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Risk Factors for Re-admission in Covid-19 Patients from a Tertiary Care Health System: Quality Control (QC) and Quality Improvement (QI) Project

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The COVID-19 pandemic has made a significant impact on public health globally and has unleashed an array of deficiencies that have already crippled our health care system. It also brought out the health care disparities among minorities and thrust health inequity to the limelight. Hospital readmission is one descriptive marker for overall patient clinical prognosis. Prior to SARS-CoV-2 Pandemic (COVID-19), 30-day-all cause readmission rates was highest in patients with heart failure, psychoses, chronic lung disease, and peripheral vascular disease status post-surgical procedure. However, pneumonia is the most common reason for unplanned patient readmission. COVID-19 continues to evolve, from the rising versality in variants to the clinical concerns of longer

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haulers. This study followed by a review will illustrate COVID-19 post-acute disease role on readmission diagnosis and rates. The aim is to identify most common reason for readmission and overall patient clinical prognosis. Readmitted patients in this study were older.
In this QC/QI project the frequent symptom on readmission was respiratory illness and the primary diagnostic codes on readmission were noted to be respiratory failure and "COVID-19 sequelae." Readmitted patients in this study were older (>61yrs of age), with an equal sex distribution, more likely to have multiple comorbidities, majority were of African American ethnicity, reflecting the disproportionate impact ofCOVID-19 on this group. About 70% of readmissions had a Charlson Comorbidity index of 3 and above reflecting the chronic conditions present in this cohort. Less than 40% of patients were up to date with their COVID 19 immunization and overall mortality rate was close to 12%. Based on our QC/QI analysis, a comprehensive and coordinated approach that addresses important metrics comprising optimal medical management of comorbidities, COVID 19/Pneumococcal immunizations, focus on mental health treatment and homelessness is essential to decrease the risk for readmissions in this population.

Keywords: COVID-19; readmissions; COVID-19 sequelae; long-haulers; multi-organ dysfunction; COVID-19 prognosis; risk factors; post COVID-19 syndrome.

1. INTRODUCTION

The COVID-19 pandemic has made a significant impact on public health globally and has unleashed an array of deficiencies that have already crippled our health care system. It also brought out the health care disparities among minorities and thrust health inequity to the limelight. Although United States has 4% of the world's population, it was hit by a majority of COVID 19 cases and deaths compared to other developing countries [1,2]. Importantly, minorities including black persons constituted 13% of the U.S. population, accounted for 20% of COVID-19 cases, 22% of Covid-19 deaths; hispanic persons, at 18% of the population, accounted for 33% of new cases; 20% of U.S. counties are disproportionately black, and these counties accounted for more than half of Covid-19 cases and almost 60% of Covid-19 deaths nationally [3]. These racial and ethnic disparities that are already entrenched in the US health care system, became more prominent during the pandemic, when minorities faced higher morbidity and mortality relative to the general population. Hence it makes it important to evaluate the impact of COVID 19 on the minority population and its long-term consequences such as "post COVID-19 syndrome" by evaluation of "long haulers" in the community. This could be performed by outpatient follow up visits, telephone calls post discharge or by evaluating the characteristics of patients discharged and readmitted within 30-60 days after COVID-19. Our understanding of COVID 19 illness has greatly improved over the last year, there are several gaps that need to be filled. Throughout the COVID-19 pandemic, the frequent surges in hospital admission have overwhelmed health care institutions around the world. Amidst this, readmissions after discharge could further destabilize the already saturated health care system. A good understanding of the prognostic indicators, risk factors and comorbidities associated with readmissions would play a crucial role in risk stratification, formulate guidelines for appropriate care, criteria required for safe discharge and follow up instructions after recovery from COVID-19. Studies on readmissions to hospital after recovery from COVID-19 are limited to date [4-10]. These studies have shown a correlation between comorbidities and readmissions. Also, the risk and characteristics of "long haulers" is a relevant problem and needs to be studied. Analysis of long-term effects of COVID-19 are essential to effectively gauge and assess health care capacity, and plan healthcare delivery in an efficient manner. Most studies of SARS-CoV-2 have been focused on the respiratory effects of the virus, but there is increasing evidence of its effects on other organ systems, including the cardiovascular, neurological, and gastrointestinal systems. Therefore, investigation of COVID-19 related long term effects on various other organ systems is urgently needed to further the understanding of the virus. Post-COVID syndrome, also known as long COVID, is categorized as a broad range of symptoms that can last weeks or months after the initial COVID-19 infection [11,12]. Due to its vague parameters, it is hard to define exactly what falls under this categorization. Therefore, by identifying common reasons for hospital readmission, we can learn more about the role of post-COVID syndrome.

1.1 Aims

The primary aims of this study were (i) to address readmission rates post COVID 19, (ii) to evaluate comorbidities associated with readmissions (iii) to identify reasons for readmission (respiratory, cardiovascular, gastrointestinal, etc. Secondary aims were (i) to evaluate the impact of COVID 19 immunization on readmissions (ii) to analyze morbidity and mortality in this group (iii) to provide specific metrics for long-term follow up in these patients.

2. MATERIALS AND METHODS

This study was a retrospective record review with a descriptive design, conducted at a tertiary care hospital in Detroit, Michigan. Medical records of index patients admitted to Detroit Medical Center with a positive COVID 19 RT-PCR test were screened for the study. Out of these patients, those who were readmitted within 30 days of discharge and had a positive RT-PCR for COVID 19 were reviewed for the study. The study period was from March 2020 through February 2021. Patient demographics, diagnosis on admission, comorbidities and Charleston comorbidity index, length of stay, requirement for intensive care unit or ventilator, laboratory inflammatory markers, infections with positive microbiology cultures and COVID 19 sequelae (defined as persistent respiratory symptoms and signs, fatigue, and gastrointestinal symptoms in the setting of a recent covid 19 discharge) were evaluated for the study.

3. RESULTS

153 readmitted patients were identified during the study period. The average age of readmitted patients was 61.2 ± 17.7 years and 51.0% of patients were female. On average, patients were readmitted 15.2 ± 8.2 days after discharge and the most common diagnoses for readmission included respiratory failure (n=30;15.7%; p<0.05), COVID-19 sequelae (n=30; 15.7%; <0.05), and altered mental status/encephalopathy (n=15;7.8%; p<0.1), . Additionally, 31 (20%) readmitted patients had an identified secondary infection with positive microbiological culture; the most common

Table 1. Common diagnoses for readmission

Sex, n (%)	Female	78 (51.0)
	Male	75 (49.0)
Ethnicity, n (%)	African American (p<0.05)	111 (72.5)
	White	19 (12.4)
	Other/Unknown	23 (15.0)
Charlson Comorbidity Index, n (%)	0 – 2	46 (30.1)
	3 – 5	50 (32.7)
	≥ 6	57 (37.3)
Length of Stay, mean ± SD	COVID-related hospitalization (days)	12.6 ± 30.6
	Readmission (days)	8.9 ± 8.9
Ventilator, n (%)	COVID-related hospitalization	7 (4.6)
	Readmission	16 (10.5)
Source of Positive Culture (readmissions), n (%)[1]	Blood	11 (35.5)
	Urine	10 (32.3)
	Sputum	4 (12.9)
	Other	6 (19.4)
Most Commonly Isolated Organism, n (%)[1]	*E. coli*	4 (12.9)
	Methicillin-Resistant *S. aureus*	3 (9.7)
	P. aeruginosa	3 (9.7)
Most Common Readmit Diagnosis, n (%)[2]	Respiratory Failure (p<0.05)	30 (15.7)
	COVID Sequelae (p<0.05)	30 (15.7)
	Altered Mentation State and/or Acute Encephalopathy (p<0.1)	15 (7.8)
		13 (6.8)
	Acute Renal Failure and/or Acute Uremia and/or Dialysis	12 (6.8)
	Pneumonia (p<0.05)	

[1] Patients without positive culture on readmission excluded
[2] Several patients had multiple readmit diagnoses

sources of infection were blood (11;35.5%), urine (10;32.3%), and sputum (4;12.9%). Majority of readmitted patients were of African American ethnicity ($p<0.05$), reflecting the population of the city of Detroit and the disproportionate impact of COVID-19 in this group. About 70% of readmissions had a Charleston Comorbidity Index (CCI) of 3 and above; in fact, 37% of patients with a CCI of ≥ 6, reflecting multiple co-morbidities including diabetes, heart disease, hypertension, and chronic kidney disease in this cohort of patients.

4. DISCUSSION

This was a retrospective, descriptive study of 153 patients from a tertiary care center in Detroit who were readmitted following an initial episode of COVID-19. Although this was a small study not powered enough to delineate specific risk factors, the findings were noteworthy. Observations from this study are similar to few other studies that have evaluated readmission characteristics in COVID-19 patients and adds valuable information to available data. This is one of the very few studies that have looked at readmission characteristics within a minority black community known to have intrinsic health care disparities. About 30-35% of readmissions were related to respiratory illness. Several patients (30; 15.7%) suffered from persistent symptoms since discharge and never returned to baseline health within the 30-day period. These patients were categorized with the diagnosis of “COVID-19 sequelae”, defined as the presence of persistent respiratory symptoms, fatigue, or gastrointestinal symptoms in the setting of recent COVID-19 discharge [11,12]. These patients clearly fit the description of “long haulers” and need to be closely followed in the outpatient clinic. A total of 31 patients were diagnosed with infections, with positive cultures (blood, sputum, or urine).

One of the largest studies from Lavery et al. that examined 126,137 patients admitted, 106,543 patients discharged, out of which 9504 (9%) were readmitted [13]. The median interval between discharge and readmission was 8 days. Readmission was more common among patients discharged to a skilled nursing facility or home health organization support compared to patients discharged to home or self-care. The chances of readmission increased with the presence of chronic obstructive pulmonary disease, heart failure, diabetes, and chronic kidney disease. Common primary discharge diagnoses after readmission were infectious and parasitic diseases. This was the only study that compared readmissions between patients from subacute nursing facility (SNF) versus home. This observation emphasizes the importance of formulating specific guidelines for follow-up care for COVID-19 patients discharged to SNF. The readmission rate of ~9% was similar to the incidence rate in our cohort of patients.

Another study conducted in England by Ayoubkhani et al. that examined post-covid syndrome included 47,780 patients, of which 14060 (29.4%) were readmitted. It was an observational, retrospective, matched cohort study that demonstrated the highest readmittance rate to date [14]. Authors found that COVID-19 admission by itself increased the risk for readmission compared to admission for any other cause. Interestingly, diabetes, major adverse cardiovascular event, chronic kidney disease, and chronic liver disease were newly diagnosed after discharge in 4.9%, 4.8%, 1.5%, and 0.3% of individuals, respectively. Rates of death, readmission, and multiorgan dysfunction after discharge from hospital remained substantially increased in individuals with COVID-19, especially those more than 70 years of age, compared with matched controls. The observation of post COVID-19 multi-organ dysfunction confirms the extrapulmonary pathophysiology of COVID-19. Individuals who needed to be admitted to the intensive care unit had higher rates of respiratory diseases and diabetes after discharge, but lower rates of death, readmission, and major adverse cardiovascular event than those who did not need to be admitted to the intensive care unit. In a study conducted in Madrid, Spain by Ramírez et al. examining 1368 discharged patients, 61 patients were readmitted, with a median time between discharge and readmission of 6 days. Interestingly, this was a matched nested case control study matched by age, sex, and period of admission [15]. Hypertension was identified as the single most risk associated with readmission, but not COPD (chronic obstructive pulmonary disease). The author also noted that presence of fever within 48 hours prior to discharge was associated with a high risk for readmission in this group. However, inflammatory markers (C-reactive protein, LDH, neutrophil/lymphocyte ratio and D-dimer) were not associated with increased risk for readmission. Nevertheless, a trend towards increased readmission was noted in patients with elevated D dimer, and elevated neutrophil/lymphocyte ratio on admission and

lymphocytopenia on discharge. One other study, conducted in a minority, underserved, black population in Philadelphia by Guarin et al. reported that, out of 275 discharged patients, 21 patients were readmitted within 1 month and 66 were readmitted within 6 months of initial hospitalization. Coronary artery disease (CAD) related causes (21%) were the most common reason for readmission, followed by respiratory (18%), musculoskeletal (18%), and neuropsychiatric (18%) causes. Patients with coronary artery disease had a significantly higher rate of readmission, and being on hemodialysis had a trend toward being significant. So far this is the only study that has reported CAD to be a major risk factor for readmission [9]. It is unclear if risk factors such as diabetes, hypertension and obesity played a role in these patients with CAD or direct myocardial injury or myocarditis secondary to SARSCoV-2 invasion via ACE2 receptors contributed to readmissions. Authors did report that in their subgroup analysis, majority of readmitted patients were his panics, with a high incidence of diabetes which is a major risk factor for CAD. Peixoto et al. specifically evaluated ICU admissions after discharge from COVID-19 and reported that longer length of stay, longer days between discharge/first readmission, and pulmonary involvement (≥50%) were associated with ICU admission in readmitted patients [16]. Readmissions evaluation is pivotal and may help in ensuring safe care transition and post-discharge follow-up.

Fin et al.,[17] conducted a multi-centered cohort study in Rhode Island, USA, between April 1st and December 31st, 2020 that included all adults (n=2062) discharged after hospital treatment for COVID-19 The main study outcomes were length of hospital stay, 30-day readmission, and post-discharge 30-day mortality. Authors observed that patients who received remdesivir were less likely to be readmitted within 30 days, (RR: 0.31; 95% CI: 0.13,0.75), had a low all-cause mortality (HR: 0.65; 95% CI: 0.49,0.85) and an increase in length of stay (estimated average increase of 3.27 days; 95% CI: 2.11,4.44) 17). One of the largest studies from around the world was a multicenter (147 hospitals) nationwide cohort study from Spain in 2020 that included 8392 patients. During the study period, 298 patients (4.2%) patients were readmitted, median time of readmission was 7 days, (IQR 3–15 days) and most frequent reasons for readmission were pneumonia (54%), bacterial infection (13%), venous thromboembolism (5%), and heart failure (5%). Age, age-adjusted Charlson comorbidity index score, chronic obstructive pulmonary disease, asthma, hemoglobin level at admission, ground-glass opacification at admission and glucocorticoid treatment were independently associated with hospital readmission. The overall rate of readmission after hospital discharge for COVID-19 was low [18]. CT lung involvement and time from symptom onset were reported to be the main determinants of hospital readmissions by Reggio Emilia COVID-19 Working Group from Italy [19].

A careful analysis of above studies and others [20-22] reveals that diabetes, heart disease, hypertension, kidney disease increase risk for readmissions. Noteworthy is the fact that management of patients during initial admission for COVID-19 includes use of intravenous fluids, corticosteroids, and prophylactic anticoagulation, all of which could collectively worsen chronic medical conditions such as congestive heart failure, hypertension, diabetes, and bleeding in elderly from trauma and falls. Hence, there is also a possibility that some of these comorbidities may act as confounding variables and may not be primary risk factors for readmission. It underscores the need for cautious use of medications and optimize plan post COVID-19 discharge, that would minimize readmission rate in this cohort of patients.

It is important to see if recent COVID 19 increased the risk of secondary infections involving the respiratory, gastrointestinal, or urinary tract due to binding to ACE-2 receptors in these organ systems with subsequent mucosal injury. Our study clearly demonstrated that preexisting cardiac, pulmonary, renal, or neurological disease increased the risk for readmission when all factors were analyzed. Long term research and follow up (on health parameters, mental health, health care access, social support system, economic burden, etc.) of index patients is indicated to recognize factors associated with a high likelihood of readmission. A significant observation of concern is that the incidence of “long haulers” could be higher than reported (16% in this study). Healthcare disparities, poverty, delayed presentation to hospital, and inadequate social support are outside factors that have possible correlation to these results. There are several limitations to this study. It is limited being a retrospective a single-center, descriptive study, from a tertiary care center in a downtown community with majority of patients being blacks and hence data cannot be

generalized to other scenarios. The small sample size precludes identification of differences between specific variables. Immunization data and its impact on readmission rates was not available. It would be important to see if COVID-19 immunization decreased the readmission rate in this group. Measurement of inflammatory markers in index patients and in readmitted patients (data not shown) did not show a statistical difference. Social determinants related to readmission were not specifically addressed, but most patients in this group were under Medicare, Medicaid, and belonged to low socioeconomic backgrounds. It is important to understand that other risk factors and reasons for readmission have been reported from around the world including hyponatremia, deep venous thrombosis [23-26]. Most importantly, at the time of this study, newer COVID-19 variants such as the Delta or Omicron variants had not yet emerged and hence readmission patterns associated with these variants is beyond the scope of this study. Other studies conducted around the world seem to arrive at similar conclusions regarding the link between comorbidities and readmission rates.

It is important to note that a majority of studies did not capture minorities as a risk factor for COVID readmissions. Our QC/QI project in a small number of patients noted an increased risk for above mentioned risk factors in the minority population. Ongoing research from several institutions around the world would help address the knowledge gaps that exist regarding risk factors associated with post COVID-19 readmission especially in the low income and minority groups. This study must be considered a hypothesis generating study designed to identify risk factors and outcomes associated with readmissions in this group. More research in this field is needed that would shed light on the long-term outcomes in this cohort of patients, identify and provide preventive measures and targeted treatment based on risk stratification not only in the general population but also in the low-income group and minorities around the world [27].

5. CONCLUSION

In this study, 153 patients initially hospitalized for COVID-19 were readmitted within the first 30 days post-discharge during the study period. The most frequent symptom on readmission was respiratory illness and the primary diagnoses on readmission were respiratory failure and “COVID-19 sequelae.” Readmitted patients in this study were older (>61yrs of age), with an equal sex distribution and more likely to have multiple comorbidities. Less than 40% of patients were up to date with their COVID 19 immunization and overall mortality rate was close to 12%. Based on our QC/QI analysis, optimal medical management of comorbidities, COVID 19/Pneumococcal immunizations, addressing both mental health concerns and homelessness were the important metrics that need to be identified to decrease rate of readmissions in this population (unpublished data from QC/QI departmental analysis).

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

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The authors have no conflict of interest. This is a QC/QI project and meets all IRB requirements for our Univestiy. None of the authors have any financial disclosures.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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