

## Mortality of covid19 in sickle cell disease systematic review

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### Abstract

The covid19 infection is pandemic disease are more commonly in chronic diseases. As covid19 case pulmonary infection, the current study focuses on sickle cell disease patients are suitable to acute chest syndrome. It will clarify the risk factors for covid19 infection and its clinical features in sickle cell disease. It also reviews the radiological findings to gain more data on this pandemic disease. The current study includes 44 cases of sickle cell disease having covid19 infection. The entire cases include sickle cell disease only in 89% whereas the other sickle cell disease cases are coexisted with beta- thalassemia in 9.1%. The fourth decade is the highest peak incidence. There are several complications found to be in sickle cell disease are acute chest syndrome, chronic leg ulcer, renal failure exceeding 10%. The bronchial asthma found to be in 6.9% and avascular necrosis found to be 11.4% whereas the cerebrovascular accident found to be in 13.8%. The radiological changes include lung tissues, alveoli, pleural cavities and pulmonary arteries in different rate. The incidence of recovery found to be in 93% whereas the death found to be in 7%. It found to be involving in respiratory and gastrointestinal systems result in different clinical features in different rate. This study compares the clinical features, findings investigation and complications between sex and decades. Further, this study clarifies recovery and mortality rate between sex and decades. Knowing and understanding covid19 infection in sickle cell disease, physicians will be able to provide high quality of medical services.

**Keywords:** Covid19; Pandemic; Pulmonary; Sickle Cell Disease; Acute Chest Syndrome; Avascular Necrosis

### 1. Introduction

As the covid19 is a pandemic disease, patients with sickle cell disease and treating physician raise several Concerns regarding the susceptible of covid19 infection as a risk factor in which the sickle cell patient is more likely to susceptible to acute chest syndrome [1-3]. Beside infection, the aggravating factors of sickle cell crisis are hypoxia, acidosis and dehydration which are also consequences of infection [1]. The acute chest syndrome is a major reason of death therefore the current study will focus on finding to identify the risk factors rate and correlate with mortality. The current study involves the duration of diagnosis based on clarification of clinical features and investigations. It measures the gender and age to provide more information of risk factors in relation to covid19 infection. The current study will describe the recovery and death incidence and duration by reviewing the entire cases considering the existence of the risk factors.

### 2. Material and methods

Current study investigates patients with sickle cell disease who have covid19 infection. It measures the risk factors of covid19 infection and its clinical features. Also, it reviews the chest- X- ray and computed tomography (CT) to measure

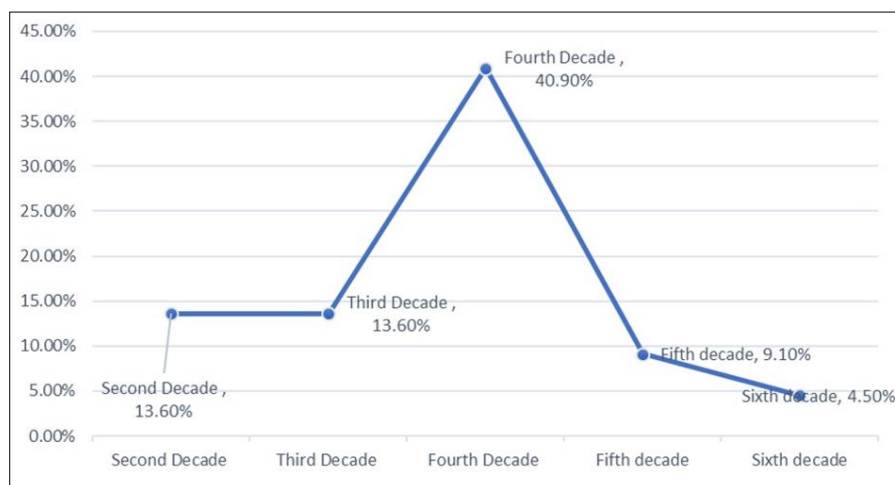
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the changes such as pulmonary embolism or other organ involves in coexistence of covid19 infection. Further, the follow up investigation will provide many findings indicating either the effectiveness or ineffectiveness of treatments. It also determines the incidence of recovery and critical fatality rate in patients with sickle cell disease. The literatures linked to sickle cell disease and covid19 are attained from PubMed and Google Scholar database. The entire articles have been published in 2020 found to be almost hundreds articles. The entire articles are founded and selected based on the keyword 'sickle cell, corona virus and covid19. The articles are selected only in English language. Out of hundreds articles, 44 cases found to be relevance to the study were collected from January to August 2020. The data is collected and analysis via Statistical Package for the Social Sciences (SPSS).

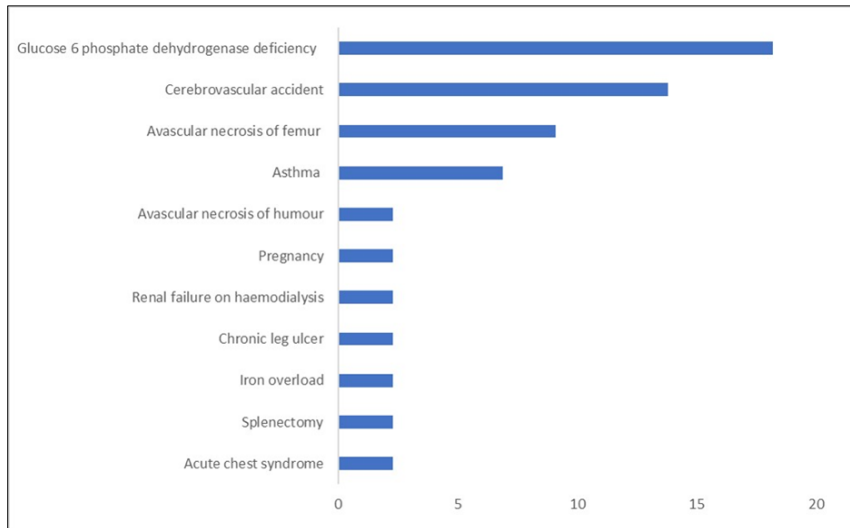
### 3. Results

The main complain of sickle cell patients attending to emergency department is pain due to vasoocclusive crises estimated in 95% in current study. The remain is due to gastrointestinal symptoms such as nausea, vomiting and diarrhoea in 2.3% as well as due to delivery of pregnancy. The entire cases include sickle cell disease only in 89% whereas the other sickle cell disease cases are coexisted with beta- thalassemia in 9.1%. The incidence of male and female is 44.4% and 55.6% respectively. Based on decade, the incidence of covid19 found to be in 18.2% of first decade, 13.6% of second, 13.6 of third, 40.9% of fourth, 9.1% of fifth and 4.5% of sixth (Figure 1). The diagnosis is based on nasopharyngeal swab taking in first day in 47.7%, second day in 6.8%, third day in 31.8, seventh day in 4.6%, eleventh day in 4.6% whereas the nasopharyngeal swab has done twice in 4.5% in the third day. Based on medical history, the sickle cell disease patients have several conditions such as acute chest syndrome in 2.3%, Splenectomy in 2.3%, iron overload in 2.3%, chronic leg ulcer in 2.3%, renal failure on haemodialysis in 2.3% whereas pregnancy found to be in 2.3%. Further, the sickle cell patient having bronchial asthma found to be in 6.9% whereas avascular necrosis of the femur and humour found to be 9.1% and 2.3% respectively. Moreover, the sickle cell patients having cerebrovascular accident found to be in 13.8%. In few cases of sickle cell disease, the glucose 6 phosphate dehydrogenase deficiency (G6PD) found to be in 18.2%. According to radiological studies such as chest- x-ray and computed tomography, the opacity found to be in 37.2% indicating involvement of lung tissues whereas the other findings such as atelectasis indicating partial collapse of lung alveoli in 2.3%, cardiac effusions in 4.6% and pulmonary embolism in 4.6%. The haemoglobin level ranges from 6 to 11.5% and haemolysis found to be in 39.3% (Figure 2). Beside the pain crisis, the main clinical features involve fever in 34.9%, cough 41.9%, shortness of breath (chest tightness) or nonspecific chest pain in 39.5%, nasal congestion in 11.6% which are classified under respiratory symptoms in 67.5% which differ in their presentation from one patient to other whereas gastrointestinal system which are nausea, vomiting and diarrhoea in 2.3% (Figure 3).

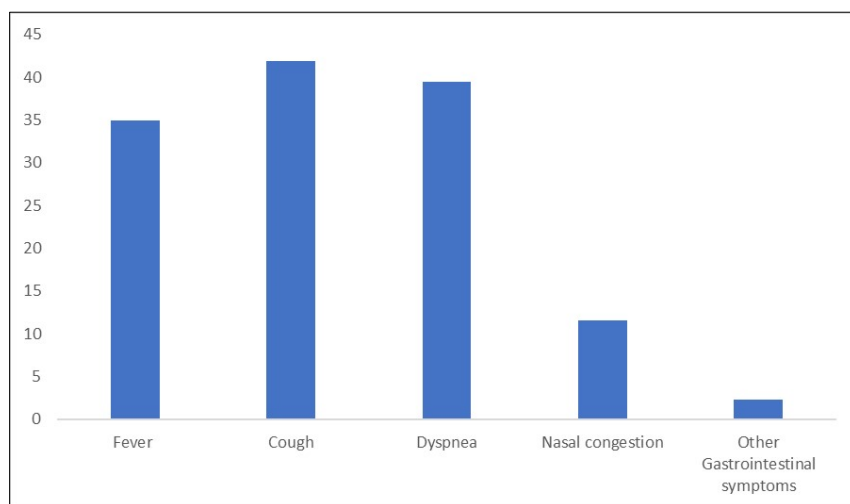


**Figure 1** The incidence of covid19 in sickle cell patient's decades

Based on laboratory, the leucocytosis found to be high in 6.9% and lymphocytopenia in 27%. The pulse oximetry shows desaturation in 45.4% however they need oxygen support in 61.4% including non-invasive 56.8% and invasive in 4.6%. The patients receive anticoagulant therapy in 54.5%. Different medications have been used in treatment are azithromycin 31.8%, cefotaxime in 27.3%, hydroxychloroquine in 11.5%, hydroxyurea in 9.2%, tocilizumab in 4.6%, ceftriaxone in 2.3%, deferoxamine in 2.3% and zosyn in 2.3%. The incidence of recovery found to be in 93% whereas the death found to be in 7%. The incidence of recovery from hospital management is 72.3% whereas 20.7% is from home management.



**Figure 2** The incidence of covid19 in sickle cell patients with coexistence of risk factor conditions



**Figure 3** The incidence of covid19 symptoms in sickle cell patients

Based on decade, the incidence of death is 5.5% in fourth decade, 16.6% in second and 50% in sixth. On the other hand, the incidence recovery is 100% in first, third and fifth whereas the recovery is 94.5% in fourth decade, 83.4% in second and 50% in sixth. Based on clinical feature, the incidence of fever is 50% of fifth and 50% of sixth, 66.6% of third, 72.2% of fourth, 100% of second whereas the first decade has not recorded any fever. Based on clinical feature, the incidence of cough is 25% of fifth, 38.8% of fourth 83.3% of sixth. 50% of third whereas the first decade has not recorded any cough. Based on clinical feature, the incidence of shortness of breath or nonspecific chest pain is 50% of fifth and sixth, 33.3% of fourth, 66.6% of second and third whereas the first decade has not recorded any chest tightness. Based on radiological findings, the incidence of opacity is 25% of fifth, 33.3% of fourth, 50% of third and 100% of second whereas the first and sixth decade has not recorded any findings. Acute chest syndrome is risk factor found to be mainly in fourth decade in 5.5% as well as chronic leg ulcer is risk factor found to be mainly in fourth decade in 5.5%. Chronic renal disease on haemodialysis is risk factor found to be mainly in fourth and fifth decade in 5.5% and 25%. The iron overload is risk factor found to be mainly in 25% of fifth decade. G6PD is risk factor found to be mainly in 100% of first decade. Avascular necrosis of femur is risk factor found to be mainly in 5.5% of fourth, 33.3% third and 50% of sixth decade. Avascular necrosis of humerus is risk factor found to be mainly in 50% of sixth decade. Cerebrovascular accident is risk factor found to be in 25% of fifth, 22.2% of fourth and 16.6% of third decade.

Based on sex comparison, the incidence of death in male is 8.3% and female 6.6% whereas the incidence of recovery is 91.7% in male and 93.4% in female. Acute chest syndrome is risk factor found to be in 6.6%. Female. Chronic leg ulcer is risk factor found to in female 6.6%. Chronic renal disease on haemodialysis is risk factor found to be in male is 8.3% and female 6.6%. The iron overload is risk factor found to be in female 6.6%. Avascular necrosis of femur is risk factor

found to be in male is 16.6% and female 13.2%. Avascular necrosis of humerus is risk factor found to be in female 6.6%. Cerebrovascular accident is risk factor found to be in 16.6% male and 19.8% female Asthma risk factor found to be in 19.8% female. The radiologic findings such as opacity found to be in male is 85.1% and female 26.4% whereas atelectasis found to be in 8.3% male and 13.2% pulmonary embolism and 13.2% cardiac effusion in female. The haemoglobin level is below 10 g\dl found to be in 66.6% male and 39.6% female. Haemolysis found to be in 33.3% male and 26.4% female.

#### 4. Discussion

Sickle cell disease is most common hemoglobin disorders of the world's population with incidence rate of 5%. The incidence of sickle cell disease is more than 75% in sub-Saharan Africa (WORLD HEALTH ORGANIZATION) [4]. The gene of entire cases sickle cell disease classified into HgbSS or HgbSC in 89%.1 whereas HgbSB (beta- thalassemia) in 9.1%. The chief complain of sickle cell patients is pain because of vasoocclusive crises estimated in 95% in current study. The incidence covid19 in entire sickle cell disease found to be more in female (55.6%) than male (44.4%). Further, the highest incidence of covid19 found to be fourth decade (40.9%) comparing to other six decades (figure 1). In fact, the infection, hypoxia, dehydration, or acidosis linked to clinical and laboratory presentation are aggravating factors to vaso-occlusive crisis [1]. Since the respiratory infection is aggravating factors to acute chest syndrome [1], the acute chest syndrome mimics clinical features and investigations of covid19 respiratory infection from mild to severe conditions [5-16]. In current study, the sickle cell anemia present with vasoocclusive pain due to covid19 infection which has been approved by nasopharyngeal swap in all cases of different days of admission with a majority of first and third days due to clinical features presentation.

The risk factors associated with sickle cell disease are acute chest syndrome, Splenectomy, iron overload, chronic leg ulcer, renal failure on hemodialysis found to be equal in 2.3% which may decrease immunity and high predispose to infection. Further, bronchial asthma may increase the mortality rate of respiratory infections in sickle cell disease found to be in 6.9%. the avascular necrosis of the femur and humour found to be 11.4% indicating insufficient blood supply of bone and its bone marrow by series of vaso-occlusions. Hydroxycarbamide (hydroxyurea) is another risk factor for suitable infection in sickle cell disease [1] found to be in 9.2% in current study. Also, the cerebrovascular accident indicates risk of thrombosis found to be 13.8%. As the thrombosis is risk factor in sickle cell disease, the anticoagulant therapy provided in 54.5% of all cases. On the other hand, hemolysis can increase the risk of sickle cell disease crisis in coexisting of the glucose 6 phosphate dehydrogenase deficiency (G6PD) with incidence of 18.2%. The chest X-ray is mandatory in Sickle cell patient presenting with respiratory features. The radiologic result of infiltration presenting as opacity in COVID-19 positive patients or Sickler patients indicating acute chest syndrome [5-16]. According to current study of radiological investigation, the infiltration of different lung lobe found to be in 37.2% indicate involvement of lung tissues however associated complication of covid19 pulmonary infection such as cardiac effusions in 4.6% and pulmonary embolism in 4.6%. According to laboratory, hemolysis found to be in 39.3%. of entire cases indication covid19 infection is high risk factors of hemolysis in sickle cell anemia (Figure 2). Further, 27% of sickle cell entire cases have lymphocytopenia indicate that covid19 decreases immunity in sickle cell disease. Hypoxia is due to covid19 and aggravating factors of sickle cell crisis found to be in 45.4%. The sickle cell patients receive oxygen support in 61.4% including non-invasive 56.8% and invasive in 4.6% due desaturation in 45.4% via pulse oximetry to eliminate hypoxia as an aggravating factor due to covid19 infection.

In fact, the clinical pictures are linked to involving organs as the COVID19 penetrates cell membrane by binding to angiotensin-converting enzyme 2 (ACE2) and causes pulmonary infection or other organs such as brain, kidney, vascular smooth muscle, and skeletal muscles [17,18]. The clinical presentation of covid19 are mainly fever dry cough, and dyspnea [19]. found to be record the majority which is almost two third of entire cases whereas the gastrointestinal symptoms record the minority. The cough, dyspnea and fever are the common feature of covid19 infection in sickle cell crisis with incidence rate of 41.9%, 39.5%, 34.9% respectively (Figure 3). The nasopharyngeal swap has different days after admission based on respiratory symptoms. Accordingly, emergency physicians need to be alert for possibility of delay of respiratory symptoms since the infection of covid19 can be the reason behind of vaso-occlusive crisis.

The fatality ratio increase as the age increases [20] therefore current study measures the risk factors, clinical presentations and mortality considering decade and sex. In covid19 Sickler, most of the death and recovery is equal in sixth decade (50%) whereas the death less than 17% and recovery rate is higher than 83% in previous decades. Based on clinical feature, fever is 50% in fifth and sixth and more than 50% in second, third and fourth. On the other hand, the fever is absent in the first decade. The cough is majority in sixth decades and less than 50% in third, fourth and fifth however cough is absent in first decade too. The incidence of shortness of breath is 50% and below in fourth and fifth whereas it is above in second and third however shortness of breath is absent in first decade. Therefore, a great attention for treating physician for first decade since patient is asymptomatic covid19 in sickle cell disease. Based on radiological

findings, the infiltration of lung tissue is 50% and below in fourth and fifth and completely in second however the infiltration is absent in first and sixth decades. This great alert for physician to be careful in diagnosis and decision of treatment as inpatient or outpatient for the first decades. Moreover, the fourth decade include majority of risk factors such as Acute chest syndrome chronic leg ulcer, Chronic renal disease, Cerebrovascular accident and Avascular necrosis of femur which increases as incidence age based on lifestyle may present with variable incidence. The risk factors are linked with thrombosis which is due to sickle cell disease producing coagulopathy therefore the physicians should have great attentive in treating immunocompromised covid19 patients who usually on hydroxyurea leading to decrease immunity too. Based on sex comparison, the atelectasis, avascular necrosis of femur and chronic renal disease on haemodialysis is risk factor found be more in male on the other hand cerebrovascular accident is risk factor found to be more in female. The other risk factors are acute chest syndrome, chronic leg ulcer, pulmonary embolism, iron overload, asthma and avascular necrosis of humerus found to be only in female. The radiologic findings found to be more in male than female. However, the pulmonary embolism and cardiac effusion found to be in female. The male is lower than female in haemoglobin level below 10 g\dl which is due to haemolysis found to be more in male than female.

The incidence of recovery in covid19 in sickle cell disease found to be in 93% which is more in female than in male. On the other hand, the incidence death in covid19 in sickle cell disease found to be in 7% of entire cases which is more male than female. The incidence of death is on sixth decades due to risk factors comparing to other decades. Since the most patent with sickle cell disease has increase rate of Intensive care unit admission, the incidence of recover and death in patient with sickle cell disease is close international rate (world meter).

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## 5. Conclusion

The first decade patients with sickle cell disease are asymptomatic patients of covid19 being high risk of spread of infections therefore great precaution must be done in clinical and laboratory from health workers such physicians, nurse and technicians through laboratorial, radiology and surgical procedures during examination, investigation and management using isolation room and personnel protecting equipment in emergency room and admission. The patient with sickle cell disease is at high risk of intensive care unit and may present with clinical features of vasoocclusive crisis behind serious covid19 infection. Emergency physician should admit him under observation for twenty-four hours to control pain and rule out of covid19. Infection control division should be providing protocol in admission procedure for health administrative management with clear plan to avoid spread of infection between patients and health workers as well as minimizing the spread in society.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

There is no conflict of interest.

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