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Original article

Hematological and Biochemical Abnormalities Associated with Mortality Among Hospitalized COVID-19 Patients: A Retrospective Single Center-Based Study.

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ABSTRACT

Background and objectives: *Severe acute respiratory coronavirus 2 (SARS-CoV-2) has emerged as a major public health threat. Characteristics of patient laboratory test results have important implications for predicting disease prognosis, especially in countries with limited health resources. This is a retrospective, cross-sectional, single-center study of 402 COVID-19 patients.* ***Methods:*** *Hematology parameters, coagulation parameters, liver function test (LFT) and renal function test (RFT) results were collected and compared between survivors and non-survivors to identify predictive biomarkers of death. Collected data were statistically analyzed using SPSS V.26.* ***Results:*** *114 patients died with a mean age of 75.8±16.3 years old which was significantly high compared to the survivors' group. (p=0.00). There was no significant difference in hemoglobin level (Hb) and blood cells count between the two cohort (all P > 0.05). non survivors group significantly has higher level of lactate dehydrogenase (LDH) than the survivors' group (P < 0.05). LFT & RFT results show no significant difference between the survivors and non-survivors' cohort (P > 0.05). Erythrocyte Sedimentation Rate (ESR) and serum C reactive protein (CRP) were high. However, the difference between the survivors and death cohort was not statistically significant (P > 0.05). D-dimer level was significantly higher among non-survivor group compared to survivors (P< 0.05).* ***Conclusion****: we conclude that some demographic features and laboratory investigation could be used to identify high risk patients especially in low resources hospitals.*

Keywords. COVID-19, Hematological Parameters, Biochemical Parameters, Mortality.

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2) was first reported in Wuhan city, Hubei, China, in December 2019.WHO (World Health Organization) declared COVID-19 as a pandemic as the virus spread across over 160 countries [1]. In March 2020, the first case of confirmed COVID-19 was recorded in Libya. As of December 2021, the total confirmed cases were about 400,000 cases [2]. considering the limited number of screening test done by the Libyan health authorities, the real number of cases is expected to be much higher [3].

however, the collapsed health care system in this war-torn country was challenged by this pandemic [4]. limited medical and logistic resources made it necessary to improve the hospital management and early diagnosis of patients [5]. demographic factors (age and gender) have been confirmed as predictors of disease severity by many studies [6]. many hematological and biochemical parameters have been identified as predictors of disease severity. Identification of these parameters will make it possible to predict disease severity and patients' prognosis [7]. This study aimed to identify the demographic, biochemical and hematological characters of hospitalized Libyan patients with COVID-19. In addition, we compared the biochemical and hematological parameters between survivors and non-survivors which may help the identification process and better management of the higher risk patients.

METHODS

Study design & data collection

We studied subjects referred to Shahat teaching hospital for respiratory diseases, which was designated as a COVID-19 quarantine hospital since March 2020. The patients were admitted to the hospital during the period from June 2020 and April 2021. epidemiological, demographic, medical history and laboratory data were retrospectively extracted from electronic medical records of the subjects. the diagnosis of COVID-19 was confirmed for all patients by quantitative real-time reverse transcriptase-polymerase chain reaction (qRT-PCR) of nasal or pharyngeal swabs Excluding criteria include patients aged less than 15, pregnancy, recent history of surgery and malignancy. All patients were treated according to the national guideline for novel corona virus, COVID-19. hematological and biochemical parameters were investigated for all patients within 24 hours of admission. we check the outcome of the patients after one month of the admission of the last patient. Outcomes included either death, or discharged after two successive negative qRT-PCR tests.

Statistical analysis

Collected data were statistically analyzed using SPSS V.26 (IBMSPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp, USA). Descriptive analysis (i.e., mean, standard deviations, median and interquartile range IGR) were calculated for the entire set of data. Independent sample t-test were performed to compare means of the clinical data between both COVID-19 survivors and non-survivors' as well as, the clinical parameters associated with normal and elevated values of D-dimer. Mann–Whitney U test was performed to compare ranked means of the symptoms and comorbidities in survivors and non-survivors' group, at significant level of $P<0.05$ two-sided.

RESULTS

Patients

A total of 402 COVID-19 patients were included: 53.7% of them were male. The mean age was 55.5 ± 23.3 range, 15-101 years **(table 1).** 114 patients died with a mean age of 75.8±16.3 years old which was significantly high compared to the survivors' group. (p=0.00). 64% of the non-surviving patients were males. Coughing, shortness of breath and a high body temperature were the most common symptoms reported among the patients (33.1%, 25.8% & 21.4% respectively) other symptoms like a sore throat, anosmia and ageusia were less frequently seen (Fig 1). about one sixth of the patients were known cases of different chronic diseases. Diabetes mellitus and hypertension were the most common co-morbidities among the subjects (Fig 2).

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Table 1: Clinical characteristics in patients with COVID-19 (N=402)

Clinical characteristics	Mean ± SD	Median (IQR)/n
ESR (mm/hr)	49.9 ± 33.6	44.5 (20 - 70)/402
S. ferritin (ng/ml)	187.9 ± 195.9	134 (10.5 - 50.5)/402
CRP (mg/l)	36.9 ± 39.9	21.2 (10.5 - 50.5)/402
D-dimer (ng/ml)	3.5 ± 2.3	3.1 (1.8 - 4.8)/402
LDH (U/l)	403.5 ± 279.9	332 (234 - 508)/402
ALP (U/l)	153.8 ± 75.2	153 (96.8 - 199)/402
AST (U/l)	40.1 ±5 4.7	29 (19 - 44.3)/402
ALT (U/l)	40.7 ± 96.6	24 (18 - 39)/402
Creatinine (mg/dl)	1.8 ± 2.1	1.35 (0.7 - 2.2)/402
Urea (mg/dL)	43.9 ± 30.9	35.5 (24 - 54)/402
Lymph (%)	4.7 ± 8.7	1.75 (0.98 - 2.9)/402
Hb (g/dl)	11.3 ± 3.1	11.5 (9 - 13.6)/402
Platelets (B/l)	243 ± 104.7	231 (177 - 297)/402
WBC (B cell/L)	9.3 ± 14.9	8 (5.6 - 10.9)/402
RBC (milli cell/L)	4.5 ± 1.3	4.5 (3.8 - 5.2)/402
Age	55.5 ± 23.3	54 (36 – 75)/402

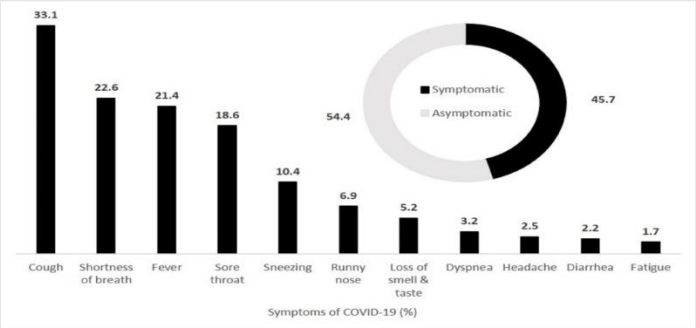

Figure 1: COVID-19 symptomatic patients (N=184)

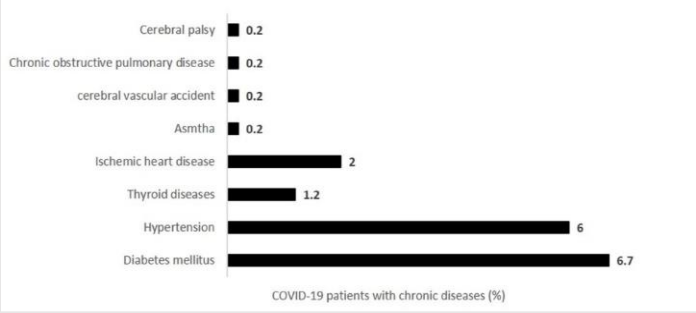

Figure 2: Chronic diseases among COVID-19 patients

Hematological and biochemical profile

Lymphopenia was observed among the patients of the study (mean 4.7±8.7), though there was no significant difference between the survivors and death cohort (P > 0.05). Besides that, there was no significant difference in hemoglobin levels (Hb), White Blood Cells (WBCs) count, Red Blood Cells (RBC) count and platelets count between the survivors and non survivors (all P > 0.05). (Table 1, Table 2).

Table 2. Comparison of clinical characteristics among patients with COVID-19 (survivors and non-survivors

Clinical characteristics	Mean SD		*P* value
	Survivors (n=288)	Non-survivors (n=114)	
ESR (mm/hr)	49.5± 32.9	50.6± 35.3	0.770
S. ferritin (ng/ml)	183.6± 168.9	193.6± 252.3	0.712
CRP (mg/l)	34.9 ± 35.6	41.7± 48.8	0.126
D-dimer (ng/ml)	3.3± 2.2	4.0± 2.5	0.002
LDH (U/l)	353.5.2 ±204.8	529.9± 386	0.000
ALP (U/l)	153.3±70.9	155.1± 85.3	0.824
AST (U/l)	39.3 ± 43.5	42.1± 76.3	0.636
ALT (U/l)	39.3± 72.1	44.4± 140.9	0.632
Creatinine (mg/dl)	1.6±1.7	1.9± 2.7	0.203
Urea (mg/dL)	45.3± 32.7	40.6± 25.9	0.175
Lymph (%)	5.2± 9.1	3.6±7.8	0.091
Hb (g/dl)	11.4± 3.1	11.1± 3.1	0.475
Platelets (B/l)	243.3± 104.8	242.5± 104.9	0.947
WBC (B cell/L)	9.5± 17.5	8.8± 4.4	0.714
RBC (milli cell/L)	4.6± 1.2	4.3± 1.4	0.069
Age	47.4.45 ± 20.7	75.8±16.3	0.000

Analysis of the biochemical profile showed that the non-survivor's group significantly had higher levels of lactate dehydrogenase (LDH) than the survivors' group (P< 0.05). In regards of liver enzymes, our results show no significant difference in level of serum aspartate transaminase (AST) level, Alanine transaminase (ALT) level and Alkaline Phosphatase (ALP) between the survivors and non-survivors' cohort (all P > 0.05). In regards of the renal biomarkers, serum creatinine level was higher among non-survivors, though there was no significant difference observed between the patients in both groups (P > 0.05). Serum urea level shows no significant difference between the survivors and non-survivors' cohort (Table 2).

Inflammatory markers and D dimer

patients of our study show high levels of the inflammatory markers namely, Erythrocyte

Sedimentation Rate (ESR) (mean 49.9 ± 33.6) and serum C reactive protein (CRP) (mean 36.9 ± 39.9). however, the difference in levels of these inflammatory markers between the survivors and death cohort was not statistically significant (P > 0.05). D-dimer level was high among the patients of our study (mean 3.5 ± 2.3), moreover D-dimer level was significantly higher amongst the non-survivor group compared to survivors (Table 2).

DISSCUSION

SARS-CoV-2 belongs to beta-coronaviruses cluster which include the much deadlier SARS-CoV, and MERS-CoV viruses. Symptoms of COVID-19 varied from mild symptoms like fever, coughing, sore throat to sever respiratory failure (acute respiratory distress syndrome) [8]. Many studies from all over the world had described the abnormalities of several hematological and biochemical parameters among patients infected with COVID-19. These abnormalities could be of great value as predictors of disease severity and prognosis [5,7,9,10]. Hence, we described a comparative analysis of hematological and biochemical parameters of 402 patients from the North African region. The demographic findings of our study are in agreement with the results of previous researches [6] state that patients aged 70 years or more were at higher risk of infection and higher risk of death if infected compared to younger patients. In accordance our results show that the median age of the non-survivor group was higher than the survived cohort. regarding gender effect on covid-19 mortality, 64% of patients in non-survivor cohort were male. Meta-analysis of data from 46 different countries concludes that men infected with COVID-19 have higher mortality rates than women [11] Besides that, during Previous coronavirus outbreaks (SARS and MERS), the male sex has been reported as a factor affecting the disease severity [12]. About one third of patients either presented with or developed cough, while dyspnea was the second most common symptom (25% of patients). however, a high fever was the most common symptom recorded by Chinese researchers during early months of the pandemic [13]. Numerous studies demonstrate the link between comorbidities and disease severity and mortality [14,15]. However, our results show no significant difference in term of the effect of chronic illnesses between the survivors and non-survivors' cohorts in accordance with Sheng et al results [16].

Comparison of total white blood cell count, red blood cell count, and platelet count showed no significant difference between the surviving and non-surviving groups. Although lymphopenia was observed amongst the patients in our study, the difference between the surviving and non-surviving groups was not statistically significant. However, many studies confirm the relation between some hematological parameters like higher WBC count, lower platelets and lymphopenia with higher mortality rate [3,7,17,18]. The enzyme lactate dehydrogenase (LDH) is a cytoplasmic enzyme which is found in almost every cell in the human body. High level of LDH has been associated with malignancies and inflammation. Furthermore, high plasma (LDH) was reported as an indicator of poor prognosis of inflammation and various malignancies [19]. in our study, statistically significant higher LDH levels were reported in non-survivor cohort in accordance with many previous studies [7,10,20]. In addition to that, LDH reported as an independent indicator of lung injury in patients with severe COVID-19 disease [21,22]. Association of higher liver enzymes (AST and ALT) with increase morbidity that was described by other researchers was not observed in our study [3,23]. Regarding renal biomarkers (blood urea and creatinine), creatinine was slightly higher amongst the non-survivor group. However, this difference was not statistically different between the two groups in accordance with Zemlin et al [10]. Nonetheless, many researches correlate high urea and creatinine level with higher disease severity and mortality [20,24,25]. Although our results show that the inflammatory markers (namely ESR and CRP) were high among the survivors and non-survivor patients, the difference

between the two groups was not statistically significant. However high level of inflammatory markers was proved to be an indicator of higher disease severity [7,26,27]. D-dimer was significantly high among non-survivors' cohort in agreement with reports from many previous studies [20, 27-29]. D-dimer is generated when the cross-linked fibrin network undergoes plasmin-mediated degradation. excessive release of the inflammatory cytokines in patients with COVID19 cause a state of coagulopathy by inducing tissue factor expression and increasing fibrinogen production and associated with high levels of D-dimer [30,31].

CONCLUSION

we conclude that, some demographic features and accessible laboratory investigations could be used to identify high risk patients to give them the appropriate care. This can be of special importance to the countries suffering of low resources health care system.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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