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The Use of Lymphocyte Count and CT Chest Imaging for Assessment of COVID-19 Severity in Sudan: A Single Center Cross-Sectional Study

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Introduction: The COVID-19 (Coronavirus Disease 2019) global pandemic has strained health systems worldwide, including in Sudan, where there have been over 37,138 cases with an estimated case fatality rate of 7.5% as of August 2021. Emergency department physicians in Sudan play an important role in the triage, diagnosis and resuscitation of patients with COVID-19. Available laboratory and imaging investigations, namely complete blood counts and computed tomography (CT) scans, are being used to help characterize disease severity and anticipated clinical course. This study is conducted to evaluate the predictive value of lymphocyte counts and CT in characterizing disease severity among Sudanese patients with COVID-19 who present for emergency care.

Methods: This was a retrospective review of patients diagnosed with COVID-19 at a single academic center in Sudan. A questionnaire was used to gather de-identified data on patient demographics, co-morbidities, vitals, symptoms, laboratory and imaging findings. Patient disease severity was stratified based on respiratory distress defined by respiratory rate, oxygen saturations and PaO2:FiO2 ratio.

Results: Among 110 included patients, shortness of breath was the dominant symptom (68.8%) and hypertension was the dominant comorbidity (49.1%). The mean lymphocyte count was in the lymphopenic range (mean: 1320/µL, reference: 2500 - 10000/µL). The correlation between lymphocyte count and severe clinical presentation was statistically significant (p=0.01). Ground glass opacities were seen in the majority of CTs (93.6%). Computed Tomography Severity Score (CTSS) had a statistically significant correlation with clinical severity (mean= 18.18, range= 16 - 25, p=0.01). Lymphocyte count did not correlate with CTSS (p=0.21).

Conclusion: Lymphocyte count and CTSS both correlate with COVID-19 severity in Sudan. The lymphocyte count may be used in hospitals with limited PCR or CT availability to assist with prognostication.

Keywords: COVID-19 Clinical Severity, Emergency Care, Sudan, Lymphopenia, Computed Tomography.

Introduction

In December 2019, a novel coronavirus was identified as the causative organism for a cluster of cases of pneumonia linked to a seafood wholesale market in Wuhan, China [1]. By March 2020, there had been rapid spread of infections worldwide and COVID-19 was declared an international pandemic by the World Health Organization [2]. In Sudan, approximately 37,138 patients have been infected to date, with a case fatality rate of 7.5%, although these values are likely an underestimation of the true incidence [3].

Emergency care physicians in Sudan face the challenge of diagnosing COVID-19 as there is limited confirmatory polymerase chain reaction (PCR) testing available. Few centers can provide this test, and it is cost prohibitive. A single SARS-COV2 PCR test costs approximately 40 American dollars and has a turnaround time of 24 to 48 hours. Accurate diagnostics are important in this context as COVID-19 patients require use of special personal protective equipment, placement in isolation, and decision-making around anticipated clinical course and need for prolonged observation. Physicians in Sudan are currently using their clinical assessment in conjunction with lymphocyte count and chest imaging to diagnose and risk stratify patients with suspected COVID-19 infection. However, there have been no studies on the effectiveness of this diagnostic approach specific to the Sudanese context.

The use of lymphocyte counts and specific imaging findings to predict COVID-19 severity is supported by the international literature. Lymphopenia, defined as a lymphocyte count of less than 1500/μL, has been found to correlate with disease severity in studies conducted in multiple countries [4]. For example, a meta-analysis of 2282 cases in China found that lymphopenia was associated with a 3-fold increased risk of severe COVID-19 infection [5]. Computed tomography has also been found to be a highly sensitive diagnostic modality. While chest radiographs have little diagnostic value in early stages of illness, CT findings are often present even before symptom onset [6]. Hallmark CT findings for COVID-19 include bilateral multilobar ground glass opacities with or without consolidation in the posterior and peripheral lungs [7].

Methods

The aim of this study is to evaluate the correlation between the lymphocyte count and CT chest findings with the diagnosis, severity and outcome of cases of COVID-19 in Sudan. This is a descriptive, retrospective cross-sectional study of COVID-19 patients seen at a single academic center emergency department (Ribat University, Khartoum, Sudan) from March 1 through July 31, 2020. Inclusion criteria include age > 18, PCR confirmation of COVID-19 infection, and full demographic and clinical data including age, gender, oxygen saturation, symptoms, and duration of illness, comorbid conditions, complete blood count and CT chest scan. Patients were excluded if they (1) did not have confirmatory PCR testing, (2) had missing data; (3) had a known chronic hematologic disorder that may affect the lymphocyte count (AIDS was not considered as HIV test is not one of the routine tests in Sudan given very low country prevalence); add reference or (4) did not provide consent. Patients included in the final analysis were stratified into two groups based on disease severity.

Severe COVID-19 pneumonia was defined as: (1) Resting respiratory rate ≥ 30 times/min (2) oxygen saturation ≤ 93%; or (3) PF ratio (defined as arterial partial pressure of oxygen/fraction of inspired oxygen) ≤ 300mmHg. This definition was derived from prior observational studies of COVID-19 in China [8]. A CT severity score was calculated for each case by joint consensus of two radiologists who were blinded to the patient history. CT severity score, a simplified version of Yang et al.'s scoring system [9], involved assessment of the extent of anatomic involvement of each of the five lobes of the lung, with a score of 0 through 5 assigned per lobe (0, no involvement; 1 < 5% involvement; 2,5 - 25% involvement; 3,26 - 50% involvement; 4,51 - 75% involvement; and 5 > 75% involvement), and summed to provide a global severity score on a scale from 0 to 25. This global severity score is then classified into mild (<8), moderate (8 - 17), or severe (>18) [10].

Data were analyzed using the IBM SPSS version 24. Categorical data were described using frequencies and percentages and continuous data were described using means and standard deviation. A two-tailed p-value of less than 0.05 was considered statistically significant.

The research was approved by the ethics committees in Ribat University Hospital and by the Sudan Medical Specialization Board Educational Development Center. Written or telephonic consent was obtained from all patients or their first-degree relatives in the case of patient death. All patient data remained confidential as it was collected through a de-identified form.

Results

A total of 204 patients with PCR-confirmed COVID-19 infection were identified during the study period and 110 had complete datasets for inclusion in the final analysis. Of 110 patients, 68% (n=75) were male, and the mean age was 66.6 (range 27 - 95 years). Over 78% of patients were above the age of 60. The most common presenting symptoms included shortness of breath (68%), fever (68%), cough (64%) and fatigue (17%). The mean duration of symptoms was 8.4 days. Frequent comorbid conditions included hypertension (49%), diabetes mellitus (41%), asthma (6%), and ischemic heart disease (5.5%). The majority of patients had severe COVID-19 pneumonia, as characterized by their respiratory distress based on our definition (n=80, 73%). The majority of severe cases were among male patients (74%).

64% of the patients in this study had a lymphocyte count below 1500/mm. The mean lymphocyte count for our study population was 1320/mm3 (range 200 - 4000 / mm3) which is low compared to the laboratory reference range (normal range is 2500 - 10500/mm3). Patients with severe COVID-19 pneumonia were more likely to have severe lymphopenia (mean ***; range 200 - 3500/mm3) compared to non-severe cases (mean ***; range 1000 - 4000/mm3) (p=0.01).

Among all-comers, common chest CT findings included ground glass opacities, crazy-paving, and focal consolidations (93%, 55%, and 50% respectively). Most cases showed bilateral lung involvement (91%) with opacification in multiple lobes. Opacities were distributed peripherally in the majority of cases (61%), followed by diffuse and perihilar patterns (22% and 11% respectively). The mean CT chest severity score was significantly higher in patients with severe disease (mean 18.2, range 16.8-25) compared to patients with non-severe disease (mean 11.8, range 9.4 - 14.2, p=0.01) CT severity score had a statistically insignificant (negative) linear correlation with lymphocyte count (r=16.16 - 18.05, p=0.21).

Discussion

This study highlights the typical patient presentation to the emergency care center in Sudan. The patients are predominantly older than 60, the majority are men, and many patients have either hypertension or diabetes mellitus. Most patients are presenting over a week into their illness with respiratory distress, with symptoms of shortness of breath, fever and cough frequently reported.

The main objective of this study was to assess how easily available emergency department testing can help assess disease severity in patients with suspected COVID-19 infection, and both lymphopenia and CT severity scoring were found to correlate with severe illness. Lymphocyte screening on admission for those with COVID-19 is a possible predictor for assessment of disease severity and clinical outcomes in patients with COVID-19, and lymphopenia substantially correlates with poor clinical outcomes [11]. Future studies in Sudan should investigate the ability of lymphocyte count to predict COVID-19 disease severity on a larger scale.

While CT imaging also correlated closely with disease severity, this imaging modality is unlikely to be used in most healthcare contexts within Sudan, given resource limitations. Furthermore, the American College of Radiology does not recommend chest imaging as a modality for risk stratification [12].

The recently released series “Pragmatic Recommendations for the Management of Hospitalized COVID-19 Patients in Low and Middle Income Countries”, supports the use of diagnostic imaging to triage patients with suspected COVID-19 with moderate to severe features, in circumstances where clinicians are unable to obtain RT-PCR confirmation (weak recommendation, very low quality of evidence) [13]. The authors also recommend the use of standardized screening questionnaires with questions incorporated to differentiate from other local endemic febrile illness, use of pretest probability to guide decision making based on local COVID-19 infection rates, and assignment of standardized severity scoring based on WHO COVID-19 disease definitions. A recent systematic review found that limited clinical tools were available for screening, triage and severity scoring for patients with suspected COVID-19 in low-resource settings [14]. Based on these data, a new tool titled “African Federation for Emergency Medicine COVID-19 Mortality Scale” (AFEM-CMS), was developed to evaluate in-hospital mortality risk using readily available demographic and clinical inputs such as age, vital signs, Glasgow Coma Scale and comorbid conditions [15].

Limitations of the present study include that it took place in a single center in an academic setting with easy access to CT imaging, which is not the case in other clinical environments in Sudan and surrounding countries. Additionally, due to use of written medical records, there was missing data for many identified cases, reducing the number of patients included in the study. Lastly, additional laboratory values which have found to correlate with COVID-19 disease severity such as C-reactive protein, D-dimer and troponin were not studied due to resource scarcity.

Conclusion

This study found a statistically significant correlation between low lymphocyte count (defined as 1.30×103/μL or less) with severe clinical presentation of COVID-19 in a cohort of patients presenting to a tertiary care facility in Sudan. High CTSS (defined as greater than 16 or more) was also found to correlate with severe cases of COVID-19. We did not find a significant correlation between lymphocyte count and CTSS and further studies are needed in this area.

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