# Hemoglobin Lansing as a Cause of Spurious Low Oxygen Saturation on Pulse Oximetry in a Neonate

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*A pulse oximeter is an easy, painless and non-invasive device to measure blood oxygen saturation ($SpO_2$). Usually, $SpO_2$ is comparable to oxygen saturation by arterial blood gas ($SaO_2$). We report a case of term infant presented with respiratory distress and low oxygen saturation measuring with a pulse oximeter. Respiratory disease and congenital heart disease were excluded. Discordance of oxygen saturation was presented. His blood was obtained to check methemoglobin level and hemoglobin (Hb) variants. Hb Lansing was detected. In addition to report the first neonate with Hb Lansing in Thailand, we draw attention to the condition as a cause of spurious low oxygen saturation. The discrepancy of oxygen saturation between pulse oximetry and arterial blood gas necessitates investigations for hemoglobinopathies.*

**Keywords:** *Hemoglobinopathy, Hemoglobin Lansing, Discordance of oxygen saturation*

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A pulse oximeter is a simple instrument to estimate a patient's arterial oxygen saturation used worldwide[1]. Some patients may be detected with spurious decreased oxygen saturation by pulse oximetry ($SpO_2$), whereas their investigations reveal test normal with oxygen saturation by arterial blood gas ($SaO_2$). Therefore, variants of hemoglobin should be suspected, rather than cardiac and pulmonary causes. Here, we demonstrated the first neonatal case of hemoglobin (Hb) Lansing in Thailand presented with discordance of oxygen saturation.

A term infant presented with respiratory distress and low oxygen saturation which did not response to oxygen therapy. He was born at 38 weeks' gestation by elective cesarean section with Apgar scores of 9 and 10 at 1 and 5 minutes, respectively. His mother was a 32 years old, previously healthy woman. Her pregnancy was unremarkable. Her prenatal investigations showed hematocrit of 35%, mean corpuscular volume (MCV) 83 femtolitre (fL) and all serology tests were negative.

At 4 hours of age, he developed tachypnea with oxygen desaturation and was transferred to the neonatal intensive care unit. His physical examination showed an increased respiratory rate of 96 times per minute, rapid shallow breathing pattern with normal and equal breath sound. His oxygen saturation by pulse oximetry was 84% in room air and slightly increased to 90% after an oxygen hood was given. He did not show any different in blood pressure and $SpO_2$ in all extremities. Other examinations were unremarkable. Initial investigations revealed a capillary blood glucose of 71 mg/dL, a white blood cell count of $6.5x10^3$ µL, with 69% neutrophils, 17% lymphocytes and 12% monocytes, a hemoglobin level of 16 g/dl, and platelets at $269x10^3$ µL. His chest x-ray (Fig. 1) and electrocardiography showed normal. To investigate for congenital heart disease, an echocardiography was done and showed a 5 mm of patent ductus arteriosus, patent foramen ovale with bidirectional flow and tricuspid regurgitation peak gradient of 30 mmHg. The echocardiography result was unremarkable. After this, he was given a heated humidified high flow nasal cannula (HHHFNC) at 5 liters per minute with a fraction of inspired oxygen ($FiO_2$) of 1.0 to support his respiration. Arterial blood gas (ABG) was obtained and the result showed partial pressure of oxygen ($PaO_2$) of 389.5 mmol/L with $SaO_2$ 100%, despite his $SpO_2$ being 90% at the same time. An ABG was repeated when he was on room air with low $SpO_2$ 90%, but it showed normal $PaO_2$ at 85.1 mmol/L and $SaO_2$ 97%. He had

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methemoglobin level of 0.5% (normal 0.5 to 1.5%). Hemoglobin variants might cause a difference between $SaO_2$ and $SpO_2$. We reviewed his peripheral blood smear and found abnormal red blood cell morphology (Fig. 2). Further studies were performed to detect variants of hemoglobin. Capillary electrophoresis found Hb A 14.7%, Hb F 69.1%, Hb A2 0.3% and Hb Bart's 15.9%. This Hb profile showed the presence of Hb Bart's, suggesting Hb H disease. Alpha-globin genotyping by a single-tube multiplex gap polymerase chain reaction (Gap-PCR) for detecting common alpha-globin deletions ($--^{SEA}$, $--^{THAI}$, $-\alpha^{3.7}$, $-\alpha^{4.2}$) and a single-tube multiplex amplification refractory mutation system (ARMS-PCR) for screening common alpha-globin mutations (Hb Constant Spring, Hb Pakse) revealed heterozygous SEA deletion. Hb Lansing (HBA1: c.264C>G; codon 87 His >Gln, CAC>CAG) was detected by PCR-restriction fragment length polymorphism (RFLP)-based analysis. In brief, alpha-1 globin gene was amplified, then the PCR product was digested with PstI restriction enzyme (Fig. 3). The globin genotyping was compatible with Hb H/Hb Lansing; compound heterozygous mutation of SEA deletion and codon 87 C>G mutation ($--^{SEA}/\alpha\alpha^{CD87}$).

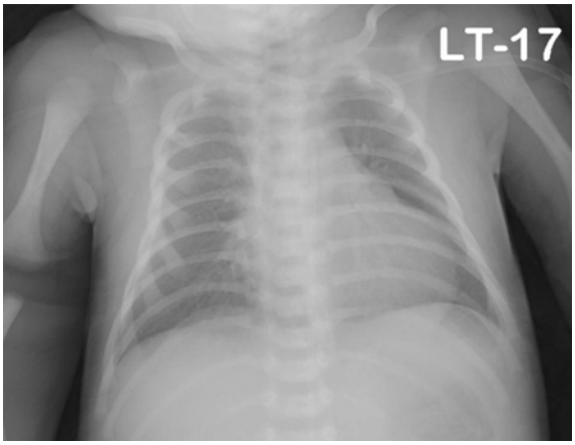


**Fig. 1** Chest x-ray showed normal.

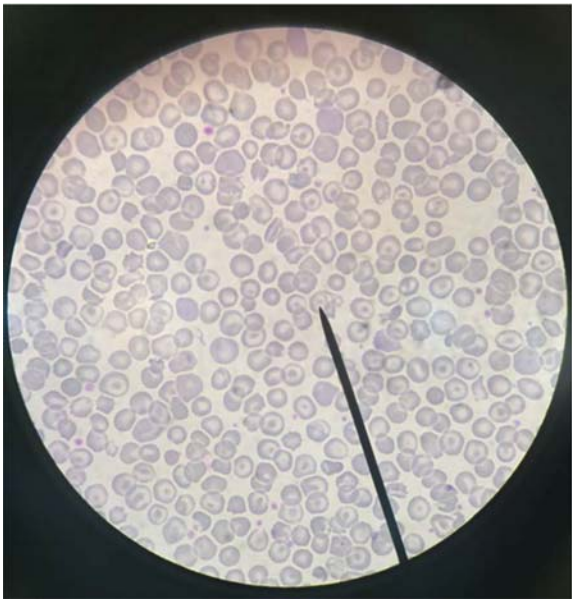

**Fig. 2** His red blood cell morphology showed hypochromia 2+, microcytic 2+ with anisocytosis 1+, poikilocytosis 2+ including target cells, schistocytes and spherocytes.

His respiratory rate decreased to normal after he was given HHHFNC for 3 days. During admission, he has pulse oxygen saturation of 88 to 94%. He was discharged to home when he was 6 days old. It should be noted that apparent spontaneous resolution of the respiratory distress would be consistent with postnatal delayed adaptation.

## Discussion

Cardiac and respiratory diseases are the most common causes of low $SpO_2$ measurement in the neonatal period. In less common incidences, Hb variants may give falsely low $SpO_2$ result with normal $SaO_2$, or concordantly low $SpO_2$ and $SaO_2$. These are caused by the different absorption spectral properties at 660 and 940 nm of abnormal Hb with the lack of

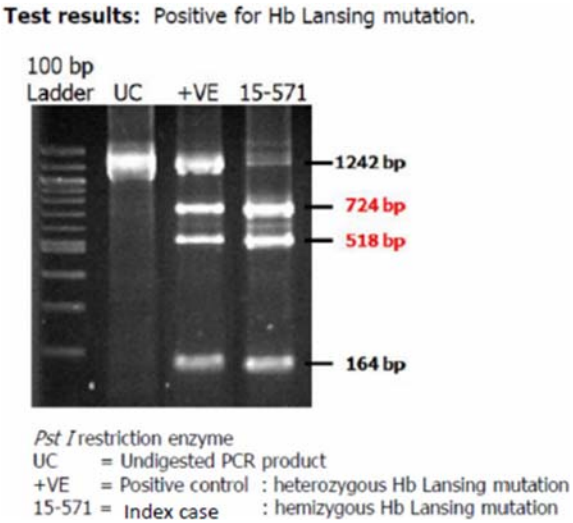


**Fig. 3** Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was positive for hemoglobin Lansing mutation.

hypoxemia or by variations of oxygen affinity[2,3]. Our case presented with spurious decreased $SpO_2$. There have been several case reports of Hb variants caused discordance between $SpO_2$ and $SaO_2$, including alpha- and beta-globin gene mutations[3]. This case suggested alpha-globin gene variant by Hb electrophoresis, which was confirmed as Hb Lansing (HBA1:c.264C>G) by specific PCR-RFLP. In our literature review, there were some reported cases of Hb variants due to alpha-globin mutations, presented with low $SpO_2$ and discordant $SaO_2$, including Hb Lansing[4-7], Hb Titusville[8], Hb Bonn[9], Hb M Iwate[10,11], and Hb M Boston[10]. Hb Lansing was first reported with heterozygous mutation of the alpha-2 gene (HBA2:c.264C>G) in an asymptomatic Hispanic man with falsely low $SpO_2$ and normal hematologic parameters by Sarikonda et al[4]. Later, Ishitsuka et al[5] described a heterozygous case of Hb Lansing (HBA2:c.264C>G) in a Japanese woman detected by falsely low oxygen saturation on pulse oximetry. Then, Akar et al[6] reported heterozygosity of Hb Lansing in a asymptomatic Turkish woman resulting from another nucleotide substitution at codon 87 of the alpha-2 gene (HBA2:c.264C>A). Recently, Hassen et al[7] had been reported a succumbed Omani newborn with presumptive homozygous Hb Lansing (HBA2: c.264C>G). In our case, a missense mutation was found at codon 87 of the alpha-1 gene. As Hb Lansing was reported previously, we named this as a new variant Hb Lansing of alpha-1 globin gene. The index case had abnormal red cell morphology due to compound heterozygosity of SEA deletion and Hb Lansing. Regarding Hb H/Hb Lansing, long term follow-up of clinical course and prognosis is necessary in this newborn patient.

## Conclusion

Our case demonstrates limitations of pulse oximetry to measure oxygen saturation and evaluation of low $SpO_2$ in neonate. The discrepancy of oxygen saturation between pulse oxymetry and arterial blood gas necessitates investigations for hemoglobino pathies, especially in endemic areas.

## What is already know on this topic?

Most of the Infants who have respiratory disease, present with respiratory distress with low $SpO_2$ measurements. After oxygen therapy, arterial blood gas should be obtained to evaluate how they response to the treatment. If there is discordant of oxygen saturation between pulse oximetry and arterial blood gas, variants of hemoglobin should be considered.

## What this study adds?

In addition to investigate congenital methemoglobinemia, infants who have discordant of oxygen saturation between pulse oximetry and arterial blood gas, molecular genetic testing for hemoglobino pathies should be explored.


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## Potential conflicts of interest

None.

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## *Hemoglobin Lansing เป็นสาเหตุหนึ่งที่ทำให้มีระดับความอิ่มตัวของออกซิเจนในเลือดจากเครื่องวัดระดับออกซิเจนต่ำเท็จในทารกแรกเกิด*

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*เครื่องวัดระดับออกซิเจนในเลือดเป็นอุปกรณ์ทำให้การวัดระดับความอิ่มตัวของออกซิเจนในเลือดทำได้ง่าย ไม่เจ็บ และไม่รุกรานผู้ป่วย ระดับความอิ่มตัวของออกซิเจนในเลือดที่ได้จากการวัดด้วยเครื่องวัดระดับออกซิเจนในเลือด ($SpO_2$) จะใกล้เคียงกับระดับความอิ่มตัวของออกซิเจนที่ได้จากการวิเคราะห์ก๊าซจากเลือดแดง ($SaO_2$) การศึกษานี้กล่าวถึงผู้ป่วยทารกเกิดครบกำหนดที่มีอาการหายใจลำบากร่วมกับมีระดับความอิ่มตัวของออกซิเจนในเลือดต่ำ ซึ่งไม่ได้มีสาเหตุมาจากโรคทางระบบทางเดินหายใจหรือโรคหัวใจพิการแต่กำเนิด ผู้ป่วยถูกตรวจพบความแตกต่างของระดับออกซิเจนที่ได้จากการวัดด้วยเครื่องวัดระดับออกซิเจนในเลือดกับที่ได้จากการวิเคราะห์ก๊าซจากเลือดแดง จึงส่งเลือดตรวจหาระดับ methemoglobin และความผิดปกติของฮีโมโกลบิน (hemoglobin variants) ผลการตรวจพบ Hemoglobin (Hb) Lansing รายงานฉบับนี้เป็นรายงานผู้ป่วยทารกแรกเกิดรายแรกที่มีรายงานการตรวจพบ Hb Lansing ในประเทศไทย ความแตกต่างของระดับความอิ่มตัวออกซิเจนของฮีโมโกลบิน โดยการใช้เครื่องตรวจวัด ความอิ่มตัวออกซิเจนของฮีโมโกลบินจากชีพจรและการวิเคราะห์ก๊าซจากเลือดแดงนำไปสู่การสืบค้นหาความผิดปกติของฮีโมโกลบิน*