second only to America in terms of the percentage of "COVID-19" cases reported compared to the previous week's "COVID-19" update.[17] The Federal Ministry of Health announced the first confirmed coronavirus disease (COVID-19) in Ethiopia on March 13, 2020. It is the first to be reported in Ethiopia since the outbreak began in China in December 2019.[18] According to the Ethiopian Federal Ministry of Health's Daily "COVID-19" report, there have been 460,602 confirmed cases and 7,212 coronavirus-related deaths reported in Ethiopia since the pandemic began on January 21, 2022. [19]

A study conducted at the millennium "COVID-19" care center in Ethiopia found that mortality was higher in "COVID-19" patients who had diabetes [20]. However, the relationship between underlying clinical and laboratory parameters on diabetic COVID-19 patients and the poorer outcome of COVID-19 patients with DM was not well understood. The purpose of this study is to determine whether diabetes has an effect on COVID-19 outcome and to identify predictors of poorer COVID-19 outcome. Finally, the findings of this study will provide critical evidence for policymakers and health care practitioners to develop novel strategies and interventions to treat COVID-19 diabetes patients.

Significance of the study

COVID-19 has become a significant global challenge, particularly in poor countries with underdeveloped health systems, such as Ethiopia. Morbidity and mortality are still major threats to global health as a result of the COVID-19 pandemic, and diabetes is one of the comorbidities associated with morbidity and mortality in COVID-19 patients. The emergence of a new COVID-19 strain adds to the difficulty of halting the pandemic's spread.

Several factors, including impaired immune response, heightened inflammatory response, and comorbidities, were thought to be associated with COVID-19 mortality. Nonetheless, there are numerous contradictory issues for which evidence is somewhat limited. As a result, it is critical to investigate the effect of diabetes mellites on COVID-19 outcome and specific COVID-19 characteristics in diabetics. This aids in the development of diabetic patient-specific treatment strategies for these individuals who have comorbidities in addition to COVID-19 infection. Although the national comprehensive COVID-19 management guidelines include a COVID-19 management strategy for pediatric, pregnant, and adult COVID-19 patients, special management for patients with comorbidities such as diabetes is not yet included.

Finally, the findings of this study contribute to the development of novel strategies and interventions for COVID-19 patients with diabetes by policymakers and health care practitioners.

Literature Review

The outbreak of the coronavirus disease 2019 has become a public health emergency of international concern,[2] caused by a novel enveloped RNA beta-coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which originated from Wuhan China.[3–5]The virus interaction with ACE2 may downregulate the anti-inflammatory function and heighten angiotensin II effects in predisposed patients and it is the enzyme, which is essential for adhesion and uptake of the virus into cells before replication. [6] “COVID-19” infects people of all ages however, there are two main groups at a higher risk of developing severe disease, these are older people, and people with underlying comorbidities such as diabetes mellitus, hypertension, cardiorespiratory disorders, chronic liver diseases, and renal failure.[6] Patients with cancer and those receiving immunosuppressive medication as well as pregnant people are also thought to be at a higher risk of developing the severe disease when infected.[6, 7]

Diabetes is a metabolic disease that occurs due to inflammation in a complex immunological process. Insulin resistance due to insulin signaling inhibition results in a series of immune responses that exacerbate the inflammatory state, which leads to hyperglycemia.[8, 9]

Many reports show that DM is a frequent pre-existing condition that is associated with severe disease and death in patients with “COVID-19”. [10] Upon infection with SARS-Cov-2 and the increased viral load due to replication of the virus in many cells throughout the body, the pre-existing chronic inflammation is further increased and plays a critical role in the progression of “COVID-19”. [10]

A vulnerable population, with chronic health conditions such as diabetes and cardiovascular or lung disease, is at higher risk of developing severe illness with “COVID-19”. This population is also faced with an increased risk of death in the event of illness. Multiple comorbidities in “COVID-19” patients are linked to severe clinical symptoms, disease complications, and critical disease progression.[7]The presence of one or more comorbidities worsened the survival rate of covid 19 patients.[7, 11] Individuals with diabetes are at higher risk of various acute and chronic infections compared with non-diabetic individuals.[2] During the SARS pandemic, the rate of admission to intensive care unit (ICU), need for mechanical ventilation, and mortality of diabetic patients was three-fold greater than that of non-diabetic patients[3]. A report showed that

diabetes triples the risk of hospitalization after influenza A (H1N1) and quadruples the risk of ICU admission and Under Middle East Respiratory Syndrome Coronavirus (MERS-Cov) infection, diabetes was considered an important risk factor for developing into severe “COVID-19” cases.[3, 5, 12]

Current evidence has demonstrated that patients with both “COVID-19” and diabetes are more likely to develop severe “COVID-19” [22] and 30.6% of patients admitted to hospitals with “COVID-19” have exposure to diabetes. Therefore, the prevalence of hospitalized patients with diabetes and “COVID-19” was seven times greater than the local population prevalence of 4.2% in Brighton and Hove, UK.[13]

Meta-analyses have indicated that individuals with type 1 or type 2 diabetes are at increased risk of suffering from a severe form of “COVID-19” and have a higher mortality rate than the non-diabetic population. Patients with diabetes have chronic, low-level systemic inflammation, which results in the whole cellular dysfunction underlying the wide variety of symptoms associated with the disease, including an increased risk of respiratory infection. [14] The increased severity of “COVID-19” amongst patients with diabetes is not yet fully understood and there is no consistent finding from related studies. [6, 15]

Another study shows that diabetes is one of the major risk factors associated with the poor outcome and mortality of “COVID-19” patients.[5, 16] “COVID-19” patients with diabetes have a higher prevalence of comorbidities such as hypertension, higher levels of inflammatory markers, lower eGFR, and a higher incidence of in-hospital complications, which illustrates the possible multifaceted pathological mechanistic pathways triggered by hyperglycemia that lead to worse outcomes and mortality. [9, 16]

Finding inconsistency is frequently observed in different articles. A study done in the United Kingdom teaching Hospital indicates that there was no association between glycemic control, before and during hospitalization, and mortality,[13] however another study indicates that patients with diabetes had longer hospital stays, greater disease severity, and increased mortality due to “COVID-19”.[13, 17, 18] Diabetes Mellitus was also found to be common comorbidity with “COVID-19”, and a study from Wuhan city China indicates Severe pneumonia caused by “COVID-19” infection predisposes diabetic patients to a higher need for critical care and mechanical ventilation.[19] a study done in America indicates the mortality rate was 28.8% in

184 diabetes and uncontrolled hyperglycemia patients, compared with 6.2% of 386 patients without diabetes or hyperglycemia.[11]

Laboratory investigations also highlighted remarkably indicate that higher C-reactive protein levels in “COVID-19” patients and lower estimated glomerular filtration rate foster the poor outcome of the disease.[16] A meta-analysis evaluated 16 retrospective studies and found that inflammatory markers, especially CRP, pro-calcitonin, IL-6, and ESR were related to the severity of “COVID-19”. [20]

Another study done at Royal Sussex County Hospital and Princess Royal Hospital indicates that age and male sex are predominantly associated with a higher prevalence of “COVID-19” and a more severe clinical course with mortality but in that study diabetes mellitus has no association with mortality and this is not consistent with another study done in Saudi Arabiya and China.[4, 13, 21, 22] In a retrospective analysis of patients with “COVID-19”, those with diabetes had a greater prevalence of hypertension, cardiovascular disease, and cerebrovascular disease than those without diabetes, and non-survivors had a greater prevalence of comorbidities than survivors.[22]

A study indicates that DM patients, compared to patients without DM, had higher National Early warning system (NEWS) rates of progression to mortality, ARDS, septic shock ICU care, and acute cardiac injury.[23] The mortality rate was 28.8% in 184 diabetes and uncontrolled hyperglycemia patients, compared with 6.2% of 386 patients without diabetes or hyperglycemia.[11]

Diabetes mellitus is associated with the pro-inflammatory state and the attenuation of the innate immune response. Individuals with diabetes have been linked to increased susceptibility to and adverse outcomes associated with infections, especially influenza and pneumonia. Metabolic disorders may impair the functions of macrophages and lymphocytes and thereby lead to low immune function, which predisposes people to disease complications.[8] A rodent study that investigated the effects of diabetes on MERS showed that diabetic mice developed the more severe disease and were found to have dysregulated immune responses following (MERS-CoV) infection, manifested as decreased and delayed recruitment of CD4⁺ T cells and inflammatory monocytes and macrophages in the lung.[8, 9]

In a report on patients with “COVID-19” by the Chinese Centre for Disease Control, Patients with diabetes who develop “COVID-19” have been seen to have a worse prognosis and increased mortality in most studies. In 201 Chinese patients with diabetes, have a higher hazard ratio of acute respiratory distress syndrome (ARDS), and have a significant relationship between the severity of “COVID-19” and diabetes. Similarly, the case fatality rate was 7.3% in patients with diabetes as opposed to 2.3% in those without diabetes.[19, 24]. A recent study in patients with “COVID-19” in centers across the USA found diabetes to be associated with a more than fourfold increase in mortality. [24] Though several factors may be responsible for the severe “COVID-19” infection, SARS-CoV-2 infects not only cells of the upper respiratory system and alveolar epithelial cells in the lung and, among others, circulating immune cells (CD3, CD4, and CD8 T cells), of lymphocytes to an extent that reflects the severity of SARS-CoV-2 infection. [9, 21] Both innate immune response defects (including dysfunction of neutrophils and macrophages) and dysfunction of the adaptive immune response (including T cells) are thought to be responsible for immune system weakness against invading pathogens in diabetic subjects.[15] But how diabetes increases the severity of “COVID-19” is yet unclear.

As T cells of the adaptive immune system inhibit the over-activation of innate immunity, the resulting lymphocytopenia might suppress the innate immune system and enhance the secretion of cytokines.[24] The overproduction of pro-inflammatory cytokines (TNF α , IL-6, IL-1 β , and CXC-chemokine ligand 10) results in a so-called cytokine storm, leading to a high vascular risk of multi-organ failure, and death.[9, 21] High blood concentrations of inflammatory markers (i.e., C-reactive protein, pro-calcitonin, and ferritin), a high neutrophil-to-lymphocyte ratio, and increased blood concentrations of inflammatory cytokines and chemokines have been associated with both “COVID-19” severity and death.[21] Post-mortem analyses of patients with “COVID-19” have revealed inflammatory infiltration of the lungs, heart, spleen, lymph nodes, and kidneys. [21]In that severe “COVID-19”, a study found higher concentrations of leukocytes-reactive protein, pro-calcitonin, and lower lymphocyte percentages as compared with patients with non-severe “COVID-19”. Moreover, C-reactive protein concentrations are higher in patients with DM[9, 21] Another study shows that “COVID-19” Patients with diabetes had higher peak inflammatory markers like CRP, and peak LDH.[25] The need for renal replacement therapy or hemodialysis (RRT/HD)was significantly higher in patients with diabetes as well as the need for vasopressors.[25]

The first confirmed coronavirus disease (COVID-19) in Ethiopia was announced on the 13th of March 2020 by The Federal Ministry of Health. It is the first one to be reported in Ethiopia since the beginning of the outbreak in China in December 2019. Studies show that severe disease seems to be determined by socio-demographic characteristics including male sex, older age, and having a history of pre-existing co-morbid illnesses particularly hypertension, diabetes, severe asthma, cancer, renal disease, cardiovascular, cerebrovascular diseases, and other co-morbidities were also found to be predictors of severe disease.[26] Another study done in the millennium "COVID-19" care center in Ethiopia indicates that mortality is higher in "COVID-19" patients having exposure to diabetes.[27] But the specific effect of DM and the relations of the clinical characteristics and laboratory parameters on the outcome of "COVID-19" patients with and without DM is not well understood yet.

The use of glucose-lowering agents might raise specific considerations in patients with "COVID-19" and despite better outcomes reported in patients with "COVID-19" with diabetes treated with metformin, the drug should be stopped in patients with respiratory distress, renal impairment, or heart failure because of a risk of lactic acidosis. A favorable effect of metformin in patients with "COVID-19" has been hypothesized as the drug might prevent virus entry into target cells via adenosine monophosphate-activated protein kinase activation and the phosphatidylinositol-3-kinase–protein kinase B–mammalian target of the rapamycin signaling pathway.[21]

Objectives

General objective

To assess the effect of diabetes mellitus and clinical characteristics on covid-19 outcome among hospital admitted covid 19- patients at alert hospital, Addis Ababa, Ethiopia from June, 2022, to August 31, 2022

Specific objectives

- To assess the effect of diabetes mellitus on clinical outcome of covid-19 patients
 - To assess the effect of clinical characteristics of COVID-19 patients on covid-19 outcome
 - To analyze the 30 days survival rate of COVID-19 patients with and without DM
-

Methods and materials

Study area and study period

The study was conducted on COVID-19 patients admitted at ALERT Hospital between March 13, 2022 and December 30, 2021. It is a medical facility in Addis Ababa; specializing in Hansen's disease, also known as leprosy. It was originally the All-Africa Leprosy Rehabilitation and Training Center (hence the acronym), but the official name is now expanded to include tuberculosis: All Africa Leprosy, Tuberculosis and Rehabilitation Training Centre and currently Highest Level of Referral Hospital for Leprosy Complications, medical, surgical, Pediatric, ophthalmology and gynecology obstetric service and also a WHO recognized international Leprosy Training Centers which was designated for COVID-19 admission and treatment service during the era of COVID pandemic and this study was conducted from June, 2022, to August, 31, 2022.

Study design

An institutional-based retrospective chart review study design was implemented to assess the effect of diabetes mellitus on covid-19 outcome

Population

Source population

All COVID 19 patients admitted to ALERT Hospital due to COVID 19 infection from March 13, 2020, to December 30, 2021, were considered as our source population.

Sampled/study population

All patients admitted to ALERT Hospital due to COVID-19 infection who were satisfying the inclusion criteria were considered as a sampled/study population.

Inclusion exclusion criteria

Inclusion criteria: All COVID-19 patients, age >18, confirmed by a real-time reverse transcriptase-polymerase chain reaction and admitted to ALERT Hospital were eligible for the study.

Exclusion criteria: COVID-19 patients who are taken to other Hospitals, with unknown diabetic status and unknown final clinical outcomes were excluded from the study.

Study Variables

Dependent variables: Effect of diabetes mellitus

Independent variables: Clinical characters (Fever, headache, cough, dyspnea, diarrhea, vomiting, Oxygen saturation) laboratory parameters (WBC Hb, Platelet PMN Lymphocyte CRP, Blood urea nitrogen (BUN) Creatinine, Na, Potassium (K) LDH, Imaging (chest X-ray, CT) Anti Hyperglycemic agent, Antibiotics, Anti-viral and anti-inflammatory drug in-take, ALT AST, Alkaline phosphatase (ALP), creatinine phosphokinase (CPK)), Sociodemographic characters (age, sex), Comorbidities (DM, Hypertension, Malignancy, chronic, Kidney disease COPD, Asthma, chronic liver disease, neurologic disorder)

Operational definitions

One of the most widely used laboratory methods for detecting the "Covid-19" virus is real-time RT-PCR. Real-time reverse transcription polymerase chain reaction (RT-PCR) is a nuclear-derived method for detecting the presence of specific genetic material in any pathogen, including viruses. Originally, radioactive isotope markers were used to detect targeted genetic materials, but subsequent refinement has resulted in the replacement of isotopic labeling with special markers, most commonly fluorescent dyes.

[28]

Acute Respiratory Distress Syndrome (ARDS) was diagnosed according to the interim guidance of WHO for “COVID-19” or patient assessment with acute respiratory syndrome by the physician [29].

Chronic Kidney Disease (CKD) and Acute Renal Injury (AKI) was diagnosed based on the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guideline or patients diagnosed as CKD by the physician [30, 31].

Cardiovascular disease (CVD) is a collective term designating all types of afflictions affecting the blood circulatory system, including the heart and vasculature and patients diagnosed with CVD by the physician [32].

Hypertension was defined according to the WHO HTN definition. Hypertension is diagnosed when it is measured on two different days, the systolic blood pressure readings are ≥ 140 mmHg,

and/or the diastolic blood pressure readings on both days are ≥ 90 mmHg and patient diagnosed as Hypertensive by the physician [34].

Diabetes mellitus was defined as having one or more of the following criteria: the known case of DM based on medical records, on anti-DM medications, $HbA1c \geq 6.5$, and fasting glucose ≥ 7.0 mmol/l considered as an exposed group, non-DM will be defined as having one or more of the following: no history of DM and/or anti-DM medication use, $HbA1c < 6.5$, and fasting glucose < 7.0 mmol/l and considered an unexposed group or patient diagnosed as diabetic by the physician [4, 35].

Sample size determination

The sample size for this study was obtained from Open Epi info 7 version open-source calculator-W/CC. The final sample size was determined with assumptions of a 5% significance level, 95% Confidence level, mortality in diabetics 28.8% and without diabetes is 6.2%[39] The risk of death is 4.6 times more likely to occur in the diabetic "COVID-19" patients than non-diabetic "COVID-19" patients which is risk Ratio of 4.6 and Probability of death in diabetic "COVID-19" patient is 6.12 times higher than non-diabetic "covid-19" patients which is an odds ratio of 6.12 both generated from epi info software while calculating sample size, power= 80%, the ratio of unexposed to exposed is 2 and finally, 20% of the calculated sample was added to compensate for the non-response/missed participants/dropout patient data. Based on this information the sample size obtained from the epi info software was 37 for the exposed and 74 for unexposed) and 20% of the total sample size was added and the final sample size was 133.[39] The study participant chart was selected using simple random sampling by using computer-assisted random number generation formula which is $=INT(N * RAND()) + 1$.

N: Population number starts from 1 up to N number of population

Data collection procedures (instrument, personnel, data quality control)

The data abstraction form was adopted from studies conducted before this study [4, 36, 37] and the "COVID-19" case report form and it was modified into context. [26] Since the data was collected retrospectively, the data collection tool was pretested on 10% (14 participant charts) of samples other than included charts, and, based on the pretest finding; the data abstraction form

was amended in a way that best fits the available data on the participant chart. The data was collected by trained health professionals who are working in the selected hospital.

Demographics, symptoms, vital signs on admission, medical history (comorbidities), medications taken, anthropometrics, serological tests (complete blood count, profiles of liver, renal, inflammatory markers, and others), and chest X-ray/CT findings were abstracted, as well as outcome (discharged, died), and time laps to the outcome was collected.

Missing data handling strategy

Variable with missing value not more than 10% was corrected using data imputations and hence numerical and categorical values was replaced by the mean and the most frequent category respectively. In this study 25 variables were imputed and 3 variables were deleted b/c high proportion of missing data.

Ethical considerations

This study was reviewed and approved by the research institutional review board (IRB) of St Paul Hospital Millennium Medical College and ALERT/AHRI ERC and an official permission letter was obtained from St Paul Hospital Millennium Medical College and ALERT Hospital. Since it was difficult to get all participants in person for written informed consent, all participants waived consent.

Data processing and analysis

Data was cleaned, coded, and entered into Redcap software before being exported to IBM SPSS 25.0 for analysis. Descriptive statistics were used to summarize the participants' baseline characteristics and clinical outcomes. Categorical variables were described as frequency and proportions, while continuous variables were described as mean and standard deviation (SD). The Shapiro-Wilk test was used to determine normality, and non-normal variables were transformed into normal. The baseline characteristics and clinical outcomes of survivors and non-survivors, as well as diabetics and non-diabetics, were compared.

The student's t-test was used to determine whether there was a significant difference in the mean of the different numerical variables. The chi-square test or Fisher's exact test was used to determine the homogeneity of the proportions of different categorical variables. Bivariate binary logistic regression and multivariate binary logistic regression were used to determine the relationships between pre-existing DM and the outcome, variables of interest. Survival analysis was also performed on time-to-event mortality data. The time-to-event was censored to the right on time-to-discharge as the exit from the time-at-risk among those who did not experience the event, i.e., mortality during the hospital stay.

The logistic regression models were adjusted for hypertension, and cardiovascular disease and asthma, which were all predetermined confounders. A p-value of 0.05 identifies diabetes history as a significant predictor of the outcomes of interest.

Kaplan–Meier curves were constructed to visualize the survival curves of DM versus non-DM, and the log-rank test was used to identify significant differences in the survival curves between diabetics and non-diabetics; a log-rank test with a p-value < 0.05 was considered significant and data was presented in terms of table and plots.

Result

Demographics and comorbidity b/n diabetic and non-diabetic “covid-19” patients

Among 133 participants studied, 74(55.6%) was male. The mean age of the participants was 52 ± 16 with an age range of 19-94 years. The age between 19-50 years were the highest proportions 71(53.4%). More than 61.7% of the population have a concomitant diagnosis of comorbidities. As shown in table 1.1, the proportion of sex across the diabetic and non-diabetic group was similar and majority of the participants were age between 19-50 years in the non-diabetic group and age >50 in the DM group. In this study the overall proportions of HTN and CVD were 45(33.8%), and 23(17.3%) respectively and the proportion of hypertension and cardiovascular disease were highest in the diabetic group than in the non-diabetic group which was 51.2% and 25.6%, respectively.

Table 1.1. Demographic Characteristics of participants segregated by the Diabetic Status

Demographic characteristics		Over all n=133	Non-DM n=90	DM n=43	P-value
Sex	Male	74(55.6%)	50(55.6%)	24(55.8%)	1
age	mean	52 ± 16	49 ± 17	58 ± 14	0.005
Age	19-50	71(53.4%)	56(62.2%)	15(34.9%)	
	>50	62(46.6%)	34(37.8%)	28(65.1%)	0.005
Comorbidity		82(61.7%)	39(37.9%)	43(100%)	
CVD		23(17.3%)	12(12.2%)	11(25.6%)	0.09
CND		2(1.5%)	1(1.1%)	1(2.3%)	0.5
Hypertension		45(33.8%)	23(25.6%)	22(51.2%)	0.006
Tuberculosis		3(2.3%)	3(3.3%)	0(0%)	0.5
COPD		1(0.8%)	1(1.1%)	0(0%)	1
Asthma		5(3.8%)	3(3.3%)	2(4.7%)	0.6
Malignancy		5(3.8%)	3(3.3%)	2(4.7%)	0.6
CKD		7(5.3%)	3(3.3%)	4(9.3%)	0.2
CLD		2(1.5%)	1(1.1%)	1(2.3%)	0.5
HIV		2(1.5%)	1(1.1%)	1(2.3%)	0.5

Clinical characteristics of COVID-19 patients with DM and without DM

As described in table 1.2, the mean age of diabetic COVID-19 patients was 58 ± 14 years and that of the non-diabetic was 49 ± 17 years with a p-value of 0.005 which was significantly different. The proportion of fever, loss of consciousness, and inability to walk within the diabetic group

were higher with the corresponding p-value <0.05 which is higher in the diabetic group than in the non-diabetic group.

Table 1. 2. Comparison of clinical sign symptoms and mortality between DM and non-DM

Clinical sign symptom	All patients		Non-DM		DM		P-value
	n=133	%(Yes)	n=90	%(yes)	n=43	%(yes)	
Cough	125	94.00%	87	96.70%	38	88.40%	0.076
dyspnea	115	86.50%	79	87.80%	36	83.70%	0.524
Loss of appetite	91	68.40%	58	64.40%	33	76.70%	0.156
Bloody sputum	6	4.50%	6	6.70%	0	0.00%	0.998
Fever	82	61.70%	50	55.60%	32	74.40%	0.039
Headache	82	61.70%	52	57.80%	30	69.80%	0.186
Vomiting /nausea	26	19.50%	16	17.80%	10	23.30%	0.457
Sore throat	13	9.80%	6	6.70%	7	16.30%	0.09
Diarrhea	11	8.30%	8	8.90%	3	6.90%	0.709
Runny nose	9	6.80%	5	5.60%	4	9.30%	0.426
LC	16	12%	7	7.80%	9	20.90%	0.035
Wheezing	12	9.00%	7	7.80%	5	11.60%	0.746
Abdominal pain	1	0.80%	0	0%	1	2.30%	0.997
Chest pain	21	15.80%	13	14.40%	8	18.60%	0.539
Conductivities	12	9.00%	8	8.90%	4	9.30%	0.938
Muscle ache	64	48.10%	39	43.30%	25	58.10%	0.112
Joint pain	74	55.60%	50	55.60%	24	55.80%	0.978
Lymphadenopathy	1	0.80%	0	0.00%	1	2.30%	0.997
Fatigue (malaise)	106	79.70%	71	78.90%	35	81.40%	0.737
Bleeding	3	2.30%	2	2.20%	1	2.30%	0.97
Inability to walk	21	15.00%	10	11.10%	11	25.90%	0.037

Comparison of laboratory parameters between diabetic and non-diabetic COVID-19 patients

As described in table 1.3. The means of the laboratory parameters were compared between the two groups using the independent Samples t-Test to see if there was statistical evidence that the population means were significantly different between the two groups.

According to laboratory results upon admission; the mean HA1C, random blood sugar label, C-reactive protein, and total bilirubin levels were greater (p-value 0.01) in the diabetic group than in the non-diabetic group. In addition to this, creatinine level was higher in the DM group than

the non-DM group's (P-value 0.042). On the other hand, WBC count and lymphocyte percentage, were lower (p-values <0.05) in the DM group than in the non-DM group.

Table 1. 3. Independent sample t-test to see significance mean difference in laboratory results segregated by diabetic status using independent sample T-test

Laboratory parameters	All patients	Non-DM	DM	P-value
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	
Hemoglobin	13.60 $\pm$ 2.16	13.54 $\pm$ 2.05	13.86 $\pm$ 2.37	0.421
HA1C	6.00 $\pm$ 1.80	5.20 $\pm$ 1.33	7.79 $\pm$ 1.34	<0.01
Hematocrit	39.70 $\pm$ 6.03	39.67 $\pm$ 5.51	39.80 $\pm$ 7.07	0.909
Creatinine	1.00 $\pm$ 1.47	0.84 $\pm$ 1.41	1.39 $\pm$ 1.54	0.042
WBC (x103/mm3)	8.50 $\pm$ 5.08	7.83 $\pm$ 4.97	9.74 $\pm$ 5.12	0.043
BUN	22.20 $\pm$ 13.27	22.34 $\pm$ 13.39	22.05 $\pm$ 13.18	0.91
Neut%	77.30 $\pm$ 14.06	75.68 $\pm$ 12.62	80.66 $\pm$ 16.30	0.056
ALT/SGPT(U/L)	37.50 $\pm$ 23.85	36.74 $\pm$ 22.95	39.17 $\pm$ 25.82	0.585
Lymph%	16.30 $\pm$ 11.35	17.90 $\pm$ 10.48	12.72 $\pm$ 12.44	0.014
ALP	103.10 $\pm$ 69.96	99.86 $\pm$ 71.73	109.69 $\pm$ 66.48	0.451
AST/SGOT(U/L)	47.80 $\pm$ 51.56	46.98 $\pm$ 50.45	49.53 $\pm$ 54.46	0.792
Plt (x 103/mm3)	232.9 $\pm$ 94.59	235.91 $\pm$ 96.07	226.90 $\pm$ 92.26	0.610
TBL (mg/dL)	0.80 $\pm$ 0.44	0.72 $\pm$ 0.43	0.94 $\pm$ 0.42	0.008
ESR	18.20 $\pm$ 13.54	18.78 $\pm$ 13.58	17.05 $\pm$ 13.55	0.494
DBL (mg/dL)	0.30 $\pm$ 0.40	0.24 $\pm$ 0.37	0.35 $\pm$ 0.43	0.153
CRP	79.35 $\pm$ 72.54	52.17$\pm$61.93	137.62 $\pm$ 58.22	0.0005
Albumin (g/dL)	4.30 $\pm$ 1.33	4.44 $\pm$ 1.3	4.14 $\pm$ 1.39	0.229
aPTT@	28.80 $\pm$ 7.73	29.25 $\pm$ 7.68	27.90 $\pm$ 7.83	0.351
Na+	136.90 $\pm$ 6.06	138.41 $\pm$ 5.14	133.85 $\pm$ 6.69	0.0005
PT	13.80 $\pm$ 9.98	13.91 $\pm$ 9.81	13.58 $\pm$ 10.43	0.862
K+	4.40 $\pm$ 0.74	4.38 $\pm$ 0.69	4.45 $\pm$ 0.83	0.630
LDH	276..6 $\pm$ 112.84	283.29 $\pm$ 117.36	262.19 $\pm$ 102.29	0.348
Ca+	3.19 $\pm$ 1.20	3.23 $\pm$ 1.22	3.12 $\pm$ 1.18	0.630
Troponin	0.98 $\pm$ 0.86	1.05 $\pm$ 0.87	0.83 $\pm$ 0.81	0.168
RBS@	217.98 $\pm$ 107.47	164.43 $\pm$ 76.33	330.07 $\pm$ 70.33	0.0005
AST VS ALT ratio	1.40 $\pm$ 1.02	1.41 $\pm$ 1.02	1.37 $\pm$ 1.04	0.837
Neut VS Lymph	8.77 $\pm$ 8.31	7.83 $\pm$ 7.52	10.77 $\pm$ 9.58	0.059

Medication received at admission segregated by diabetic status

In this study 129(97.7%) received antibiotics (azithromycin and ceftriaxone) at the time of admission, while 67% of diabetic patients received anti-diabetic medication. Corticosteroid (dexamethasone) was administered to 68.4% of the participants, with the majority of diabetics

(67.4%) receiving the drug. The majority of participants (87.2%) received vitamin B/C. The majority of diabetics (67.4%) were also given an anti-diabetic medication at the time of admission.

Table 1. 4. Medication received at the time of admission segregated by diabetic status

medication received during hospitalization		Diabetes mellites					
		All patients		Non-DM		DM	
		n	n %	103	n %	n	n %
Oral/Orogastric fluid	Yes	7	5.3%	3	2.9%	4	9.3%
Intravenous (IV)fluid	Yes	32	24.1%	20	19.4%	12	27.9%
Antibiotics	Yes	129	97.0%	87	84.5%	42	97.7%
Antifungal agent	Yes	1	0.8%	1	0.9%	0	0.0%
Corticosteroid	Yes	91	68.4%	62	60.2%	29	67.4%
Systemic anticoagulant	Yes	113	85.0%	71	68.9%	42	97.7%
CCB (amlodipine)	Yes	28	21.1%	14	13.6%	14	32.6%
Vitamins like VB /VC	Yes	116	87.2%	76	73.8%	40	93.0%
Anti-diabetic agent (Insulin, NPH)	Yes	29	21.8%	0	0.0%	29	67.4%

Comparison of vital sign between diabetic and non-diabetic group

The mean systolic blood pressure of all patients was 124± 22. The mean systolic blood pressure among the diabetic group was 131± 21 and that of the non-diabetic group was 121± 21 respectively. The mean systolic blood pressure was significantly different (p-value 0.016) in the two group.

Table1. 5. Vital sign segregated by diabetic status

Vital sign	Diabetes mellitus status						P-value
	All patients		Non -DM		DM		
	Mean	SD	Mean	SD	Mean	SD	
Temperature °C	36.8	0.9	36.8	1.0	36.7	0.8	0.429
Respiratory rate	23	6	23	6	24	6	0.510
Pulse rate	96	18	97	19	95	16	0.560
SBP	124	22	121	21	131	21	0.016
DBP	73	15	73	15	74	16	0.805
O2saturation	90	10	89	8	92	13	0.114

Demographic characteristics segregated by the outcome

The overall mean age of the participants was 52 ± 16 and that of the non-survivors and survivor was 58 ± 3 and 50 ± 2 respectively, which was significantly different (P-value= **0.032***). The proportion of Glasco coma scale ≥ 14 at presentation was 107(80.5%) and < 14 at presentation was 26(19.5%) respectively. In addition to this the proportion of GCS < 14 among the non-survivor and survivor was 16(53.3%) and 10(9.7%) respectively which was significantly associated with mortality from COVID-19 (P-value<**0.01***). The overall proportion of mortality among chronic liver disease, HIV and chronic neurological disorder was 1(1.5%).

Table1. 6. Demographic characteristics and comorbidities segregated by the outcome

Demographic characteristics		All patients	Death n=30	Discharge alive n=103	P-value
Sex	Male/Female	133(74/59)	30/17/13(56.7%)	103/57/46(55.3%)	0.898
age	Mean age	52 ± 16	58 ± 3	50 ± 2	0.032*
age group	19-50	71(53.4%)	13(43.3%)	58(56.3%)	0.21
	>50	62(46.6%)	17(56.7%)	45(43.7%)	
GCS	<14	26(19.5%)	16(53.3%)	10(9.7%)	< 0.01*
	≥ 14	107(80.5%)	14(46.3%)	93(90.3%)	
HTN		45(33.8%)	15(50%)	30(29.1%)	0.036*
CVD		23(17.3%)	12(40%)	11(10.7%)	0.001*
CND		2(1.5%)	1(3.3%)	1(0.9%)	0.379
Tuberculosis		3(2.3%)	1(3.3%)	2(1.9%)	0.655
Asthma		6(4.5%)	3(6.9%)	3(2.9%)	0.128
Malignant Neoplasm		5(3.8%)	2(6.7%)	3(2.9%)	0.355
Chronic kidney disease		7(5.3%)	2(6.7%)	5(4.9%)	0.697
Diabetes mellites		43(32.3%)	15(50%)	28(27.2%)	0.021*
Chronic liver disease		2(1.5%)	1(3.3%)	1(0.9%)	0.379
HIV		2(1.5%)	1(3.3%)	1(0.9%)	0.379

Clinical presentation of patients at admission segregated by the outcome

As shown in table 1.7, the most common clinical symptoms observed at admission were cough, 125(94%), Shortness of breath/dyspnea, 115(86.5%), Fatigue ,106(79.7%), Loss of appetite, 91(68.4%), fatigue, 106(79.7%) fever, 82(61.7%), headache, 82(61.7%). inability to walk, 21(15.8%) (p-value<0.01), vomiting/nausea, 26(19.5%) (p-value=**0.03***), wheezing, 11(8.3%) (p-value <0.01) and LC, 16(12%) (p-value<0.01). lymphadenopathy and abdominal pain were among the least prevalent symptoms with a proportion of 1(0.8%) at admission. The proportion

of vomiting, inability to walk and loss of consciousness were higher (p-value <0.01) in the non-survivor than survivors. Additionally, wheezing was highest (p-value =0.03) in the non-survivor group than survivor group.

Table1. 7. Clinical presentation of patients at admission segregated by the outcome

Clinical presentation at admission	Outcome			P-value
	All patients (133)	Death (30)	Discharge alive (103)	
	n (%)	n (%)	n (%)	
Cough	125(94%)	27(90%)	98(95%)	0.379
Dyspnea	115(86.5%)	25(83.3%)	90(87.3%)	0.554
Cough with sputum	32(24.1%)	10(33.3%)	22(21.4%)	0.225
Loss of appetite	91(68.4%)	21(70%)	70(67.9%)	1.000
Cough with hemoptysis	6(4.5%)	2(6.7%)	4(3.9%)	0.617
Fever	82(61.7%)	17(56.7%)	65(63.1%)	0.53
Headache	82(61.7%)	18(60%)	64(62.1%)	0.834
Vomiting /nausea	37(27.8%)	19(63.3%)	18(17.5%)	<0.01*
Sore throat	13(9.8%)	4(13.3%)	9(8.7%)	0.489
Diarrhea	11(8.3%)	5(16.7%)	6(5.8%)	0.123
Runny nose	9(6.8%)	4(13.3%)	5(4.9%)	0.116
LC	16(12%)	9(30%)	7(6.8%)	<0.01*
Wheezing	11(9%)	7(23.3%)	4(3.9%)	0.03*
Abdominal pain	1(0.8%)	0(0%)	1(0.9%)	1.0
Chest pain	21(15.8%)	7(23.3%)	14(13.6%)	0.254
Conductivities	12(9%)	5(16.7%)	7(6.8%)	0.141
Muscle ache	64(48.1%)	17(56.7%)	47(45.6%)	0.307
Seizures	1(0.8%)	0(0%)	1(0.9%)	1.0
Joint pain	74(55.6%)	15(50%)	59(57.3%)	0.534
Lymphadenopathy	1(0.8%)	1(3.3%)	0(0%)	0.226
Fatigue (malaise)	106(79.7%)	27(90%)	79(76.7%)	0.129
Bleeding	3(2.3%)	1(3.3%)	2(1.9%)	0.539
Inability to walk	21(15.8%)	13(43.3%)	8(7.8%)	<0.01
Imaging findings	39(29.3%)	16(53.3%)	23(22.3%)	0.068

Vital signs at admission

Table 1.5. shows that the mean respiratory rate and corresponding SD of the “COVID-19” patient at admission was 23 ± 6 beats/minutes (p -value=0.014) which is significantly different in the two group. The mean of most vital signs was phenotypically higher in the non-survivor than the survivors and the mean oxygen saturation was less in the non-survivors.

Table1. 8. Vital signs of patients segregated by the outcome

Vital sign	All patients		Death		Discharge alive		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	
Temp °C	36.8	0.9	36.9	0.8	36.8	0.9	0.581
RR	23	6	27	9	22	4	0.014*
Pulse rate	96	18	103	22	94	16	0.058
SBP	124	22	125	26	124	21	0.796
DBP	73	15	74	18	73	14	0.814
O2 saturation	90	10	87	12	91	10	0.053

Laboratory parameters of patients segregated by the outcome

The Independent Samples t-Test compares the means of two independent groups in order to determine whether there is statistical evidence that the population means are significantly different. As shown on table 1.9 that Results from laboratory test reveals that the mean HA1C level was 6.8 among the non-survivors and 5.8 among the survivors which was significantly different (p -value=0.021) in the two group. On the other hand, the mean platelet count, in the non-survivors was 200.1 and 242.9 in the survivor (p -value of 0.030*) which was significantly different.

Table1. 9. Independent sample t-test to see significant mean difference in laboratory results of patients segregated by the outcome

Laboratory parameters are segregated in terms of outcome	All patients		Death		Discharge alive		p-value
	Mean	SD	Mean	SD	Mean	SD	
Hemoglobin	13.60	2.16	13.30	2.69	13.70	1.98	0.309
HA1C	6.02	1.80	6.80	1.89	5.80	1.71	0.021*
Hematocrit	39.70	6.03	38.00	7.31	40.20	5.55	0.083
Creatinine	1.01	1.47	1.30	1.70	0.90	1.40	0.268
WBC (x 103/mm3)	8.50	5.08	8.80	6.04	8.40	4.79	0.677
BUN	22.24	13.27	26.20	16.77	21.30	12.15	0.183
Neut%	77.30	14.06	79.50	14.38	76.70	13.97	0.331
ALT/SGPT(U/L)	37.50	23.85	31.58	16.06	39.28	25.36	0.122
Lymph%	16.25	11.35	14.80	11.68	16.70	11.28	0.442
ALP	103.00	69.96	111.70	68.29	100.50	70.57	0.443
AST/SHOT(U/L)	47.80	51.56	45.80	58.48	48.50	49.64	0.772
Plt (x 103/mm3)	232.97	94.59	200.10	90.66	242.6	93.96	0.030*
TBL (mg/dL)	0.90	0.44	0.80	0.32	0.80	0.47	0.53
ESR	18.20	13.54	15.70	13.01	18.97	13.67	0.24
DBL (mg/dL)	0.28	0.40	0.30	0.46	0.30	0.38	0.6
CRP	79.40	72.54	93.20	77.35	75.30	70.96	0.237
aPTT	28.80	7.73	30.30	8.84	28.40	7.36	0.237
Na+	136.90	6.06	137.00	7.16	136.90	5.74	0.910
PT	13.80	9.98	13.90	10.18	13.80	9.97	0.961
K+	4.40	0.74	4.50	0.73	4.40	0.74	0.477
LDH	276.70	112.84	294.70	123.84	271.60	109.72	0.359
Ca+	3.19	1.20	3.10	1.15	3.23	1.22	0.508
RBS	217.90	107.30	246.90	99.33	209.6	108.75	0.095
AST VS ALT	1.40	1.02	1.70	1.11	1.31	0.99	0.068
Neut VS Lymph	8.80	8.30	9.90	8.48	8.40	8.28	0.377
HA1C (Hemoglobin A1 C), White blood cell count (WBC), Activated prothrombin time(aPTT),							

Medication at admission segregated by the outcome

As indicated in table 1.10. majority of COVID-19 patients received antibiotics like Azithromycin and ceftriaxone 129(97%) vitamins like vitamin B/C, 116(87.2%), systemic anticoagulation, 113(85%) Corticosteroid drugs 91(68.4%). The proportion of patients who received corticosteroid drugs like dexamethasone among the non-survivor was 10(11.0%),

which was lower than the proportion of patients who received dexamethasone among the survivors with ap-value less than 0.01.

Table1. 10. Medication received at the time of admission across the outcome

Medications received at admission	All patients		Death (30)		Discharge alive (103)		P-value
	n	%(yes)	n	%(yes)	n	%(yes)	
Orogastric fluid	7	5.3%	2	6.7%	5	4.9%	0.655
IV fluid	32	24.1%	11	36.7%	21	20.4%	0.089
Antibiotics	129	97.0%	30	23.3%	99	76.7%	0.574
(NSAID)	13	9.8%	4	30.8%	9	69.2%	0.489
(Dexamethasone)	91	68.4%	10	11.0%	81	89.0%	<0.01*
Systemic AC	113	85%	28	24.8%	85	75.2%	0.162
CCB (amlodipine)	27	20.3%	7	25.9%	20	74.1%	0.615
(Amitriptyline)	6	4.5%	0	0%	6	100%	0.336
VB /VC	116	87.2%	29	25.0%	87	75.0%	0.118
(Insulin, NPH)	29	21.8%	10	34.5%	19	65.5%	0.129

Comparison of outcome b/n diabetic and non-diabetic groups

The overall proportion of mortality was 22.6% and 34.9% with the presence of DM. On the other hand, the proportions of ICU admission were 26(60.5%) which was significantly higher (p-value 0.028). in in the diabetic group.

Table1. 11. Bivariant binary logistic regression for the outcome of COVID-19

Outcome	All patients	Non-DM	DM	COR (95% CI)	P-value
Death	30(22.6%)	15(16.7%)	15(34.9%)	2.68(1.2-6.2)	0.021
ARDS	62(46.6%)	38(42.2%)	24(55.8%)	1.7 (0.8-3.6)	0.14
ICU admission	62(46.6%)	36(40%)	26(60.5%)	1.5(1-2.3)	0.04

Factors associated with death from covid 19

Variables selected for multivariate binary logistic regression with p-value below 0.2. based on this CVD, HTN, DM and Asthma were selected. Finally, CVD was significantly associated with mortality from COVID-19 with p-value (0.001). and DM was significantly associated with ICU admission with p-value 0.028.

Table1. 12. Fitted Multivariant Binary logistic regression model for mortality from COVID-19

Variables	COR (95% CI)	P-value	AOR (95% CI)	P-value
CVD	1.7(1.1-2.7)	0.001	6.7(2.4-19.1)	0.001
Hypertension	1.2(0.9-1.6)	0.048	2.4(0.9--6.0)	0.072
DM	1.3(1.0-1.6)	0.021	1.9 (0.7-4.8)	0.20
Asthma	1.5(0.7-3.5)	0.128	5.6 (0.9-33.4)	0.06

Fitted multivariate binary logistic Regression model for ICU admission from covid-19

Variable	COR (95% CI)	P-value	AOR (95% CI)	P-value
DM	1.5(1-2.3)	0.04	2.3 (1.1-4.8)	0.028

Survival analysis

As showed on fig1 there was no significant different on 30-day probability of mortality b/n diabetic and non-diabetic COVID-19 patients with p-value of 0.141.

Survival analysis

The survival probability

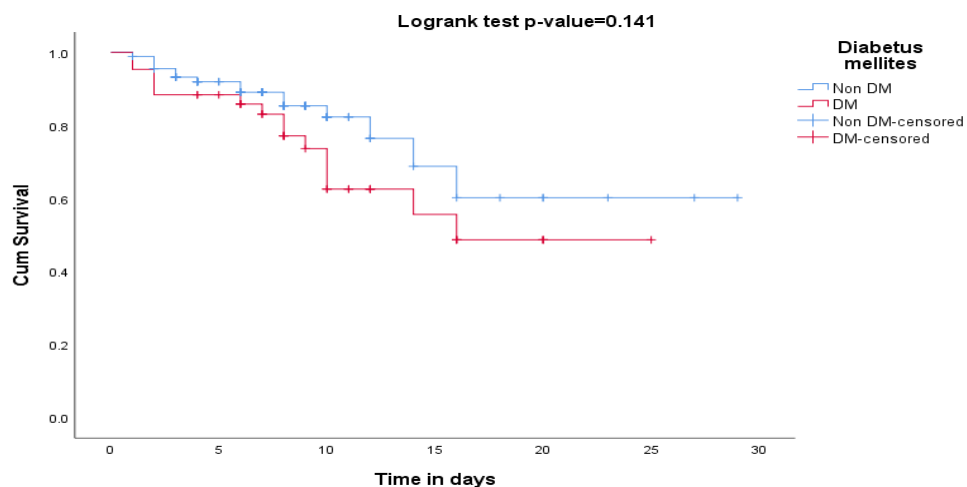


Fig1: Kaplan-Meier estimates of survival for “covid-19” patients with and without diabetes mellites1

Discussion

Diabetes Mellitus (DM) is one of the four priority non-communicable diseases (NCDs) identified by the World Health Organization (WHO).[38]Emerging evidence suggests that comorbid diabetes in patients with COVID-19 and previous SARS-related pandemics was associated with disease deterioration and death. [3] This study aimed to assess the effect of diabetes mellites on COVID outcomes among hospital admitted COVID-19 patients at ALERT Hospital, Addis Ababa Ethiopia.

Characteristics of all patients admitted with COVID-19

In this study, most patients were male 74(55.6%). The Mean age of the participants were 52 ± 16 and the proportion of age between 19-50 years were higher (53.4%) compared with age >50 years. [39] In most studies elder age and male sex were associated with COVID-19 mortality [40, 41] and this was not consistent with the current study. [39, 41] This might be due to majority of the participants were younger age and medications received that can improves the outcome of COVID-19. In a dozen of studies DM was significantly associated with COVID-19 related mortality. But in the current study DM was not associated with COVID-19 related mortality which is similar with studies done in United kingdom.[39] This might be due to the effect of younger age and other co-existing co-morbidities like a chronic cardiac disease which was significantly associated with COVID-19 related mortality.

The overall proportion of COVID-19 mortality was 22.6%. This finding was slightly higher than the findings of most studies arising from Europe US and Ethiopia [42, 43]and lower than the finding of a study done in Kuwait and that difference might be the quality of health care given there could reduce the COVID-related mortality [44]. Cardiovascular disease was significantly associated with COVID-19 mortality Which ,was similar with the findings of systematic and meta-analysis studies done in other countries.[45, 46] In this study DM was associated with ICU admission of COVID-19 patients and this was observed in many other studies. [47, 48] On the other hand DM was not associated with ARDS even with adjustment which contradicts the findings of other study.

Cough, shortness of breath, fatigue, loss of appetite, fever and headache were common clinical presentations at admission, which is similar to most studies done in China and Bangladesh.[49] The proportions of Vomiting/nausea, loss of consciousness, inability to walk, and wheezing were significantly higher in the non-survivor group and which is in line with other studies [43, 50] In different studies tachypnea was associated with mortality from COVID-19 [51] and the current study also revealed that tachypnea was associated with COVID-19 mortality. The mean RR was 27 breath/minutes in non-survivors and 22 breath/minutes in survivors with p-value of 0.001 which was significantly different in the two group.

In this study, the proportion of corticoid steroidal drugs like dexamethasone received at admission was lower (11%) with p-value <0.01 in the non-survivor group which, was in line with the findings of the study on the effect of dexamethasone on hospitalized “COVID-19” patients [52]. This study also indicates significant mean difference on HA1C and alanine transaminase(ALT) level b/n the non-survivor and the survivor group and this finding was similar with studies done in India.[53] On the other hand, platelets count was significantly lower in the non-survivors than survivor.[54] In many other studies c-reactive protein and neutrophil were significantly higher and lymphocytes were significantly lower in non-survivor COVID-19 patients[54]But this was not observed in the current study. This might be due to that majority of the COVID-19 patients received dexamethasone which possibly reduce inflammation and that will end up with relatively normal biomarker level.

Clinical characteristics between DM and non-DM COVID-19 patients

In many studies, the average age of the diabetic COVID-19 patients were higher than the non-diabetic COVID-19 patients[55] and the current study confirms that the average age of the diabetic COVID-19 patients was significantly higher than the non-diabetic group. The proportion of fever, loss of consciousness, and inability to walk at admission were higher in the diabetic group as compared with the non-diabetic group which was similar with studies done in Iran and China [55, 56]

Many studies suggest that laboratory results like WBC, HA1C, RBS, CRP, creatinine, and total bilirubin level were higher in diabetic than in non-diabetic COVID-19 patients. [57, 58] . This

study also reveals that WBC, HA1C, RBS, C-reactive protein, TBL, and creatinine levels were significantly higher in diabetic patients than in non-diabetic COVID-19 patients. On the other hand, diabetic COVID-19 patients have lower lymphocyte percentage than non-diabetic COVID-19 patients and this finding was in line with a study done in Wuhan China.[59] In many studies electrolyte imbalance were seen either it increased or decreased the electrolyte level in the body and the coexistence of DM and covid can cause severe electrolyte disturbance.[60, 61] The current study tells that sodium was significantly lower in diabetic COVID-19 patients than in non-diabetic “COVID-19” patients. This might be due to impaired renal function also leads to fluid and electrolyte disturbances.[61] It is known that The kidneys have a wide range of roles, including urine formation, hormone secretion, blood pressure regulation, acid-base balance, and osmolality regulation, so their normal function is essential.[61] kidney impairment is not uncommon in diabetic and COVID patients, so impaired kidney function will end up with electrolyte imbalance. The other reason for lower sodium levels in the diabetic group could be uncontrolled DM can also induce hypovolemic-hyponatremia due to osmotic diuresis. Moreover, in diabetic ketoacidosis ketone bodies (b-hydroxybutyrate and acetoacetate) obligate urinary electrolyte losses and aggravate renal sodium wasting.[60]

Survival analysis

Kaplan-Meier survival curves demonstrated no difference in the 30 days survival rate of hospitalized COVID-19 patients with DM and without DM (Figure 2). This might be due to the majority of the patient receiving medications having better survival outcomes like dexamethasone which significantly reduces hospital mortality from COVID-19.

Limitations

Due to lack of recorded information, this study was not addressing the association of behavioral factors like Alcohol drinking, Cigarette smoking, Chat chewing and shisha smoking. Additionally anthropometric parameters like BMI which would have a possible association with the clinical outcome COVID-19 patients also not addressed due to similar reason and another important issue that was not addressed in this study was complications that COVID-19 patient develops during hospitalization b/c of high percentage of unknown complication status and the finding from this study might be overestimated or under estimated due to small sample size. finally, I suggest more prospective study to see the possible association b/n DM and those factors and long-term consequence of COVID-19.

Conclusion

In the current study age, sex DM were not associated with mortality from covid-19. On the other hand, DM was significantly associated with ICU admission. Significant mean difference was observed on the HA1C and platelet count b/n survivors and non-survivors. Cardiovascular disease was significantly associated with mortality from COVID-19. The proportion of COVID-19 patient presented with vomiting/nausea, loss of consciousness, wheezing, and inability to walk at admission were significantly higher in the non-survivor COVID-19 patients.

The proportion of fever, loss of consciousness, and inability to walk at admission were significantly higher in the diabetic group than in the non-diabetic group. Significant difference was observed in biomarkers, hematologic profiles, liver function test renal function test, endocrinology test and electrolyte status like Na⁺ CRP, WBC, lymphocyte percentage, creatinine, HA1C, RBS total bilirubin b/n DM and non-DM COVID-19 patients. COVID-19 patients who received corticosteroid drugs like dexamethasone have better outcomes as compared with those not received the drug considering all other factors remain constant.

Recommendation

From the findings of this study, the health practitioner should work on glycemic control and give attention for patient presented with additional comorbidities like chronic cardiac disease and Special emphasis should be given to COVID-19 patients who are presented with vomiting/nausea, loss of consciousness, wheezing, and inability to walk at admission. Special emphasis is also needed for patients having atypical laboratory findings. It is also important promoting medications like dexamethasone for COVID-19 patients.

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Annexes

Waiver of consent request

1. For this study the information is not sensitive in nature, and the data are derived from clinically indicated procedures. There is an extremely low probability of harm to subjects' social status. Names and any other personal identifiers will not be analyzed and published and for better confidentiality, the participants will be represented by code. Any changes to the research protocols generally need to be submitted to the research ethics review board for reapproval/amendment this further minimize the major risk, which is breach of confidentiality.
 2. The rights and welfare of the individual would not be adversely affected because clinically indicated laboratory investigations and the associated blood chemistry values were already completed, regardless of the research. None of the results of the research would affect the clinical decisions about the individual's care because the results are analyzed after the fact and subjects are not deprived of clinical care to which they would normally be entitled.
 3. The research could not be practicably carried out without a waiver. Identifying and contacting the hundreds of potential participants, would not be feasible for a review of their medical records for information that would not change the care they would have already have received.
 4. The results would have no effect on the participant's hospitals and post-hospitals care have both been completed for these participants. There is no anticipated benefit to participants that would change what has already occurred. The official permission letter will be written from St Paul Hospital millennium medical college and ALERT Hospital.
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Questionnaire

The purpose of this study is to assess the effect of diabetes mellitus on clinical outcomes among “covid-19” patients admitted at alert hospital Addis Ababa Ethiopia. The findings of the study will be treated with high confidentiality and will be used in accordance with ethical principles and there will be no mentioning of participant identity like name while data collection, analysis and data sharing.

1. General Information

1.1. Institution ID _____

1.2. Participant ID _____

1.3. Admission date (dd/mm/yyyy) _____

2. Demographic Characteristics

2.1. Sex: ☐ Male

☐ Female

2.2. Age _____

3. Clinical characteristics at admission

Vital sign	
Temperature in °C _____. ____	Respiratory rate _____ breath/min
Heart rate _____ beat/min	
Systolic blood pressure _____ mmHg	Diastolic Blood pressure _____ mmHg
Oxygen saturation _____ %	Glasco coma scale (GCS) _____/15

4. Anthropometric measurements

Hight: _____ cm	Weight: _____ kg	BMI: _____ kg/m ²	MUAC: _____ cm
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5. Comorbidities

Any type of comorbidity	☐ Yes		☐ No	
Cardiovascular disease	☐ Yes	☐ No	Chronic neurological disorder	☐ Yes ☐ No
Hypertension	☐ Yes	☐ No	Tuberculosis	☐ Yes ☐ No
Chronic obstructive pulmonary disease	☐ No	☐ No	Asplenia	☐ Yes ☐ No
Asthma	☐ Yes	☐ No	Malignant Neoplasm	☐ Yes ☐ No
Chronic kidney disease	☐ Yes	☐ No	Diabetes	☐ Yes ☐ No
Chronic liver disease	☐ Yes	☐ No	HIV	☐ Yes ☐ No
Other			☐ Yes ☐ No	

6. Clinical sign symptom at admission

Cough	☐ Yes	☐ No	Shortness of breath/dyspnea	☐ yes ☐ No
Cough with sputum	☐ Yes	☐ No	Loss of appetite	☐ Yes ☐ No
Cough with hemoptysis	☐ Yes	☐ No	Loss of Test	☐ Yes ☐ No
Fever	☐ Yes	☐ No	Loss of smell	☐ Yes ☐ No
Headache	☐ Yes	☐ No	Vomiting /nausea	☐ Yes ☐ No
Sore throat	☐ Yes	☐ No	Diarrhea	☐ Yes ☐ No
Runny nose(rhinorrhea)	☐ Yes	☐ No	Loss of consciousness	☐ Yes ☐ No
Wheezing	☐ yes	☐ No	Abdominal pain	☐ Yes ☐ No
Chest pain	☐ Yes	☐ No	Conductivities	☐ Yes ☐ No
Muscle ache (myalgia)	☐ Yes	☐ No	Seizures	☐ Yes ☐ No
Joint pain(arthralgia)	☐ Yes	☐ No	Lymphadenopathy	☐ Yes ☐ No
Fatigue (malaise)	☐ Yes	☐ No	Bleeding	☐ Yes ☐ No
Inability to walk	☐ Yes	☐ No	Other	☐ Yes ☐ No

7. Medications received at the time of admission

Oral/Orogastric fluid	☐ Yes	☐ No	Intravenous (IV)fluid	☐ Yes	☐ No
Antibiotics (Azithromycin, Ceftriaxone)	☐ Yes	☐ No	Antifungal agent	☐ Yes	☐ No
Antimalarial agent ☐ Yes ☐ No If yes specify _____			Non-steroidal anti-inflammatory drug (NSAID)	☐ Yes	☐ No
			Corticosteroid like dexamethasone	☐ Yes	☐ No
Angiotensin receptor blocker(ARBs) ☐ Yes ☐ No			Systemic anticoagulation	☐ Yes	☐ No
Calcium Chanel blocker (amlodipine) ☐ Yes ☐ No			Antidepressant (Amitriptyline)	☐ Yes	☐ No
Vitamins like VB /VC ☐ Yes ☐ No			Anti-diabetic agent (Insulin, NPH)	☐ Yes	☐ No

8. Laboratory parameter at admission

Parameters	Done	Not Done	If done result	Parameters	Done	Not done	If done result
Hemoglobin (g/dL)	☐	☐		HA1C	☐	☐	
Hematocrit (%)	☐	☐		Creatinine (mg/dL)	☐	☐	
WBC ($\times 10^3/\text{mm}^3$)	☐	☐		BUN (mg/dL)	☐	☐	
Neut (%) ANC	☐	☐		ALT/SGPT(U/L)	☐	☐	
Lymph (%) TLC	☐	☐		AST/SGOT(U/L)	☐	☐	
NLR (ANC/TLC)	☐	☐		ALP	☐	☐	
Plt ($\times 10^3/\text{mm}^3$)	☐	☐		Total bilirubin	☐	☐	
ESR (mm/hr)	☐	☐		Direct bilirubin	☐	☐	
CRP(mg/L)	☐	☐		Albumin (g/dL)	☐	☐	
INR	☐	☐		APTT	☐	☐	
Na ⁺ (mEq/L)	☐	☐		PT (seconds)	☐	☐	
K ⁺ (mEq/L)	☐	☐		LDH(U/L)	☐	☐	
Ca ²⁺ (Total)	☐	☐		Troponin (ng/mL)	☐	☐	
Mg ²⁺	☐	☐		Random blood Glucose	☐	☐	

9. Supportive care at list once at any time during Hospital stay

ARDS	☐ Yes	☐ No	Oxygen therapy	☐ Yes	☐ No
ICU Admission	☐ Yes	☐ No	Invasive ventilation	☐ Yes	☐ No
Inotropes/vasopressor	☐ Yes	☐ No	Dialysis	☐ Yes	☐ No

10. Imaging result

Imaging finding at admission	Imaging finding at discharge or prior to discharge
Yes ☐ No ☐ ☐ Unk	Yes ☐ No ☐ ☐ Unk

11. outcome

Outcome	☐ Discharged alive ☐ Death Length of Outcome in days _____
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Declaration

I, the undersigned, MPH student at ST Paul Hospital Millennium medical college declare that this research thesis is my original work for the partial fulfillment of the requirement for the Master' of public health in Epidemiology.

Name: Abraham Tekola G/Medhin

Signature: _____

Date: _____

Place of submission: ST Paul Hospital millennium medical college.

Addis Ababa, Ethiopia

Submission date: November,2022

This thesis proposal work has been submitted for examination with my/our university advisor(s) approval.

Advisors

Name of advisor:

Mr. Kinf Haile (MPH)

1. Signature _____

2. Place _____

3. Date ____/____/____

Mr. Getachew Tilahun (MPH)

1. Signature _____

2. Place _____

3. Date ____/____/____