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Case Report

Case Report Study on the Integrated Management of Sickle Cell Patient with Re-Infection of COVID-19

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ABSTRACT

The entire world has been impacted and devastated by coronavirus infection. Coronavirus infection requires no more introductions. Sickle cell patients are more prone to coronavirus infection and its complications. There is plenty of research done on the management of coronavirus infections, options and combinations initially found effective, but at the end of 2nd year revealed no potential benefit. An integrated treatment approach always becomes a possible option in the management of any complications. The case study mentioned here provides information about integrated treatment in patients of sickle cell anemia re-infected with coronavirus infection presented with positive RT-PCR, HRCT score 03/25 with moderate hepatomegaly, gall bladder sludge and auto splenectomy. The patient was previously infected with coronavirus and recovered completely with integrated treatment. He had received his vaccination for coronavirus. The patient was re-infected with coronavirus infection and developed sickle cell crisis complications for which he was hospitalized. Despite continuous monitoring SpO_2 (78%) was dropping, after discussion with family members a patient was shifted to clinic from hospital. With prior knowledge and consent, the 300 mg T-AYU-HM Premium along with integrated treatment was initiated. There was an observational improvement in clinical conditions and oxygen saturation was restored to 95% within five days. Post-discharge, he adhered to treatment and recovered from clinical complications like hepatomegaly. This approach was economical, safer and therapeutically effective. Further well-organized studies are requires to evaluate the effectiveness of the integrated treatment approach.

Keywords: Autospelenectomy, Hepatomegaly, HRCT, COVID-19, T-AYU-HM Premium.

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INTRODUCTION

Several studies have discussed the issue of SARS-CoV-2 re-infection, which is a subsequent infection after recovery from a prior episode of the infection and reactivation, also known as relapse, which is a re-detectable positive SARS-CoV-2 viral RNA in a recovered patient within the first 4 weeks of a previous infection.[1] Hansen C *et al.* (2021) mentioned in their study that a population-based observational study in Denmark consisting of 4 million individuals with possible re-infection of 2.11%.[2] The incidence of fatal complications in re-infected COVID-19 cases dropped by 68% when compared to that of the initial phase of COVID-19 infection.[3] Sickle cell anaemia is an autosomal recessive condition that reduces haemoglobin's affinity for oxygen. Patients with sickle cell anaemia are more likely to be infected with a coronavirus infection because the virus's alveolar entry site raises the possibility that it could induce acute chest syndrome or a vaso-occlusive crisis in sickle cell patients. A prominent clinical indicator of sickle cell disease and coronavirus infection is hypercoagulation.[4-7] The herbs-mineral formulation T-AYU-HM Premium (300 mg) is manufactured by ATBU Harita Pharmaceuticals Pvt Ltd, Vyara for sickle cell anemia. An onion, a common vegetable in meals, has strong antiviral properties and can be used for 1 minute steam vaporization. For sickle cell patients who have coronavirus infections, this combination proved beneficial and was presented through case reports. With the combined therapy, which included the formulation T-AYU-HM Premium, the patient had already made a full recovery from coronavirus infection in the first wave.[4-7] In this case presentation; we discuss the comprehensive management of severe problems in sickle cell patients brought on by re-infection with COVID-19. T-AYU-HM Premium 300 mg tablet is a herbo-mineral composition intended to act as an anti-sickling agent. In vitro, the formulation demonstrated antioxidant and anti-sickling action. Preclinical investigations such as acute oral

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and sub-chronic, as well as immunomodulatory activity studies of formulations, have already been established.[4-7]

CASE BACKGROUND AND CONSENT

The case report discussed here is on Re-infection of coronavirus in sickle cell anemia patients. The case study advanced to gather more information for the future benefit of the community after a thorough conversation and getting consent from patient for the use of data. The study was reported at Dhanvantatari Clinic, Vyara-Gujarat. The ayurvedic and modern medicine practitioner are available continuously in support and care for pandemic situation.

CASE PRESENTATION

Mr X is a 26-year-old male suffering from sickle cell disease with a history of being infected with a coronavirus a year ago. He recovered from it and later stages received a coronavirus vaccination which was started for above 18 years population. Mr X, with no travelling history, was hospitalized with complaints of weakness, body aches and hypoxic conditions. He is having an "O" positive blood group. His RTPCR report performed on 22/01/2022 found positive. During hospital admission, his vitals like pulse 84/min, blood pressure 140/90 mmHg, SpO_2 100 with non-invasive ventilation support (nebulizer) and respiratory rates were 26/min. Based on his clinical conditions mentioned in (Figure 1) his interventional treatment is mentioned (Figure 2) to gain a detailed idea about his history.

When Mr. X was infected previously with COVID-19, he recovered with integrated treatment only within 21 days. Mr. X is a regular patient at the designated clinic for sickle cell anemia and has been taking T-AYU-HM Premium. There was no previous history of acute splenic sequestration crises due to sickling before this visit. Mr. X was outside the town and therefore when he was infected with such clinical presentation, he was admitted to the nearest hospital for immediate management. Considering his co-morbid sickle cell disease condition, existing second-wave seriousness and dropping SpO_2 condition his family members decided to shift him to a designated day care centre. On 24/01/2022, Mr. X reported at Dhanvantari Clinic, Ayurvedic Health Care and Research Centre, Vyara, Gujarat, India.

Before proceeding with any further execution of Upasaya (therapeutic tests), Ashtavidha Pareeksha (physical examination), Purvarupa (prodromal symptoms), Rupa (manifested symptoms) and Samprapti (pathogenesis). Clinical parameters examined on the baseline day (24/01/2022) and follow-up visits are mentioned in the following Figure 3.

The ayurveda and modern medicine team prescribed treatment of T-AYU-HM premium 300 mg twice a day orally, Nebulizer, O2 supports, IV and other oral supportive treatment mentioned in (Table 1). For any further medical assistance, the consultant remained in contact with them. Regular follow-ups for monitoring pain episodes, Blood pressure, SpO_2 (%) and other vital parameters to assess safety were maintained.

On 28th January patient didn't present any clinical symptoms like body ache, weakness and nausea or something. His RTPCR report performed on 29/01/2022 found positive. On 28/01/2022, USG (ultrasound sonography) examination of abdomen and pelvis suggested moderate hepatomegaly, moderate gall bladder sludge and spleen not visualised (possible autosplenectomy).

He received discharged from day care centre. His discharge medications are mentioned in Table 1 which he has to adhere for 15 days.

On 08/02/2022 Temp was 37, Blood pressure 96/55, SpO_2 98 without oxygen, Pulse rate 106 per minute, weight was 53 Kg. On 08/02/2022 he was prescribed with tablet B. Folcine plus (Folic Acid 1.5 mg+Lactic Acid Bacillus 60 million spores+Niacinamide 100 mg+Riboflavin 10 mg) Tab. T-AYU-HM Premium 300 mg BD prescribed for 15 days.

DISCUSSION

During the second wave, many cases have come up in which people were re-infected with the virus, a few weeks after taking both vaccine doses. A few of them have died, some have fallen sick, some had bad pneumonia and some needed ventilator support after complete vaccination. Though a vaccine helps produce antibodies in advance to fight against the virus, every individual doesn't develop the same amount of antibodies. The amount of antibodies vaccination will produce in an individual depends on his or her immune system. The quantity of antibodies is measured in humans by its level of titres and a higher titre value means more antibodies in that person. So is there a benchmark level for antibodies at which the virus will not cause any harm. There are not many instances of sickle cell patients who have had vaccinations, have previously contracted coronavirus, recovered and then been re-infected. Therefore, many aggravating factors or etiological reasons are considered vital for the complicating condition of the patient.

During hospitalization, the patient received cefoperazone plus sulbactam, possibly because the lung was infected as per the HRCT score and therefore consideration of Cefoperazone, a third-generation cephalosporin and sulbactam sodium, a beta-lactamase inhibitor, are combined to form cefoperazone/sulbactam. According to a study by Bin W *et al.* 2013, mentioned that coagulation malfunction occurred in 25.8% of the patients treated with cefoperazone/sulbactam, most frequently 3-12 days following drug administration.[8-11]

The prescription-provided injection of artesunate is an antimalarial class of drug that might have a beneficial effect against COVID-19. In his study Stephane Jaureguiberry *et al.* 2014 mentioned although 20% to 25% of travellers with severe malaria

Investigation (Mr Y)		22.01.22	Investigation(Mr Y)	22/01/2022
Hb (gm/dl)		7.90	D-dimer (FEU/mL)	3.3
RBC (m/cmm)		3.60	LDH (IU/L)	-
WBC (/cmm)		20200	Interleukin-6 (pg/ml)	-
Platelets (per microliter)		219000	HRCT	-
ESR (mm/hr)		-	BP (mmHg)	-
Neutrophils (%)		85	SpO2 (%)	-
Lymphocytes (%)		11	CRP (mg/l)	59.52
PR (in minute)		-	MCV (fl)	72.80
Random Blood Sugar (mg/dl)		133		
S.Creatinine		0.55		
S.Na+ (mmol/L)		129		
S.K+(mmol/L)		4.19		
S.Cl-(mmol/L)		96		
S.Bilirubin	Total (mg/dL)	6.0		
	Direct(mg/dL)	1.3		
	Indirect (mg/dL)	4.7		
Serum urea (mg/dL)		16		
HBsAG/HIV I-II		Negative		

Figure 1: Clinical condition during hospitalization phase.

Date	Dosage form	Treatment	Active ingredient
22/01/2022	Injection	Magtam (2g) 12 hourly	Sulbuactam and Cefoperazone
	Injection	Rapeed (20) 12 hourly	Rabeprazole
	Injection	Grandem (1A) 8 hourly	Granisetron
	Injection	NKG (1A) in 10ml NS IV	Neurokind Gold
	Injection	Ketorolac (1A) IV 6 hourly	Ketorolac
	Injection	Contramal(1A) in 100ml NS	Tramadol 100mg
	Injection	LMWH (0.4) s/c BD	Low molecular weight heparin
	Nebulizer	Duolin 6 hourly	Levosalbutamol (50mcg) + Ipratropium (20mcg)
	Nebulizer	Budacort 8 hourly	Budesonide (0.5mg)
	IVF	D5% pint IV BD	Dextrose
	IVF	RL 1 pint IV	Ringer Lactate
	Injection	Falcigo 120 OD	Artesunate

Figure 2: Interventional treatment during hospitalization.

treated with parenteral artesunate recently reported to experience delayed anaemic crises, is a large and potentially exaggerated percentage. Although all of these patients recovered, 60% of them needed blood transfusions. Hence, post-parenteral artesunate anaemia does complicate patient treatment even though it does not compromise the life-saving benefit of parenteral artesunate. [12] Although Bae *et al.* 2020 found that artesunate may be useful for patients with COVID-19 and/or influenza.[13,14]

The intensity of sickle cell complications associated with pain requires adequate management in such kind of viral complications. During hospitalization, the patient was prescribed a combination of tramadol and ketorolac. The combined antinociceptive effects of tramadol and ketorolac were significant and indicate that using these medications in combination may be clinically useful for treating pain.[15]

Sickle cell patients who have a severe COVID-19 infection are more likely to die from thrombosis and related complications.[8] During hematological evaluation D-Dimer elevation is a representation of autosplenectmy and sickling episodes in a patient. A faster rate of hemolysis, demonstrated by higher reticulocyte counts and

Table 1: Integrated treatment of Mr. X.

Date	Parenteral	Ayurvedic Treatment	Allopathic Treatment
24/01/2022	i.v. LMH Oxygen/Nebulizer (24 hourly) i.v. Dexa i.v. Deriphyllin.	Tab T-AYU-HM Premium 300 mg BD Tab ACUPEN 300 mg BD.	Tab Eupod 200 Tab Levocet M Tab Rekool D
25/1/2022 BP:130/78 SpO_2:88 PR:105.	Nebulizer+Oxygen (18 hourly) i.v. LMH i.v. Dexa i.v. Deriphyllin.	Tab T-AYU-HM Premium 300 mg BD Tab ACUTAC 300 mg BD.	Tab Eupod 200 Tab Levocet M Tab Rekool D.
26/01/2022 No backache No headache Weakness.	i.v. LMH Nebulizer+ Oxygen (12 hourly) i.v. Dexa i.v. Deriphyllin	Tab T-AYU-HM Premium 300 mg BD.	Tab Eupod 200 Tab Levocet M Tab Rekool D.
27/1/2022 No backache No headache Constipation.	Nebulizer+oxygen (6 hourly) i.v. LMH.	Tab T-AYU-HM Premium 300 mg BD Tab ACUTAC 300 mg BD.	Tab Eupod 200 Tab Levocet M Tab Rekool D.
28/1/2022	Nebulizer+oxygen (2 hourly).	Tab T-AYU-HM Premium 300 mg BD Tab ACUTAC 300 mg BD.	Tab Eupod 200 Tab Levocet M Tab Rekool D.
29/1/2022 Relief No nebulizer oxygen requires discharged requested with follow-up medicines.	No parenterals and oxygen support required.	T-AYU-HM Premium tablet 300 mg BD Tab ACUTAC 300mg BD.	Tab. B folcin pls Tab. Levoflox 250 Tab.Ecosprin 75 Cap.Rezol D Inh.Budacort Dolo 650 SOS.

Eupod 200 (cefpodoxime 200 mg), Budacort (Budesonide 200 mcg), Ecosprin (Acetyl Salicylic Acid 75 mg) B- folcin Plus (riboflavin, folic acid, niacinamide, lactic acid bacillus spores), Levoflox 500 tablet (levofloxacin 500 mg), Razol-D (rabeprazole sodium and domperidone), Levocet 10 (levocetrizine 10 mg), LMH: Low molecular weight heparin, Inj Dexa (Dexamathasone), Dolo (Paracetamol 650).

lactate dehydrogenase levels, also correlated positively with higher levels of coagulation activation markers in a sickle cell patient. The pathophysiological link between hemolysis and hemostatic activation is probably heme, a product of intravascular hemolysis, which is capable of inducing TF expression by endothelial cells and inducing neutrophil extracellular trap formation in sickle cell disease. Elevated white blood cell count and platelets are considered as post splenectomy clinical markers in a patient.[16]

Increased usage of emergency rooms is indicated by elevated steady-state WBC and platelet counts, which may indicate maximising therapy. Activated platelet counts are higher in sickle cell disease patients in a steady state and they increase during a Vaso-Occlusive Crisis (VOC). Research has indicated that patients with sickle cell disease experience more acute pain episodes when specific leukocyte adhesion molecules are expressed at higher levels.[17,18]

The complex management during emergency conditions might be the reason for autosplenectomy acquired through etiological factors like hemolysis which could be the reason for delaying the recovery and inducing sickling in the patient. During the course of hospitalization, the oxygen saturation was dropping gradually over time. Overall the patient was not improving and requires patient-centric and integrated treatment which suits its existing comorbidities.[19]

T-AYU-HM Premium prevents sickle haemoglobin from polymerizing and forming sickle cells by increasing the ability of RBCs to carry oxygen and preserving the integrity of the RBC membrane.[8] When the patient was shifted to the integrated treatment patient's clinical profile was observationally improvised. The admitted patient's oxygen needs improved gradually over time with an integrated therapy strategy. The improvement can be observed through the oxygen saturation (95% without support) was previously dropping below 76%. Therefore, no hypoxia-induced complications progress further in patients.

Investigation (Mr Y)		24.01.22	25.01.22	28.01.22	8.02.22	22/08/2023
Hb (gm/dl)		6.3	4.6	5.7	6.8	9.8
RBC (m/cmm)		2.47	1.97	2.02	2.56	4.31
WBC (/cmm)		35900	40,100	35000	8,200	20160
Platelets (per microliter)		121000	80000	1,01,000	5,45,000	527000
ESR (mm/hr)		130	82	50	130	35
CRP (mg/l)		48.9	45.8	37.7	44.7	1.9
D-dimer (ng/ml)		>10000	4675.2	10000	9835.9	-
LDH (IU/L)		3722	-	2820	584.5	-
Interleukin-6 (pg/ml)		267.4	7.95	44.3	14.2	-
HRCT		3/25	-	-	-	-
BP (mmHg)		115/77	-	128/70	-	-
SpO2 (%)		78	-	95%	-	-
PR (in minute)		112	-	98	-	-
Random Blood Sugar (mg/dl)		118	-	197	82	-
S.Creatinine		0.4	-	0.61	-	-
S.Bilirubin	11.8	6.72	-	-	2.29	11.43
	4.77	2.40	-	-	1.65	1.25
	7.03	4.32	-	-	0.64	10.18
S.G.O.T(IU/L)		158.8	103	45.4	22.7	51.5
S.G.P.T(IU/L)		57.6	36.7	24.5	12.2	28.9
S.Na+		123	125	131.4	-	134
S.K+		4.2	5.3	4	-	4.49
S.Cl-		95	108	99.6	-	101.2

Figure 3: Clinical profile of Mr. X.

The outcomes of the instances revealed that the patient's haemoglobin and red blood cell counts had significantly improved. Additionally, the formulation keeps haemoglobin levels within a range that prevents sickle cell disease patients from experiencing difficulties due to viscosity. Therefore, viscosity, coagulation and polymerization-induced sickling complications were not transpiring further.

This improves the alveolar gaseous diffusion and alleviates the patients' breathing problems. T-AYU-HM Premium and onion vaporisation therapy helped patients avoid needing blood transfusions or to stay in the hospital. Some hematological parameters do appear abnormal but splenectomy might be the reason behind the same.

CONCLUSION

Previously recorded information on the usage of Cefoperazone/sulbactam, artesunate in sickle cell anemia during comorbidities like coronavirus infection requires a lot more attention and continuous observation. During our 21-day observation period, sickle cell anaemia patients who were coronavirus re-infected exhibited remarkable improvement without the need for blood transfusions or hospitalisation. The integrated treatment approach importantly did not produce any untoward complications and simultaneously improved the condition of the patient gradually over some time. Further detailed and planned observational studies are required to establish the approach's effectiveness.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

SCD: Sickle cell disease; **SCA:** Sickle cell anemia; **TSH:** Thyroid stimulating hormone; **HbF:** Fetal hemoglobin; **CRP:** C-reactive protein; **ESR:** Erythrocyte sedimentation rate; **RBC:** Red blood corpuscles; **WBC:** White blood cells.

ETHICAL APPROVAL

For single case report study no ethical approval has been provided based on minimum requires to prepare case series is 3-5 patients. Patient consent has been received and mentioned already in case introduction.

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