70 with mean ± standard deviation of 27.69 ± 24.51. Approximately 63.7% had mild disease, 13.2% moderate disease, and 35.7% severe disease, according to our severity score grading system. Comparison of international score with our score was done with a matching of 64.9%. Some minor modifications was done in a validated score due to local factors and clinical diversity.Present samples cohort (171) was divided randomly into two groups; Discovery group (N=100) and Validation group (N=71). Validation was done with overall matching of 81.5% after including parameters which was not present in an international score as per Indian patients. Score matching increased from 65% to 82% All weightings demonstrated a significant difference between the scores of mild, moderate, and severely affected patients, as classified by a subjective rating or with an existing index ($P < 0.01$).
Conclusion: Routine evaluation of disease severity in children with SCA will help to prospectively identify children at higher risk for a turbulent clinical course who may need more active management and monitoring. Assessment of patients objectively after any type of intervention like counselling, treatment(pre and post hydroxyurea) can be done by score.

References

1. Hockham et al, The spatial epidemiology of sickle-cell anemia in india, *Sci Rep*. 2018;10.1038
2. W.van den Tweel et al, Develepment and validation of pediatric severity index for sickle cell patients, *Am.J.hematology*.85 (2010);746–751

P110 CLINICAL CHARACTERISTICS OF COVID-19 IN SICKLE CELL DISEASE (SCD) PATIENTS

Malhan, H; Iqbal, B; Ghazwani, Y; AlHakim, A; Ali, S; Omar, H; Dammag, E; Khalifah, H; Alqurbi, A; Ekpenyong, U;Subahi, N; Alqahiry, W; Bakkar, M

Prince Mohammad Bin Naser Hospital, Jazan, SAUDI ARABIA

Introduction SCA is a common genetic disorder in Saudi Arabia with estimate of 1.4 % of population[1,2]. The prevalence of SCD in Jazan region is around 24 per 10,000 which consider the second region with high prevalence of SCD after eastern province. COVID 19 infection outbreak has affected SCD with different outcome.
Objectives: This research aims to determine the clinical picture of COVID-19 in patients with sickle cell disease SCD. The study represented the risk factors for severe COVID-19 presentation and predictors for poor prognosis in this group of patients.
Methods: This study is a retrospective, descriptive, observational study of SCD adult and pediatric patients in Prince Mohammed Bin Nasser Hospital, Jazan, Saudi Arabia, who were diagnosed with COVID-19 virus infection at the study center from March 2020 to September 2021. To describe clinical presentation of SCD patients of different severities, who got COVID-19 during the study, socio-demographic data, clinical presentations, laboratory parameters, medications use, as well as COVID-19 symptoms and severity were extracted and analyzed from the medical record files.
Results: 43 medical records for adult and pediatric sickle cell patients with COVID-19 were collected, in order to determine the impact of COVID-19 on the clinical presentation of SCD patients. (53%) were females, (47%) were males with a mean age of 24 years (±1.9). (37%) of the sample suffered from major comorbidities, out of which 44% had ACS. and 11.6% have pulmonary embolism. The most prevalent clinical symptoms were fever (56%) and Shortness of Breath (37%). (16%) of included patients were admitted to the ICU with an average length of stay equals to 3.9 days (±0.6).
CBC showed normal averages of PLT with a mean equal to 327 K/uL (±21.6), Basophils 0.05 K/uL (±0.01), Lymphocytes 3.6 K/uL (±0.4). High averages were found for WBC 13.8 K/uL (±1.1), Neutrophils 8.8 K/uL (± 0.9) and PT 14.2 seconds (±0.3). The only laboratory parameter that showed low average reading was Hemoglobin, with a mean equal to 8g/dl (±0.2). Out of the 41 patients who undergone CRP test, 85% were positive. The main CT chest finding were ground glass appearance in 30% of the patients 88% of the studied patients were on Hydroxyurea, 76% were on 1000 mg dose. For COVID-19 management, majority of patients were on Antibiotics 93%, 70% of patients started Anticoagulants, 51% of the patient has received antiviral treatment. 32.5% of the patient were treated with steroids. 70% of the patients have received blood transfusion. 5 patients 12% were managed at home. One patient had coinfection with falciparum malaria.
Total deaths was 2 patients represented 4.6 % out of total SCD patients with COVID-19 who were included in the study.
Conclusion: After exploring the impact of COVID-19 on SCD patients, the main presenting symptom were fever and shortness of breath. The major complication were acute chest syndrome 44% and pulmonary embolism in 12%.
The overall prognosis was excellent and most of the patient have recovered. The death was reported in 2 patients only. Outpatient treatments were feasible in 12% of the patients.

References

1. AlHamdan NA, AlMazrou YY, AlSwaidi FM, Choudhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. *Genet Med*. 2007;9:3727.
2. Nasserullah Z, Alshammari A, Abbas MA, Abu-Khamseen Y, Qadri M, Jafer SA, et al. Regional experience with newborn screening for sickle cell disease, other hemoglobinopathies and G6PD deficiency. *Ann Saudi Med*. 2003;23:354–7

P111 COVID-19 IN PATIENTS WITH THALASSEMIA AND SICKLE CELL DISEASE: A SINGLE CENTER EXPERIENCE

Dimopoulou, M; Komninaka, V; Flevari, P; Bartzi, V; Repa, K; Voskaridou, E

Laikon General Hospital, Athens, GREECE

Background: Thalassemic patients present complications such as iron overload, cardiac disease or diabetes that are expected to make them more vulnerable to COVID-19. Acute complications of SCD triggered by a viral infection include painful vaso-occlusive episodes, acute chest syndrome (ACS) and venous thromboembolic disease (VTE). Published data report variable rates of severe COVID-19 in thalassemia whereas for SCD more robust data exist suggesting a strong association with severe disease and mortality.
Aims: The aim of the present study was to report the severity and mortality of COVID-19 in thalassemic and SCD patients of a Greek Center and investigate possible risk factors for severe disease.
Patients and Methods: The patient population of our Center includes 200 thalassemic patients and 320 SCD (of which 73 and 53 transfusion dependent, respectively). Baseline clinical and laboratory data and manifestations, clinical course, treatment and outcome of COVID-19 were collected from medical files for all the patients that had a PCR-documented COVID-19 infection since the pandemic initiation. Association of characteristics with severe disease or hospitalization was investigated with Fisher's exact test.
Results: Since August 2020 until November 2021 34 patients (21 thal and 13 SCD) were infected by SARS-CoV2 corresponding to 10.5% and 4% of our patient population, respectively. Their median age was 47 yrs and 14 of them were male. Baseline patients characteristics as well as COVID-19 manifestations and outcome are presented on Table 1. None of the patient had cardiac iron overload, 2 had medium and 1 severe hepatic iron overload. Five patients had commorbidities (pulmonary hypertension 2, heart failure 1, atrial fibrillation 3, diabetes mellitus 2, arterial hypertension 1, malignant disease 1). Five patients had been vaccinated for COVID-19 before they presented with disease.
The majority of patients (32/33) devepoped symptomatic disease of mild (26) or moderate (6) severity according to established criteria. Only one patient presented severe disease. Only 6/33 patients required hospitalization (4 thalassemic and 2 with SCD). In 4/6 hospitalized patients oxygen therapy with a nasal cannula was required and only one patient required a Venturi mask. None of the patients were intubated. One of the SCD patients developed an acute painful episode but there was no ACS post COVID-19. No increase in transfusion requirements was observed. There were no deaths in our patient population. All but one patients completely recovered whereas one SCD patient who was hospitalized is suffering from long-COVID.
History of heart failure was associated with severe disease (p=0.03) and history of AF was associated with need for hospitalization (p=0.02). History of splenectomy, pulmonary hypertension or ACS and the degree of iron overload were not associated with disease severity or hospitalization requirement.
Conclusion: COVID-19 had mild to moderate severity in the majority of our patients and only a minority of the patients required hospitalization. No ICU admissions or deaths were observed, comparing favourably to published data. Factors predisposing for severe COVID-19 in the general population, especially cardiac disease, seem to play a role also in patients with hemoglobinopathy.

BASELINE PATIENTS CHARACTERISTICS	
DIAGNOSIS	
TRANSFUSION DEPENDENT β-THALASSEMIA (TDT)	11
NON-TRANSFUSION DEPENDENT β-THALASSEMIA (NTDT)	7
HEMOGLOBINOPATHY H	2
SCD (ON CHRONIC TRANFUSIONS)	13 (4)
TOTAL	33
AGE (YRS)*	47 (26–69)
SEX (M/F)	14/17
SPLENECTOMY/FUNCTIONAL ASPLENIA	11/4
COMMORBIDITIES	5
SERUM FERRITIN* (ng/µl)	738 (49–2900)
HYDROXYUREA TREATMENT	6
CHELATION THERAPY	14
MONOTHERAPY	10
COMBINATION	4
ANTICOAGULANTS	3
ANTI-PLATELETS	8
HISTORY OF ACS/MULTIPLE RELAPSES	3/1
HISTORY OF VTE	3
LIC (mg/gr)*	4.7 (1.1–21.4)
ANTI-COVID VACCINATION	5
SEVERITY OF COVID INFECTION	
ASYMPTOMATIC	1
MILD (NO DYSPNEA)	27
MODERATE (DYSPNEA, SpO2 ≥94%)	5
SEVERE DYSPNEA, SpO2 <94%)	1
FEVER	23
COUGH	20
PAINFUL CRISIS	1
PULMONARY INFILTRATES	3
VTE	0
HOSPITALIZATION	6
TREATMENT	
ANTIBIOTICS	13
STEROIDS	6
REMDESIVIR	4
LMWH	7
anti-TNF	1
OXYGEN THERAPY	5
DEATHS	0
*:MEDIAN (RANGE)	

References

1. Mucalo L et al, *Blood Adv*. 2021; 5(13):2717–2724.
2. Clift AK, et al, *Ann Intern Med*. 2021; 174(10):1483–1487.
3. Vilela TS, et al, *Hematol Transfus Cell Ther*. 2021;43(1):87–100.

P112 ENERGIZE AND ENERGIZE-T: TWO PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDIES OF MITAPIVAT IN ADULTS WITH NON--TRANSFUSION-DEPENDENT OR TRANSFUSION-DEPENDENT ALPHA- OR BETA-THALASSEMIA

Kuo, K[1]; Layton, D[2]; Al-Samkari, H[3]; Kattamis, A[4]; Sheth, S[5]; Taher, A[6]; Viprakasit, V[7]; Chamberlain, C[8]; Czapla, L[8]; Gheuens, S[8]; Lynch, M[8]; Tong, B[8]; Uhlig, K[8]; Cappellini, M[9]

[1]Division of Hematology, University of Toronto, Toronto, ON, CANADA; [2]Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, UNITED KINGDOM; [3]Division of Hematology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, UNITED STATES; [4]First Department of Pediatrics, National and Kapodistrian University of Athens BR, Athens, GREECE; [5]Weill Cornell Medical College, New York, NY, UNITED STATES; [6]American University of Beirut, Beirut, LEBANON; [7]Siriraj-Thalassemia Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, THAILAND; [8]Agios Pharmaceuticals, Inc., Cambridge, MA, UNITED STATES; [9]University of Milan, Milan, ITALY

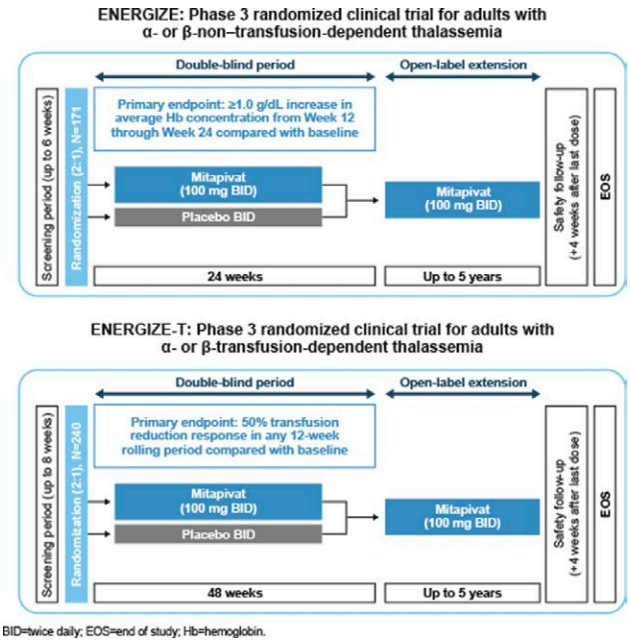
Background: Thalassemias are characterized by imbalanced globin-chain production resulting in excess α- or β-globin precipitation, hemolytic anemia, and ineffective erythropoiesis.[1,2] ATP levels are reduced in thalassemic red blood cells (RBCs), despite increased energy demands.[3,4] Mitapivat is an oral activator of RBC pyruvate kinase (PKR), a glycolytic enzyme that regulates ATP production.[5] In a phase 2 study of patients with α- or β-non–transfusion-dependent thalassemia (NTDT), twice-daily (BID) dosing with mitapivat increased hemoglobin (Hb) levels by ≥1.0 g/dL in 80% of patients,[6] supporting the broadening of mitapivat's development in thalassemia.

Aims: To report the study designs of ENERGIZE (2021-000211-23) and ENERGIZE-T (2021-000212-34), two phase 3 trials to assess the efficacy and safety of mitapivat in adults with α- or β-NTDT or transfusion-dependent thalassemia (TDT), respectively.

Methods: Both studies are phase 3, multicenter, randomized, double-blind, placebo-controlled trials (Figure). In ENERGIZE, approximately 171 eligible adults with NTDT will be randomized (2:1) to receive 100 mg mitapivat BID or placebo for 24 weeks. Upon completion, eligible patients can transition to a 5-year, open-label extension. Key inclusion criteria: documented diagnosis of thalassemia (β-thalassemia ± α-globin mutations, Hb E β-thalassemia, or α-thalassemia [Hb H disease]), Hb concentration ≤10.0 g/dL, and NTDT defined as ≤5 RBC units during the 24-week period before randomization and no RBC transfusion ≤8 weeks prior. The primary endpoint is an Hb response defined as a ≥1.0 g/dL increase in average Hb concentration from Week 12 through 24 compared with baseline. Secondary endpoints include patient-reported outcomes, changes in Hb, markers of hemolysis and erythropoiesis, and safety. In ENERGIZE-T, approximately 240 eligible adults with TDT will be randomized (2:1) to receive 100 mg mitapivat BID or placebo for 48 weeks. Upon completion, eligible patients can transition to a 5-year, open-label extension. Key inclusion criteria: documented diagnosis of thalassemia (same genotypes as detailed for the ENERGIZE study), and TDT defined as 6–20 RBC units transfused and no transfusion-free period ≥6 weeks during the 24 weeks before randomization. The primary endpoint is a transfusion reduction response, defined as a ≥50% reduction in transfused RBC units with a reduction of ≥2 units of transfused RBCs in any consecutive 12-week period through Week 48 compared with baseline. Secondary endpoints include additional measures of transfusion burden, changes in iron markers, and safety.

Results: Not yet available.

Conclusions: ENERGIZE and ENERGIZE-T are the first pivotal studies to assess a potential treatment across a broad spectrum of patients with thalassemia (ie, patients with TDT and NTDT; α- and β-thalassemias). ENERGIZE and ENERGIZE-T will evaluate the efficacy and safety of mitapivat, a novel, first-in-class oral activator of PKR. Both studies are actively recruiting.



BID=twice daily; EOS=end of study; Hb=hemoglobin.

References

1. Taher et al. *Lancet* 2018; 391:155–67.
2. Cappellini et al. *Blood Rev* 2018; 32:300–11.