

**Table: 5 Treatment and outcome of the condition**

Study ID	G6PD	Management	Outcome
Jung et al.(15)	Deficient, G6PD: 8.1 units per gram of haemoglobin	methylene blue not administered due to suspected G6PDD, Ascorbic acid IV 1500mg, oxygen nasal cannula at 6 L/min and then on a Venturi mask with a fraction of inspired oxygen 0.4, and 2 units of packed red blood cells	recovered within next 24hours
Bachmann et al. (22)	Deficient	Non- Invasive ventilation	decrease in MetHb level over time
Raru et al.(24)	Deficient	Methylene blue 1mg/kg, mechanical ventilation and bi-valve positive airway pressure for 4 days, haemolysis due to rasburicase were so severe that patient required around 8 units of blood, steroids, vitamin C and continued with IV fluids. Due to repeated transfusion patient developed ARDS.	Pt developed acute renal failure due to pigment nephropathy and acute tubular necrosis therefore pt received haemodialysis throughout the hospital stay
Cooling et al.(11)	Deficient	Methylene blue 25% test dose, 2L of oxygen supplementation, 1unit RBC within 3 hr of rasburicase administration, and 8 units of group O RBC (2693 mL) for replacement, i.e. Total 9 units of RBC and erythrocytapheresis	The patient became normal after 3 days
Ibrahim et al.(28)	5.4 Units per	Methylene blue 1 mg/kg IV, and supported with PRBC transfusion,	patient's haemoglobin

	gram of haemoglobin at the time of an acute haemolytic episode		remained stable
Reeves et al.(14)	6.0 units per gram of haemoglobin	Methylene blue was not Administered due to suspected G6PDD, Ascorbic acid 5 g IV every 6 hours for a total of six doses, oxygen 15 L/min via a non-rebreather mask, and on day 4, the patient received 3 units of blood, on days 5 and 6 received a unit of blood on each day; i.e. a total of 5 units, the patient also received two sessions of haemodialysis for volume overload	Within 24 hours of initiating ascorbic acid, the patient's oxygen saturation values and symptoms improved
Montgomery et al.(10)	Deficient	single dose of 132 mg IV methylene blue, Continuous ascorbic acid treatment, supplemental oxygen, and 1600 mL (1 red cell volume) automated red cell exchange via the right internal jugular central venous catheter	36 h following exchange the patient was discharged
Sleutel et al.(21)	Pt 1: NR Pt 2: likely more deficient than the laboratory values i.e. 9.6 (normal range = 7–20.5	Pt 1: Methylene blue was not administered due to suspected G6PDD, allopurinol 300 mg, and dialysis Pt 2: on day 1 patient received a unit of packed RBC, during the next three days pt received	Pt 1: On day 2 Pt became asymptomatic and 8 days later, Pt was transferred from the ICU to the oncology

	U/g haemoglobin)	additional 2 units of PRBC and supplemental oxygen	unit and discharged home in 2 weeks, Pt 2: Pt noticed improving laboratory results and was discharged on day 7
Sherwood et al. (5)	Suspected	Methylene blue was not administered due to suspected G6PDD, Ascorbic acid 1 gm daily, 100% oxygen via non-rebreather and double volume red cell exchange transfusion with 5.1 L of allogeneic packed red blood cells and therapeutic plasma exchange for elevated free plasma haemoglobin levels.	Pt slowly improved clinically and was eventually able to be extubated and transferred to the haematology service on hospital day 25.
Alessa et al.(26)	Normal	Methylene blue was not necessary as the condition resolved with blood transfusion, supplemental oxygen therapy-100% non-breathing mask	methemoglobinemia resolved with blood transfusion
Oluwasanjo et al. (25)	Deficient, 1.5 units per gram of Haemoglobin	Methylene blue IV, 100% oxygen via a non-rebreather mask at 10 l/min, 4 units of PRBC were transfused along with other supportive treatment.	By 24 h, methemoglobin levels had dropped to zero.
Zhang et al.(30)	Deficient, 10 IU/g Hb	11 units of PRBC transfusion over 1 week	After 1-week haemolysis resolved
Roberts et al.(27)	Pt 1: Normal, 20 (reference range of 0–60 MINS), Pt 2:	Pt 1: Oxygen through facemask was administered Pt 2: Ascorbic acid 500 mg twice daily, supplemental oxygen, and transfusions of 3 units	Pt 1: hypoxia, liver failure, and overwhelming

	Deficient, 3.4 U/g/Hb (reference range 6–12.4).	of PRBC	metastatic disease. The patient was made comfort measures only and passed within 24 h of MICU admission, Pt 2: discharged 9 days after initial presentation once haemolysis stopped.
Bucklin et al.(20)	Deficient	Methylene blue (reduced dose) 0.75mg/kg and second dose of 0.75 mg/kg, bilevel positive airway pressure (BiPAP), Pt received 2 units of PRBC each on day 2 and 3 and from day 3 to 8 total of 12units of PRBC accounting total of 16 units of PRBC	By day 8, methemoglobin was less than 1% and remained the same throughout his stay, on day 16 patient died
Cheah et al.(23)	Deficient, 4.8 IU/g Hb (reference range 8.8–17.6)	Methylene blue was not administered due to suspected G6PDD, ascorbic acid 1 g discontinued after 5 days, O2 flow rate (10Hudson mask and 40 high-flow nasal prongs) l / method, transfusion of PRBCs to maintain Hb 7.0 g/dl and IV fluids	On day 4, the patient stabilized clinically and biochemically and was discharged to the ward.
Sonbol et al.(16)	Deficient, 3.3 U/g Hb (normal, 8.8–13.4)	Methylene blue was not administered due to suspected G6PDD, ascorbic acid 1,000 mg oral daily, a total of eight units of packed red blood cells over the next 4 days	Over the next 4 days, his methemoglobinemia resolved and his O2 saturation

			normalized
Ng et al. (19)	Deficient, G6PDD suspected without a confirmatory blood test	Methylene blue and ascorbic acid were not administered due to suspected G6PDD, 4 L oxygen via nasal cannula, and then elevated oxygen delivery to a venti-mask at 50% oxygen. Within 4 h post rasburicase infusion, oxygen delivery was again elevated to a non-rebreather 15 L at 100% oxygen, and 4 units of PRBC was transfused during the entire hospital stay	By day 2 of hospitalization, MetHb and plasma haemoglobin levels had returned to normal without further interventions and by day 8, the patient had made a complete recovery and was discharged
Bauters et al.(17)	Normal	Methylene blue and ascorbic acid was not administered due to suspected G6PDD, Supplemental Oxygen administration	All complications resolved after 3 days of supportive treatment.
Bhat et al.(12)	Deficient, 3 U/gm Hb (normal 4.6– 13.5 U/gm Hb).	2 doses of methylene blue, Supplemental Oxygen, and double- volume exchange transfusion	After double-volume exchange transfusion methemoglobin level was 0% and his oxygen saturation was normal.
Borinstein et al. (18)	Deficient	Methylene blue was not administered due to suspected G6PDD, Supplemental Oxygen, and double-volume exchange transfusion, PRBC transfusions at 34, 72, and 181 hrs after	Haemolysis resolved, and the patient achieved a complete remission at the end of induction chemotherapy for Burkitt lymphoma/leukaemia

		rasburicase administration	.
Kizer et al.(29)	Pt 1: Normal, Pt 2: Not tested	Pt: 1 Methylene blue was not administered due to suspected G6PDD, 15 L nasal cannula and quickly decompensated to requiring a 100% nonrebreather face mask, and 2 units of PRBC, Pt: 2 methylene blue 50 mg IV and second dose of 50 mg, Oxygen through Venti-mask, and 2 units of PRBC	Pt 1: within 24hrs methemoglobin levels decreased and shortness of breath resolved, Pt 2: patient remained stable with no altered mental status throughout his hospital stay
Brownin g et al. (13)	Deficient, 5.0 units/g of haemoglobin (reference range 7.0–20.5	Methylene blue was not administered due to suspected G6PDD, from Day 5-8 of hospital stay patients received a cumulative volume of 8 units of PRBC	After 10 days of hospitalization, the patient made a full recovery and was discharged

g/gm: grams; Hb: Haemoglobin; G6PD: Glucose-6-phosphate dehydrogenase; G6PDD: glucose-6-phosphate dehydrogenase deficiency; RBC: Red Blood Cells; NR: Not Reported; Pt: Patients; MetHb: Methaemoglobin; PRBC: Packed Red Blood Cells; Hrs: hours; IV: Intravenous; ICU: Intensive Care Unit; MICU: Medical Intensive Care Unit.