International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Minz EE et al. Int J Reprod Contracept Obstet Gynecol. 2026 Aug;15(8):3274-3279
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20262573

Case Report

A parturient with congenital methemoglobinemia: navigating the oxygen saturation gap

Evelyn E. Minz*, Deepa K. Khurana, Preeti Agrawal, Arpana Sinha, Parminder S. Bhatia, Priyanka Kalra

Department of Anaesthesiology, VMMC and Safdurjung Hospital, Ansari Nagar West, Delhi, India

Received: 27 May 2026
Accepted: 20 July 2026

***Correspondence:**
Dr. Evelyn E. Minz,
E-mail: lynminz281993@gmail.com

ABSTRACT

Congenital methemoglobinemia (CMH) presents unique anesthetic challenges due to oxidative stress risks. We report a primigravida with type 1 CMH presenting with a profound oxygen saturation gap. Labor analgesia was successfully managed using a continuous epidural infusion of ultra-low dose bupivacaine (0.0625%) and fentanyl. The protocol strictly mandated avoiding oxidizing agents, notably substituting lidocaine with epidural bupivacaine for perineal repair. The patient was hemodynamically stable and delivered a healthy neonate. This case validates ultra-low dose epidural bupivacaine as a safe, effective strategy for labor analgesia in CMH, minimizing systemic drug load and oxidative risks.

Keywords: Congenital methemoglobinemia, Oxygen saturation gap, Co-oximetry

INTRODUCTION

Congenital methemoglobinemia (CMH) is a rare hemoglobinopathy, typically caused by a deficiency in the NADH-cytochrome b5 reductase enzyme, leading to the accumulation of oxidized hemoglobin (Fe^{3+}) that cannot effectively transport oxygen.[1,2] In the obstetric setting, the primary anesthetic goal is to prevent further oxidative stress while providing effective analgesia. Systemic opioids, such as remifentanil, have been described for these patients but carry risks of maternal sedation and neonatal depression.[3] Neuraxial analgesia is preferred but requires the meticulous avoidance of oxidizing local anesthetics (e.g., prilocaine, lidocaine).

Furthermore, monitoring is complicated by the "oxygen saturation gap," where standard pulse oximetry provides falsely low readings in the presence of dyshemoglobinemias.[4]

We describe the successful management of a parturient with CMH using an ultra-low-dose bupivacaine epidural regimen. Written informed consent was obtained from the patient for publication purpose.

CASE REPORT

A 22-year-old primigravida (G1P0) at 38 weeks and 3 days of gestation presented for elective induction of labor with a significant history of shortness of breath and low SpO_2 reading of 44%, requiring intubation and mechanical ventilation in the 2nd trimester of her pregnancy. She was diagnosed with autosomal dominant heterozygous type B CMH. The patient was later discharged and optimized with vitamin C 1 gram three times a day antenatally.

Admission and diagnostic findings

Our team was requested to assist for a vaginal delivery with an epidural for painless labor. On examination, she had a greyish skin tone with bluish discoloration of lips and nail beds (Figure 1). The patient appeared clinically stable with normal cardiovascular and pulmonary examination. However, standard pulse oximetry showed a concerning SpO_2 of 46-55% on room air. An arterial blood gas (ABG) analysis was performed to investigate this drastic discrepancy between the low saturation reading and the patient's stability. The ABG results showed a normal pH of 7.421, a partial pressure of oxygen (PaO_2) of 75

mmHg, a hemoglobin level of 11 g/dl, a lactate level of 0.8 mmol/l and a raised fractional methemoglobin (FMetHb) of 13%. This confirmed that the low SpO_2 was an artefactual reading driven by the elevated methemoglobin (MetHb), consistent with the oxygen saturation gap phenomenon.

Anesthetic management

A multidisciplinary plan was established involving anesthesiology, obstetrics, neonatology, and hematology. The protocol mandated the strict avoidance of known methemoglobin-inducing agents, specifically listing lidocaine (lignocaine), metoclopramide, nitroglycerin, nitroprusside, nitrates, phenytoin, and valproate. A contingency plan for methylene blue administration (1 mg/kg) was in place in case MetHb levels exceeded 20-30%. Table 1 lists the common drugs and their safety profiles used in obstetrics and anesthesia.

The patient was electively taken for lumbar epidural placement at 3 cm dilation, inserted in the L2-L3 intervertebral space. The test dose of lignocaine adrenaline was not given; instead, an incremental dose of a solution of 0.0625% Inj. Bupivacaine with Inj. Fentanyl 2 mcg/ml 3 ml was given. After no signs of intrathecal catheter placement, 0.0625% Inj. Bupivacaine with Inj. Fentanyl 2 mcg/ml was started at an infusion rate of 5 ml/hour. Continuous fetal and maternal vital monitoring was done (Table 2).

Intrapartum course

The patient remained hemodynamically stable throughout labor. Despite low SpO_2 levels and an elevated baseline MetHb of 13%, she remained asymptomatic, with normal lactate and PaO_2 levels (Table 3). Supplemental oxygen was given throughout this time.

Table 1: Common drugs and their safety profile used in obstetrics and anesthesia.

Drug	Classification	Safety	Reason
Local anesthetics			
Bupivacaine	Amide (pipecoloxylidide)	Safe	Does not produce oxidative metabolites. Preferred in epidural/spinal
Ropivacaine	Amide (pipecoloxylidide)	Safe	Structurally like bupivacaine; safe alternative
Lidocaine	Amide (Aniline)	Avoid	Potent trigger of MetHb
Prilocaine	Amide (Aniline)	Avoid	Highest risk of MetHb
Benzocaine	Ester	Avoid	Found in topical sprays. Potent trigger of MetHb
Anesthetic induction and maintenance			
Propofol	Induction agent	Safe	Standard induction agent of choice
Fentanyl	Opioid analgesic	Safe	Safe for neuraxial and systemic use
Ketamine	Induction/analgesic agent	Safe	Useful for hemodynamic stability
Etomidate	Induction	Safe	Safe alternative for cardiac stability
Succinylcholine	Muscle relaxant	Safe	Safe for rapid sequence induction
Rocuronium	Muscle relaxant	Safe	Safe non-depolarizing muscle relaxant
Cardiovascular and antihypertensive			
Phenylephrine	Vasopressor	Safe	Preferred for spinal induced hypotension
Ephedrine	Vasopressor	Safe	Safe alternative
Labetalol	Antihypertensive	Safe	Safe for preeclampsia and hypertension
Hydralazine	Antihypertensive	Safe	Safe for preeclampsia and hypertension
Nitroglycerin	Antihypertensive/uterine relaxation	Contrain-dicated	Nitrates are potent oxidizers and a classic trigger for MetHb
Nitroprusside	Acute hypertension crisis	Contrain-dicated	Release of nitric oxide; high risk for MetHb
Obstetrics uterotonics			
Oxytocin	1st line for induction of labor (IOL)/post-partum hemorrhage (PPH)	Safe	No known oxidative stress
Carboprost	Prostaglandin (PGF2α)	Safe	Safe for PPH
Misoprostol	Prostaglandin (PGE1)	Safe	Safe for PPH
Methylergometrine	Ergot alkaloid	Safe	Safe
Antiemetics and gastrointestinal			
Ondansetron	1st line antiemetic	Safe	Do not cause MetHb
Metoclopramide	Antiemetic/prokinetic	Contrain-dicated	Know oxidizing agent

Continued.

Drug	Classification	Safety	Reason
Antibiotics			
Cefazolin		Safe	Standard prophylaxis for caesarean section
Clindamycin/Gentamycin		Safe	Alternatives to penicillin allergy
Sulfonamides		Avoid	Potent oxidizing agent
Nitrofurantoin		Avoid	Risk of MetHb

Table 2: Observation chart.

Time	BP (mmHg)	SpO_2 (%)	PR (/min)	Epidural infusion rate	NST
12:00 pm	104/72	48	76	5 ml/hour	Reactive
2:00 pm*	110/80	48	80	5 ml/hour	Reactive
4:00 pm	116/80	40	75	5 ml/hour	Reactive
6:00 pm	107/70	45	89	5 ml/hour	Reactive
8:00 pm	117/60	44	80	5 ml/hour	Reactive
10:00 pm	122/70	46	90	5 ml/hour	Reactive
12:00 am	118/88	45	88	5 ml/hour	Reactive
2:00 am	110/80	45	90	5 ml/hour	Reactive
4:00 am	108/72	49	92	5 ml/hour	Reactive
6:00 am	106/74	50	96	5 ml/hour	Reactive
8:00 am	102/64	50	94	5 ml/hour	Reactive
10:00 am	133/89	55	88	5 ml/hour	Reactive
12:00 pm	128/80	56	95	5 ml/hour	Reactive
2:00 pm**	124/88	56	98	5 ml of bolus of 0.125% Bupivacaine	Healthy baby delivered

*Induction of labor **normal vaginal delivery

Table 3: ABG of the patient.

Time	pH	PCO_2 (mmHg)	PO_2 (mmHg)	HCO_3^- (mmol/l)	BE	Hb (g/dl)	SO_2 (%)	FMeth	Lactate
ANC	7.50	28.8	114	22.3	+0.3	8.5	99.9	9.9	0.7
6:00 pm	7.45	32.7	123	22.7	−0.3	11.2	84.0	13.0	0.8
12:00 pm*	7.46	30.8	101	21.9	+1.4	10.9	81.7	14.7	1.2
6:30 am	7.41	30.0	162	22.7	−0.1	11.8	87.8	13.4	1.1
12:00 pm	7.46	36.4	138	25.9	+2.4	12.7	86.7	14.1	1.2
2:58 pm**	7.40	29.6	158	18.1	−5.2	10.3	88.1	13.1	3.3

*Epidural placement, **post delivery

Table 4: Safety classification of labor analgesia in congenital methemoglobinemia.

Analgesia type	Specific agents/methods	Safety	Rationale and clinical recommendations
Non-pharmacological	Transcutaneous electric nerve stimulation (TENS), massage, water immersion, sterile water injections	Yes	Safe, these methods involve no pharmacological agents and carry no oxidative risk to the hemoglobin.
Inhalational	Entonox (50% nitrous oxide 50% oxygen)	No	Best avoided, nitrous oxide is an oxidizing gas.
Systemic (intravenous)	•Remifentanil	Yes	Preferred systemic option, metabolized by blood and tissue esterases (hydrolysis); this pathway bypasses the oxidative hepatic P450 system, avoiding the production of oxidizing metabolites.
	Pethidine (Meperidine)	Yes (likely)	Likely safe, listed as "likely safe" in specific CMH literature. However, it is generally less preferred in modern obstetrics due to active metabolites causing neonatal sedation.

Continued.

Analgesia type	Specific agents/methods	Safety	Rationale and clinical recommendations
	Fentanyl (systemic)	Caution	Controversial, metabolized by the hepatic cytochrome P450 system which carries a theoretical risk of inducing methemoglobinemia. Low doses (e.g., in epidurals) are generally accepted, but high systemic doses are controversial
Neuraxial (epidural/spina)	Bupivacaine, Ropivacaine, Levobupivacaine	Yes	Gold standard, these amide local anesthetics have an excellent safety profile regarding oxidative stress. Bupivacaine was not implicated in large reviews of methemoglobinemia cases.[5]
	Lidocaine (often used for test dose)	No	Lidocaine is metabolized into oxidizing intermediates.
	Prilocaine	No	Contraindicated, metabolizes into o-toluidine, a potent oxidizer that causes rapid and severe methemoglobinemia.
Paracervical and pudendal nerve block	Benzocaine (spray/gel)	No	Strictly contraindicated, a direct oxidizer causing severe, rapid methemoglobinemia.
	Lignocaine (infiltration)	No	Potent oxidizer
	Bupivacaine (infiltration)	Yes	Preferred, use for perineal repair instead of Lidocaine.

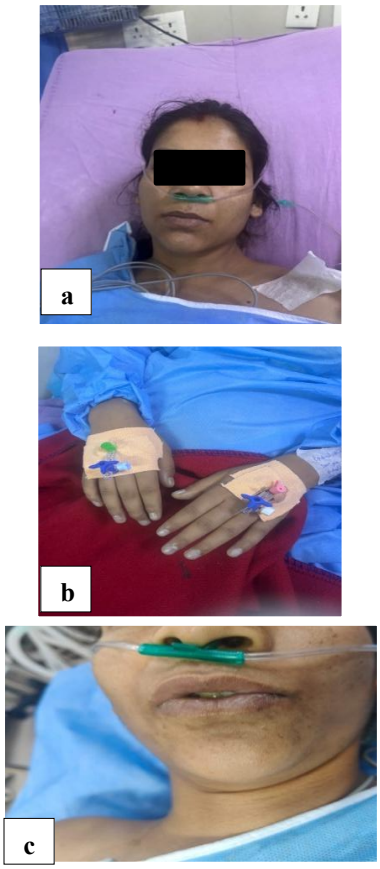

Figure 1: (a) a) Clinical Appearance, (b) cyanosis of nails, and (c) cyanosis of lips.

Delivery and outcome

The first stage of labor lasted for 24 hours, and the patient was pain-free throughout with a visual analogue scale (VAS) of 2-3. An episiotomy given during the second stage of labor was effectively repaired by a 5 ml bolus of 0.125% Inj. Bupivacaine, administered via the epidural catheter. Consistent with the safety protocol, all forms of local infiltration (lidocaine) were avoided to minimize systemic drug absorption and potential complications.

Table 5: Correlation between methemoglobin levels and clinical severity.

MetHb concentration	Clinical feature
<2%	Normal level in adults
>10%	Clinically detectable cyanosis
~30%	Systemic hypoxia begins to appear
60-70%	Often fatal

The patient delivered a healthy female infant weighing 3 kg. A venous blood gas analysis of the neonate immediately after birth showed a pH of 7.372 and an FMetHb of 2.1%, ruling out vertical transmission or drug-induced methemoglobinemia in the newborn.

DISCUSSION

Methemoglobinemia is a rare hemoglobinopathy characterized by decreased oxygen-carrying capacity due to oxidation of the iron molecule present in the hemoglobin from ferrous (Fe^{2+}) to the ferric state (Fe^{3+}). The oxidized hemoglobin is unable to bind or transport oxygen, causing a leftward shift of the oxygen dissociation curve, leading to cyanosis and tissue hypoxia.

The normal MetHb values are usually maintained below 1% by NADH cytochrome b5 reductase enzyme, which converts methemoglobin to reduced hemoglobin. Methemoglobinemia manifests as either decreased activity of the cytochrome b5 reductase enzyme (congenital) or as overproduction of MetHb by oxidizing agents (acquired).

There are two types of CMH. In type 1, there is a deficiency of cytochrome b5 reductase enzymes limited to erythrocytes. Such patients are usually cyanosed since birth and have very few symptoms. While in type 2, there is a generalized systemic deficiency of this enzyme in all tissues, including the brain, causing life-threatening neurological symptoms.

The inheritance of CMH is autosomal recessive except in HbM disease, an autosomal dominant condition wherein the production of abnormal hemoglobin resists the enzymatic reduction of Fe^{3+} to Fe^{2+}.

Labor analgesia can be divided into three categories: pharmacological, non-pharmacological, and regional methods. Table 4 briefly describes the different methods of labor analgesia and their safety in methemoglobinemia.

We opted for lumbar epidural labor analgesia with ultra-low dose of bupivacaine (0.0625%) and Fentanyl (2 mcg/ml). An epidural needle was placed in the L2-L3 epidural space by loss of resistance technique. Confirmation of correct catheter placement was done by negative aspiration followed by an incremental dose of bupivacaine. We avoided the conventional test dose of using 2% of lignocaine with adrenaline (1:2,00,000) keeping in mind the risk of precipitation of MetHb by lignocaine.

Pregnancy is a stressful state where worsening of methemoglobinemia may be triggered by pain and the use of oxidizing drugs. Furthermore, oxygen monitoring is hampered and cannot be solely relied on pulse oximetry. This case addresses the above points in the management of CMH in pregnancy with the provision of lumbar epidural analgesia for maximizing maternal and neonatal safety.

Neuraxial anesthesia has been avoided in patients with CMH due to the fear of worsening methemoglobinemia by use of local anesthetics. The four reported local anesthetics causing methemoglobinemia are prilocaine, tetracaine, benzocaine, and lidocaine.[5] No such event has been documented with the use of neuraxial bupivacaine.[6] Incorporation of continuous lumbar epidural infusion for pain management avoided the unnecessary systemic exposure to anesthetic agents used in general anesthesia. By utilizing ultra-low concentration bupivacaine (0.0625%) for the continuous epidural infusion and administering a low-volume bolus of 0.125% bupivacaine via the catheter for the second stage of labor, we successfully minimized both systemic drug load and oxidative stress.

The oxygen saturation gap

The discrepancy between the initial SpO_2 of 46-55% and the patient's clinical stability is a classic example of the "oxygen saturation gap." Standard pulse oximeters measure oxygen saturation based on only two wavelengths (990 nm and 660 nm) corresponding to oxyhemoglobin and deoxyhemoglobin. Methemoglobin absorbs light at both wavelengths, leading to an absorbance ratio towards unity and a fixed value SpO2 of 85% or lower.[7] Reliance on standard oximetry in this context is perilous and may trigger unnecessary interventions. Previous reports have documented cases where patients with persistently low SpO_2 (e.g., 66–70%) underwent emergency caesarean section (C/S) under general anesthesia due to anesthetic concern.[8,9] Our case, involving a patient with an even more dramatic reading (46-55%), demonstrates the successful, non-operative management of labor through planned vaginal delivery under labor epidural analgesia, providing a crucial decision-making algorithm for these high-risk patients.

Co-oximetry is the standard method for monitoring oxygenation and methemoglobin levels in such patients.[10] It uses four wavelengths to examine blood. Not only its gives accurate saturation percentage but also detects dyshemoglobinemia (carboxyhemoglobin and methemoglobin). Modern blood gas analyzers with inbuilt co-oximeters can also be used to measure methemoglobin levels, as done in our case. The clinical severity of methemoglobinemia correlates directly with the concentration of MetHb in the blood (Table 5).[11]

Our patient had a baseline MetHb of 10% with clinically detectable cyanosis. It's also seen that patients with CMH remain stable despite MetHB of as high as 40%.[12] This is the result of chronic physiological adaptation to elevated methemoglobin levels.

The management of life-threatening methemoglobinemia (MetHb >20%) is done with the injection of methylene blue in a dose of 1 mg/kg. Methylene blue is an FDA pregnancy category X drug (teratogenic). At high dose may act as an oxidizing agent and worsen methemoglobinemia. The clinical stability of the patient validated the decision to reserve this antidote for life-threatening hypoxia only.

The newborn's FMetHb of 2.1% was sub-clinical, confirming that the neuraxial strategy effectively limited fetal drug exposure. Neonates are susceptible to oxidative stress due to lower reductase levels and easily oxidized fetal hemoglobin (HbF). The use of neuraxial bupivacaine avoided the "ion trapping" associated with systemic opioids in the acidic fetal environment, leading to a favorable outcome.[13]

CONCLUSION

Epidural analgesia using ultra-low-dose bupivacaine (0.0625%) and fentanyl is a safe and effective strategy for parturients with CMH. Management necessitates ABG analysis with co-oximetry for monitoring oxygenation and FMetHb levels. To acknowledge that tissue oxygenation can be preserved despite alarmingly low peripheral saturation values. Furthermore, the rigorous exclusion of

lidocaine from all peripartum procedures, including local infiltration, is vital to maternal and neonatal safety.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Barberio G, Ivaldi G. Varianti instabili dell'emoglobina: una sfida per il Laboratorio? Biochim Clin. 2022;46:2.
2. Cefalu JN, Joshi TV, Spalitta MJ, Kadi CJ, Diaz JH, Eskander JP, et al. Methemoglobinemia in the Operating Room and Intensive Care Unit: Early Recognition, Pathophysiology, and Management. Adv Ther. 2020;37(5):1714-23.
3. Yin W, Jung F, Adams D, Konig G, Romeo RC, Lim G. Case Report of Remifentanil Labor Analgesia for a Pregnant Patient With Congenital Methemoglobinemia Type 1. AA Pract. 2021;15(1):e01373.
4. Akhtar J, Johnston BD, Krenzelok EP. Mind the Gap. J Emerg Med. 2007;33(2):131-2.
5. Guay J. Methemoglobinemia Related to Local Anesthetics: A Summary of 242 Episodes. Anesth Analg. 2009;108(3):837-45.
6. Büyükcavlak M. Anesthetic management of congenital methemoglobinemia in emergency caesarean delivery: a case report. Int J Obstet Anesth. 2026;65:104807.
7. Chan ED, Chan MM, Chan MM. Pulse oximetry: Understanding its basic principles facilitates appreciation of its limitations. Respir Med. 2013;107(6):789-99.
8. Verma S, Sachdeva P, Gandhi G. Rare Case of Methemoglobinemia Complicating Pregnancy. Case Rep Obstet Gynecol. 2016;2016:1-3.
9. Rajmane SH, Anand MN, Senapati JB. A rare case of congenital methemoglobinemia in pregnancy. Int J Reprod Contracept Obstet Gynecol. 2024;13(7):1845-7.
10. Haymond S, Cariappa R, Eby CS, Scott MG. Laboratory Assessment of Oxygenation in Methemoglobinemia. Clin Chem. 2005;51(2):434-44.
11. Nascimento TSD, Pereira ROL, Mello HLDD, Costa J. Metemoglobinemia: do diagnóstico ao tratamento. Rev Bras Anestesiol. 2008;58(6):651-64.
12. Paudel S, Adhikari N, Mandal S, Srivatana P. A Case of Congenital Methemoglobinemia: Rare but Real. Cureus. 2022;14(4):e24152.
13. Da-Silva SS, Sajan IS, Underwood JP. Congenital Methemoglobinemia: A Rare Cause of Cyanosis in the Newborn - A Case Report. Pediatrics. 2003;112(2):e158-61.

Cite this article as: Minz EE, Khurana DK, Agrawal P, Sinha A, Bhatia PS, Kalra P. A parturient with congenital methemoglobinemia: navigating the oxygen saturation gap. Int J Reprod Contracept Obstet Gynecol 2026;15:3274-9.