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Risk Assessment of COVID-19 on Patients with Chronic Kidney Diseases in Libya

(Original Research Article)

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ABSTRACT: The Sars covid 19 virus is an extremely contagious disease that originated in Wuhan, China, in late 2019[1,2]. Widespread panic over the news of the infectious disease

quickly followed, and despite most countries inflicting lockdown restrictions, the virus spread nonetheless, reaching over 230 countries and territories as of October 2022. This study is to provide insight into managing CKD patients' with COVID-19, and to declare that the diseases' outcome was affected by individual factors on Libyan CKD patients. Data of 635 CKD patients were collected from Al-Shatt Road Kidney Diseases Center in Tripoli, from January to September 2020. Statistical analysis was conducted to assess the risk of this pandemic on kidney patients and to evaluate the impact of several related factors: gender, age, and CKD associated diseases. The rate of mortality among CKD patients COVID infected was determined as well. The results of this study showed that 18.5% of CKD patients tested positive for COVID-19, while 81.5% tested negative. The highest number among CKD with COVID-19 were males 58.8% vs female 41.2%. Patients with hypertension and diabetes age >45 were more vulnerable to COVID-19 than other CKD patients. In additions, 74% of CKD patients developed diabetes after COVID 19 infection. The fatality rate of CKD- COVID 19 positive was significantly higher than CKD- COVID 19 negative (29.8 % vs 2.3%) and male's mortality rate was significantly higher than females, p-value <0.05 through the nine months of observation. Hemodialysis is a significant variable for Corona's chance of infection. These results may be beneficial for CKD patients who may benefit from appropriate, specialized and efficient medical treatment. Further research considers studding the long-term damage of COVID-19 on public health.

KEYWORDS: COVID-19. Pandemic. Chronic Kidney Disease (CKD). Mortality. Diabetes. Hypertension.

INTRODUCTION

Throughout the past few centuries, the world has been exposed to infectious diseases of varying degrees, such as the Spanish Flu and the Bubonic Plague, each one surpassing the former in severity and mortality rates. What scientists didn't expect was that in the 21st century, a time widely renowned as the pinnacle of medical and scientific advancement in the world's leading countries, is that billions of people globally would be exposed to a pandemic of a larger magnitude than any of the aforementioned diseases.

The Sars covid 19 virus is an extremely contagious disease that originated in Wuhan, China, in late 2019 (Li, 2020 & Zhao et.al, 2020). Widespread panic over the news of the infectious disease quickly followed, and despite most countries inflicting lockdown restrictions, the virus spread nonetheless, reaching over 230 countries and territories as of October 2022. The record for the largest number of daily COVID-19 cases reaches a new peak regularly, with the highest being in January 2022, during the time in which the Omicron variant, assumed to be the deadliest of the virus, surged worldwide.

The World Health Organization (WHO) named the modern "SARS-CoV-2" as COVID-19 [Ali, S. A et.al, 2020 & WHO, 2020] and stated it as a global public health pandemic on March 11th (Ali et.al, 2020). Among the countries greatly impacted by the pandemic are African countries, arguably more so than first-world countries due to their unstable living conditions and scarce resources to provide the necessary

protocols for disease prevention, such as sanitation products and face masks, as well as a disproportionate number of vaccinations available in comparison to the large number of cases in these countries.

One of the most impacted African nations is Libya (Figure1), which is located in the Northern-African region. Similar to many African nations, the country's political turmoil, instability, and irresponsibility of the appointed government officials led to a lack of awareness on the disease, which contributed greatly to the spread, among other factors such as the unavailability of vaccinations immediately after their production, and a lack of awareness on sanitation among civilians.

These factors all contributed to the fact that Libya having the highest number of COVID-19 cases among all African nations during the middle stage of the pandemic (WHO, 2021). In the Eastern Mediterranean region, Libya occupies the 10th place in terms of the highest number of cases, and the 6th in terms of mortality rates, which leads to the inference that the country's case to mortality rate is higher than that of some of its peer countries (WHO, 2021).

As one of the most life-threatening chronic diseases, chronic kidney disease (CKD) is a global common complicated condition, has a world-wide heavy burden on patients, society, and health sector authorities alike. In the United States of America about 15 percent of adults suffer from CKD (Mohanty et.al, 2020).

In Libya the number of CKD dialysis was increased since 2009 from 2116 to 2417 in 2017 [Akkari, K., 2013]. It has been previously proven that people with chronic kidney disease, especially those on dialysis, who underwent the kidney transplant, or are on immunosuppressive medications, are more likely to have high hospitalization frequency, higher incidences of ICU admissions, longer hospital stays, and a higher mortality rate compared to individuals with other chronic diseases [Lee & Lee et.al, 2018]. COVID-19 impacted healthcare services for many chronic diseases especially chronic kidney disease services.

Throughout the spread of this pandemic, several studies have clarified that people with CKD are key susceptible individuals for a severe route of corona disease (Akalin .& Azzi et.al, 2020, Henry & Lippi, 2020, Ma et.al, 2020). They are three times more prone to develop serious symptoms and side effects of COVID-19 than others (Schiffrin et.al, 2020). In addition to their vulnerability which puts them at risk of dying, infection with COVID - 19 may accelerate and further incline their fatality rate.

The first coronavirus (COVID-19) death in Libya was reported in Tripoli as acute kidney failure in an 86 years old lady with no close-to-date moving history. She had type 2 diabetes mellitus and the human immunodeficiency virus (HIV) infection. Her reported death cause was as non-responding to the treatment (Schiffrin et.al, 2020, Askari et.al, 2021). More severe COVID-19 cases were reported with high rates of mortality among old people and individuals with chronic diseases such as kidney dysfunction, cardiovascular disease, diabetes, or hypertension.

However, the elderly was not the only age group affected by the virus, as death has also struck young and healthy patients (Hilbrands et.al, 2020, Karami, et.al, 2021, Salvadori, 2021).

In 2020, Hilbrands and his group conducted an observational analytical study. They analyzed collected data from the ERACODA (European Renal Association COVID-19 Database) database. Their investigation involved 1073 CKD patients; 305 (28%) kidney transplant, and 768 (72%) were dialysis patients with a

mean age of 60 ± 13 and 67 ± 14 years respectively. Their results revealed that 8 out of 148 dialysis patients and 7 out of 23 kidney transplant patients died throughout the 28 days' observational period (Kliger & Silberzweig, 2020).

Many clinical outcomes, for instance sepsis, acute respiratory distress syndrome (ARDS), respiratory failure, septic shock, acute myocardial injury, and coagulopathy, were higher in mortal patients (Mohanty et.al, 2020, Elhadi et.al, 2020).

However, according to the Centers for Disease Control and Prevention (CDC), reports showed that one of the highest causes of mortality by COVID-19 is CKD and vice versa. Especially people on dialysis who have weaker immune system, which making it harder for their bodies to survive COVID-19 (Mohanty et.al, 2020).

Patients with end-stage kidney disease marked as the most vulnerable group for COVID-19 with an infection rate of 16% (Akalin, et.al, 2020).

Chronic systemic inflammation may associate with high morbidity and mortality among CKD patients. Akalin2020 and Salvadori 2021 and their colleagues showed a remarkably high premature death (28% according to Akalin2020) amongst COVID-19 infected recipients of kidney transplant in comparison to the overall population (Akalin et.al, 2020, Salvadori, &Tsalouchos 2021).

Considering the impact COVID-19 on patients with CKD can have on morbidity, mortality, and hospital costs. It is mandatory to understand the risk factors that contribute to their occurrence. There is an urgent need for additional measures to be taken in high-risk CKD patients to prevent or reduce their COVID-19 infection.

Therefore, identifying risk factors for CKD of great clinical value could prevent the occurrence of COVID-19, speed recovery, and reduce health care costs.

Factors such as: ageing, hyperglycemia, a proinflammatory, and hypercoagulable state, and comorbidities. Understanding these risks and the most effective ways to mitigate them in the short and long term is critical to have the right treatment choices during and after the COVID-19 infection (Gansevoort .& Hilbrands, 2020).

MATERIALS AND METHODS

Data Collection

In this study, 635 CKD patients (age 19+) with chronic kidney disease (CKD) were observed at the Al-Shatt Road Kidney Diseases Center in Tripoli between January 1st, 2020, and September 31st, 2020.

All patients were undergoing continuous hemodialysis. Most of them had other chronic diseases associated with kidney disease. For instance: diabetes, hypertension, congenital malformation, and cysts.

PCR assay was conducted to detect the presence of SARS-CoV-2 in their respiratory specimens of nasal or pharyngeal swabs with compatible findings on a computed tomography (CT) scan of the lungs.

The PCR was performed in accordance to the protocol established by the WHO [WHO,2020]. The CKD database used in this work consisted of eight risk factors, as shown in Table 1.

These factors were considered for this work and identified from the literature and expert clinical opinions.

Table 1. Description of Dataset

ID	Attribute	Type	Description
1	Age	Numerical	Female; Male
2	Sex	Categorical	Independent; Partially dependent; Totally dependent
3	Hemodialysis risks	Categorical	Inpatient; Outpatient
4	Blood group heparin	Categorical	Positive; Negative
5	Corona virus Infection	Categorical	No, Yes
6	CKD associated diseases	Categorical	Hypertension; Diabetes; Hypertension& diabetes; Congenital malformation (CM); Cysts etc.
7	Death	Categorical	No, Yes

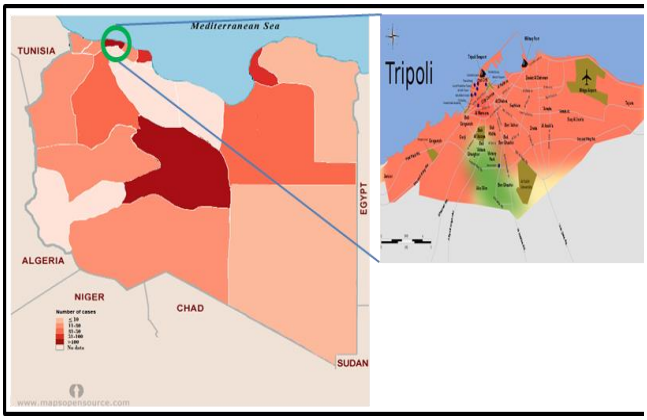

Figure 1. Geographical Distribution of COVID-19 in Libya

Statistical Analysis

Data collected was analyzed using Excel and MINITAB-19 (Askari, et.al, 2021, Lai, et.al, 2020). Clinical and demographic patients' characteristics were charted using relative frequencies according to the type of variables.

A descriptive statistic was used to calculate proportions and frequencies. Significantly was determined at P-value <0.05. The least significant differences test (LSD) was performed using T table to indicate means' significant differences.

RESULTS AND DISCUSSION

Characteristics of the Study Cohort

Out of the 635 CKD patients who were admitted to Al-Shatt Road Kidney Diseases Center in Tripoli from January to September 2020, 616 CKD patients met the study before analysis, and 19 missing observations were excluded.

The Effect of Age and Genders

Kidney failure-COVID 19 patients' ages were between 19-74 years old. The mean patient age was 45 years. Most of CKD- COVID 19s who had significantly older age, suffered from higher severity of illness's symptoms, and high comorbidity index as well.

As shown in Figure 2, of the 114 confirmed COVID-19 infected CKD patients, 67 were males (58.8%) and 47 were females (41.2%). These results agreed with Gansevoort and Lai 2020 results which their results demonstrated that CKD males were highly promoted to catch COVID 19 than females.

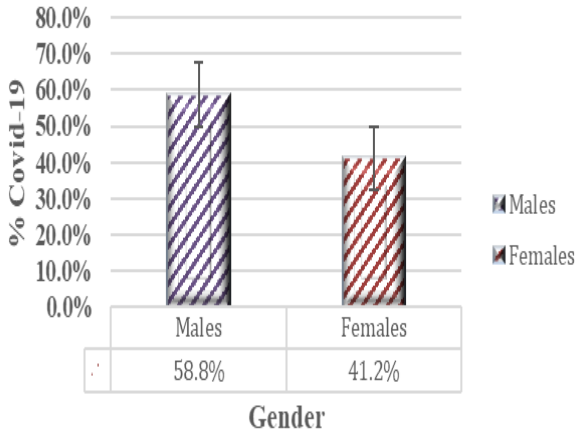

Figure: (2). Distribution of CKD Patients with COVID-19 by Gender.

Table 2. Patient with Kidney Failure Associated with COVID-19

Kidney Failure Associated Diseases	Disease% Percentage %	Count (n)		
		Female	Male	Female
			% Male %	
Hypertension	36.8	19	23	45.2[a, b] 54.8[b]
Diabetes	22.8	10	16	38.5[a] 61.5[b]
Hypertension& diabetes	4.38	2	4	40[a] 60[b]
Congenital Malformation (CM)	8.77	3	7	30[a] 70[b]
Hypertension	7.01	2	6	25[c] 75[d]
Cysts	9.64	4	6	36.4[a] 63.6[b]
Other reasons	10.6	7	5	58.3[b] 41.7[a]
Total	100	47	67	41.2[a] 58.8[b]
Means	14.3	6.71[e]	9.57[f]	39.1[a] 60.9[b]

Different lower cases letters indicated a significant diff.

Kidney failure Associated Chronic Diseases

Increasing numbers of CKD patients infected by COVID-19 were directly influenced by CKD associated diseases. This study results shows that hypertension and diabetes were common among patients with chronic kidney disease (CKD) and the prime cause of COVID-19. Hypertension was the most promoter to COVID-19 in CKD patients. Among the 616 CKD observed patients 316 were developed hypertension followed by 161 patients developed diabetes. These results agreed with Schiffrin 2020 and Mohamed 2021's results. Males with hypertension or diabetes were at higher risk of having deadly sever COVID-19 [13,14,18].

In this study, CKD-Hypertension patients were infected by COVID 19 more likely than CKD patients with other associated diseases. Table 2 shows that the percentage of CKD-Hypertensions with COVID 19 patients was 36.84% (54.8%, males and 45.2% females).

Secondly the CKD-diabetes with COVID 19, their percentage was about 22.81% (61.5 %males, 38.5% females). Bothe results showed that men were more vulnerable to hypertension-COVID19 and diabetes-COVID19 than women. This result was similar to Mohammed 2021's results which showed that the majority of the CKD patients with hypertension were males [9, 22, 23]. In diabetes disease-COVID19 cases alone, males were two times higher than females (Table 2, figure 3).

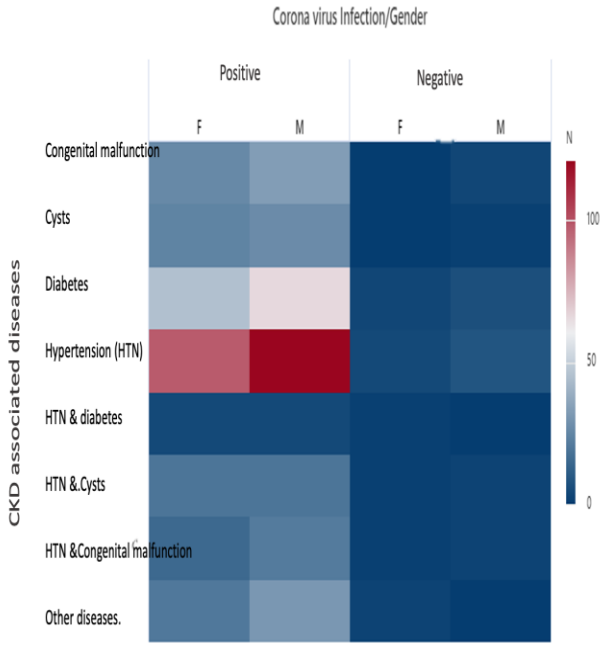

Figure 3. Kidney failure associated diseases patients with COVID 19

Association between CKD and COVID-19 Related Mortality in Libya.

From the 114 CKD patients with COVID-19 in this study's sample, 29.8% had died because of COVID-19 in the period between January to September 2020, as shown in Table 3. The rate of mortality was increasing over the nine months.

The death percentage of CKD patients associated with COVID-19 during the nine recorded months was high compared to other countries recorded results. Figure 7, revealed that the highest mortality rate was in August 2020 with a death percentage of 8.77%. Thirty-four almost one third of the patients out of 114 CKD patients were died at the same KD center in Tripoli because of the COVID-19 sever infection. Most death happened to older people. People with age higher than 45 years old. These results showed that Libyan-CKDs were died in younger age than other countries' CKD patients. Similar studies clarified that Almost one- quarter (22.6%) of patients aged 65 years and older died as compared to 6.9% and 0.9% among 45 to < 65 years old and < 45 years old, respectively (Lee et.al, 2018, Elhadi et.al, 2020).

While in this study's results 10.4% CKD patients ages <45 have died from COVID 19. Table 3 and figure 4 showed that males death numbers were significantly higher than females which agreed with WHO several reports in many places around the world (Kliger & Silberzweig, 2020).

Results showed that the mortality rate was significantly proportional to the progression in time, which means that the pandemic was spreading at a rapid pace and CKD patients were in degradation health status during and after their infection period.

According to the results, COVID-19 caused an increase in the death rate among CKD patients in Tripoli in compression with the control (non-COVID-infected dialysis patients) (Figure 4).

Eleven patients among the 519 patients were died through the nine months. The mortality rate among kidney patients was 2.31% if compared with the COVID-infected CKD patient's mortality rate

which was 29.8% (Table 3). This result agreed with Mohamed et al., 2021 study of evaluating the mortality risk of CKD patients infected with COVID-19.

Their results showed that COVID-19 mortality rate was significantly higher in CKD patients (23.1% vs 10.2%) [Askari, H.& Sanadgol et.al, 2021].

Table (3). The mortality rate of COVID-19

Month	CKD-Male death n) COVID	CKD-Male death n) COVID	CKD-Female death n) COVID	CKD-Female death n) COVID	*Mortality rate % COVID*	*Mortality rate % COVID*
1	3	5	0	2	0.58	6.14[b]
2	0	0	1	0	0.19	0[a]
3	0	2	0	0	0	1.75[a]
4	0	0	0	0	0	0[a]
5	1	1	0	0	0.19	0.9[a]
6	0	1	0	2	0.19	2.63[a]
7	2	1	1	2	0.39	2.63[a]
8	1	5	0	5	0.19	8.77[b]
9	2	7	0	1	0.39	7.02[b]
Total	9[b]	22[d]	0	12[c]	2.31[a]	[b]29.8[f]
			1[a]			

Death n= death numbers, different lower cases letters indicated a significant difference among results at p-value<0.05.

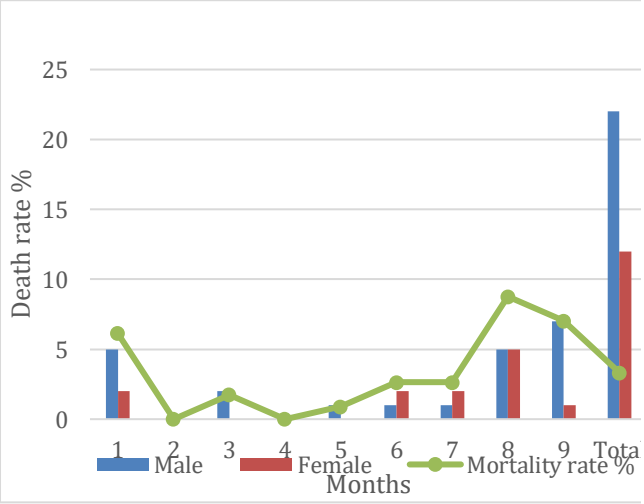

Figure 4. The Mortality Rate of CKD-COVID-19 from Jan to Sep, 2020.

In addition, there were similar results by Gansevoort 2020. This investigation included data for more than 17 million people in the UK. In this study the mortality rate among CKD patients who had COVID-19 was very high. It reached to 192 deaths among 23978 CKD dialysis cases. These CKD data indicate that these patients especially those on dialysis or living with a kidney transplant deserve special attention with regard to COVID-19 (Gansevoort and Hilbrands, 2020).

Other factors associated with CKD patients affected by COVID-19 among Libyan patients

Determining the variables that have the most influential effect on CKD patients with COVID-19 was critical to enhance the model's performance and efficiency. For better understanding to the associations between risk factors and COVID-19 in CKD patients, the relative feature importance of the model was calculated and shown in Table 5.

As shown in Figure 8, important variables in a descending rank were hemodialysis risks, heparin doses (to avoid blood clotting problems normally used for dialysis patients), virus (Veral load), and blood group. This research exposed that the novel proposed model was hemodialysis risks with the most impact on the COVID-19 with CKD patients, which was100% relative importance. Using important variable models showed that hemodialysis risks were the most important variable involved in the occurrence of COVID-19 in CKD patients.

To our knowledge, this is the first study to evaluate analysts of COVID-19 in a single cohort in Libya and how this has potentially impacted the health care system. However, this study had several limitations. Initially, the study was displayed in a country that has a continuing civil war and severe economic crisis, which will illuminate the high mortality rate.

According to the results, the hemodialysis risks were the most important variable involved in the occurrence of COVID-19 among CKD patients (figure 8). These results agreed with Ma et al., 2021's results [9]. Patients with CKD were highly susceptible to COVID-19 and were at an increased risk of progression to a severe or critical form of the disease because of impaired immunity. In addition, they are at increasing risk of SARS-CoV-2 infection due to their frequent hospital attendance. Given the un appropriate environment and poor hygiene in most Dialysis centers for CKD patients' low immunity.

Factors such as ethnicity, race, and other laboratory findings were not provided due to the limited availability of resources, which incomplete our capacity to analyze these factors. One more limitation; that the study was revealed data from a single country, and the results were not comprehensive to other parts of the world.

CONCLUSION

In conclusion, this observational study confirmed essential information about the under belt hit of COVID-19. It's the first to demonstrate the importance of CKD as a risk factor for COVID-19 mortality in Libya, and the consideration of renal diseases as a strong predictor of mortality in patients diagnosed with COVID-19. Therefore, prioritizing the CKD patients with COVID-19 in hospital admissions and supportive care with closer monitoring is an urgent matter.

Results should be considered by clinicians and healthcare policymakers in the future when planning support for hospitals and healthcare workers during the ongoing COVID-19 pandemic. In addition, some CKD cases developed diabetes during the study after getting COVID infection. These pro COVID accumulative symptoms such as: diabetes, blood clotting, hair failing, vision and hearing problems, and other COVID-19 penalties deserve to be further investigated.

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We would like to thank all of the medical and nursing staff at the Al-Shatt Road Kidney Diseases center for their dedicated care of our renal patients during the COVID-19 pandemic.

ETHICS

Ethical approval for this study was obtained from the Bioethics Committee at Biotechnology Research Center in Libya. All participants on the condition that consent before participating in the study. All patients were asked for consent prior to participation in the study.

CONFLICT OF INTEREST

The authors stated that they have no conflict of interest.

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