COVID-19 Infection in Thalassemia Patients

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بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

{وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ ۖ

وَسَتُرَدُّونَ إِلَىٰ عَالِمِ الْغَيْبِ وَالشَّهَادَةِ فَيُنَبِّئُكُم بِمَا كُنتُمْ تَعْمَلُونَ }

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Supervision Certificate

I certify that this thesis was prepared under my supervision at Department of Pediatrics- College of Medicine/ Diyala University.

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Abstract

Background:COVID-19 is a contagious respiratory infectious disease whose causative agent has been demonstrated to be a novel virus of the coronavirus family, SARSCoV-2. Thalassemia is a chronic haematological disease in children.

Aim of study: To study the incidence of COVID-19 infection in thalassemia patients and the association of demographic and the other criteria of the thalassemia patients with COVID-19 infection.

Patient and method: This is a hospital based cross sectional, case-controls study. The study was conducted from 1st of October 2020 to 1st of December 2020 in Thalassemia Centre, Baaquba, Diyala, Iraq. The study enrolled 100 thalassemia patients, involving children, adults and elderly. COVID-19 infections were confirmed by Antibody Rapid Test by using Kit (The: Biocomma limited, Industry: China, Code:51818). Control group was random selected from the community by simple random method involving different age groups without chronic diseases. a questionnaire form was performed involving many characters of thalassemia patients, beside COVID-19 infected or not, family history of COVID-19. SPSS version 21 was used for statistical analysis.

Result: During the study, 13 of thalassemia patients were infected with COVID-19, male gender were more predominant than female with ratio of M:F 1.4:1. The study showed the COVID-19 infection of thalassemia group were 13 (13%), while 39 (39%) of control group were infected. Rate of COVID-19 infection in thalassemia patients increase in those who have hepatitis (29.4%) and those who kept on deferoxamine (28.6%), while splenctomized patients had low rate(8.7%).

Conclusion: Hemoglobin disorders including thalassemia are generally not risk for COVID-19 infection but iron-overload, chronic liver hepatitis, diabetes and even the immune system might encounter these patients to have higher risk of COVID-19 infection than normal population.

Key words: COVID-19, thalassemia, hepatitis.

Introduction

COVID-19 is a contagious respiratory infectious disease whose causative agent has been demonstrated to be a novel virus of the coronavirus family,SARSCoV-2.This virus is a single-stranded and enveloped RNA. Its genomic is 29891 nucleotides in size and encoding 9860 amino acids.COVID-19 was first discovered in December 2019 in the South China Seafood Market Hubei Province, China.It rapidly spread throughout the world.transmission via direct contact through droplets spread by coughing from an infected person.The clinical symptoms of the disease varies from asymptomatic infection, mild upper respiratory symptoms to pneumonia with respiratory failure and death.The symptoms develop within 14 days after exposure to someone who has COVID-19 infection, including dry cough, dyspnea,difficulty in breathing, fever,Loss of taste and smell, tiredness,pain and diarrhea.[1,2,3,4,5]

Generally, the symptoms more sever in immunocompromised, older people, and those with chronic conditions like diabetes, cancer and lung disease. Most deaths are related to respiratory complications and Thrombotic complications such as acute pulmonary embolism.[6]

Thalassemia is the most common inherited disorder,result from defect in production of haemoglobin. Ineffective bone marrow erythropoiesis and excessive red blood cell hemolysis together account for the anemia.Since reticulocytes manufacture equimolecular portions of alpha and beta chains, mature erythrocytes contain essentially equimolecular quantities of each chain.[7] Patients with thalassemia do not produce enough hemoglobin (Hb) A ($\alpha 2\beta 2$) due to the fact cells cannot manufacture either the alpha or beta polypeptide chain of human hemoglobin. Alpha-thalassemia depresses only the production of the alpha chains, and beta-thalassemia depresses only the production of the beta chains. Clinically, each alpha and beta-thalassemia may occur in the major (homozygous), intermediate, and minor (heterozygous) genetic forms and also can interact with the presence of abnormal hemoglobins in the same individual Thalassaemia patient often have underlying complications including heart disease, liver disease, diabetes and intense iron overload.[8,9]

The studies show that ORF8 and surface glycoproteins of the COVID-19 could combine to the porphyrin to form a complex. Orf1ab, ORF10, and ORF3a proteins could coordinate attack the heme, formed into the mitochondria, on the 1-beta chain of hemoglobin to dissociate the iron ions from the heme. Furthermore, it revealed that Favipiravir could inhibit the envelope protein and

ORF7a protein bind to porphyrin, thus preventing the virus from entering host cells, and catching free porphyrins.[10]

Patients with preexistent chronic morbidities are likely to be more severely affected by severe acute respiratory syndrome coronavirus-2 infection. Infectious complications, are a common cause of mortality and morbidity in thalassemia patients.If these patients have stress erythropoiesis, iron overload, splenectomy and adrenal insufficiency may contribute to increased susceptibility to infection.[11].

Aim of the study

To study the incidence of COVID-19 infection in thalassemia patients and the association of demographic and the other criteria of the thalassemia patients with COVID-19 infection.

Patients and Methods

This is a hospital based, cross sectional, case-controls study. The study was conducted from 1st of October 2020 to the 1st of May 2021, data collection was done from 1st of October-1st of December 2020 at Thalassemia Centre, Baaquba, Diyala, Iraq.

The study enrolled 100 thalassemia patients involving children of different age group, in addition to adults and elderly. COVID-19infections were confirmed by Antibody Rapid Test (blood test to detect IgM and IgG antibodies specific for nucleocapsid protein of COVID-19) by using Kit(The: Biocomma limited, Industry: China, Code:51818). Control group was also 100 person, they were randomly selected from the community by simple random method, they involved different age groups.

A questionnaire was performed including age, gender, type of thalassemia, COVID-19 infected or not, family history of COVID-19, symptoms, chelating therapy, had hepatitis or not, splenectomised or not. Data collection was done by a well- trained personnel.

Statistical analysis

It was performed by using SPSS (Statistical package for Social Sciences), version 21, Chi square test was used to analyse the relationship between variables, p value was taken significant at level of less than (0.05).

Results

The study enrolled 100 thalassemia patient, M:F rate are 1.4:1. One third of patients were at 6-12 years old and the other third were above adolescence, 2 of them were elderly, while the remainder were distributed to other age groups, table(1).

Table 1: Demographic criteria of the thalassemia patients

Age	Male n.(%)	Female n.(%)	Total
Birth-<3yrs	2 (66.7%)	1 (33.3%)	3 (100%)
3-<6	6 (60%)	4 (40%)	10 (100%)
6-<12	21 (67.7%)	10 (32.3%)	31 (100%)
12-<18	10 (47.6%)	11 (52.4%)	21 (100%)
18-<25	14 (82.4%)	3 (17.7%)	17 (100%)
25-<40	8 (80%)	2 (20%)	10 (100%)
40-<60	3 (50%)	3 (50%)	6 (100%)
60 and more	0	2 (100%)	2 (100%)
Total	64 (64%)	36 (36%)	100 (100%)

Number of cases with COVID-19 infection of thalassemia group were 13 (13%), while 39 (39%) of control group were infected, p value = .000, table (2).

Table 2:-Infection rate of thalassemia and control groups for COVID-19.

Groups	COVID-19 infection		Total Number (%)	p value
	Positive Number (%)	Negative Number (%)		
Case	13 (13%)	87 (87%)	100 (100%)	.000**
Control	39 (39%)	61 (61%)	100 (100%)	
Total	52 (26%)	148 (74%)	200 (100%)	

It was found that number of thalassemia patients who had exposed history for Covid- 19 infection, family history of Covid- 19 infection, was only 3 (3 %), while for control group was 31 (31 %). It was obvious that decreased infection of thalassemia was accidently due to decreased family exposure for Corona virus.

It was clear that all Covid- 19 infected individual from general population were above 12 yrs old, while in thalassaemia patients, 4 infected patients, which form about half of infected thalassemia patients, were below 12 yrs old. Covid- 19 infection insignificantly (p value= .331) affect male gender more than females, this effect was more clear among thalassemia group. table (3).

Table 3:- Demographic criteria associated with COVID-19 infection.

		COVID-19 infection		Total n.(%)	p value
		Thalassemia patient	Control group		
		Positive n.(%)	Positive n.(%)		
Age	Birth– 12yrs	4 (8)	0	4 (8)	-
	More than12yrs	9 (17)	39 (75)	48 (92)	
Gend	Male	9 (17)	21 (40)	30 (57)	.331
	Female	4 (8)	18 (35)	22 (43)	

Thalassemia patients who have hepatitis had higher rate and patients with splenectomy had lower rate for infection with COVID-19. Thalassemia patients who were kept on deferoxamine were infected in rate more than that of patients on deferasirox. Type of thalassemia not affected the incidence of COVID-19 infection, table (4).

Table 4:- Association of the thalassemia patients criteria with COVID-19 infection rate

Criteria	COVID-19 infection		Total	P value
	Positive n.(%)	Negative n.(%)		
Hepatitis				
- Positive	5 (29.4%)	12 (70.6%)	17 (100%)	.027
- Negative	8 (9.6%)	75 (90.4%)	83 (100%)	
Splenectomy				
-Positive	2 (8.7%)	21 (91.3%)	23 (100%)	.484
-Negative	11 (14.3%)	66 (85.7%)	77 (100%)	
Chelating agent				
-Deferoxamine	4 (28,6%)	10 (71.4%)	14 (100%)	.072
-Deferasiroxe	9 (10.8%)	74 (89.2%)	83 (100%)	
Type of thalassemia				
-Major	9 (13.6%)	57 (86.4%)	66 (100%)	.792
- Minor	4 (11.8%)	30 (88.2%)	34 (100%)	

Discussion

COVID-19 are known for their mild presenting symptoms like common cold. However, the world has recently seen a huge outbreak caused by sever acute respiratory syndrome coronavirus which was highly pathogenic and spread rapidly starting from China to all over the world with increase in mortality rate. [12]

Thalassemia is one of the most common forms of the hemoglobinopathies. It is mainly due to either alpha or beta chains hemoglobin reduction leading to defects that cause a wide range of clinical presentations. Thalassemia can also be categorized into transfusion dependent or independent. [13]

Thalassemiahas not been linked directly to respiratory conditions, yet close monitoring is necessary as thalassemia patients could have multi-organ damage including heart, lung, liver, endocrine, and immune system damage due to the iron overload that might increase their COVID-19 infection risk. [14,15]

Thalassemia patients are usually splenectomized as part of the therapeutic interventions.Besides predisposing to infections by encapsulated bacteria, splenectomy has also been correlated with quantitative lymphocyte changes and aggravation of the immunological effects of multiple transfusions, due to the reduced clearance of immune cells. [16]

At present there is no evidence that splenectomy is correlated with an increased risk of COVID-19 infection and complications. However, patients whose spleen has been removed should be evaluated for concomitant bacterial infection, which may happen along with COVID-19 and start antibiotics if needed. [17]

Chronic liver hepatitis is common complication of thalassemia. This study shows thalassemia patients with hepatitis are at increase risk of COVID-19 infection due to cirrhosis associated immune dysfunction. The same can be true for patients after liver transplantation. [12]

Iron chelating agent that reduces liver iron concentration and serum ferritin levels. There is no evidence indicating relation between iron chelation and susceptibility toCOVID-19 infection or COVID-19 severity but according to this study patients who take deferasirox are low risk to infection than other who take deferoxamine. Onother hand, thalassemia patients who became positive for COVID-19 and develop symptoms should discontinue their iron chelation therapy.[17]

We suggest that even if thalassemia patients seem to have a smooth clinical course of COVID-19 infection, screening them for COVID-19 infection should be done at each healthcare visit to provide close monitoring, avoid unexpected deterioration and control the spread of infection.

Conclusion and Recommendations

Hemoglobin disorders including thalassemia per se are generally seemed not a risk for COVID-19 infection but complications like iron-overload, chronic liver hepatitis, diabetes and even the immune system might encounter these patients to have higher risk of COVID-19 infection than normal population.

The few reported cases of COVID-19 infection in people with thalassemia might reflect the efforts to minimize the social contacts or other unclear reasons to get Covid- 19 infection.

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