

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20242095>

Case Report

Navigating antenatal complexity: a case report of Bombay blood group and anaemia challenges

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Received: 26 May 2024

Accepted: 29 June 2024

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ABSTRACT

The Bombay blood group is a rare blood type, predominantly found in regions with a high prevalence of consanguineous marriages due to its autosomal recessive inheritance pattern. This blood group is unique because individuals lack the H antigen, a precursor to the A and B antigens found in other blood types, making their blood type exceptionally rare. Managing antenatal patients with the Bombay blood group presents significant challenges, especially in cases of anaemia or any instance of blood loss. The primary difficulty arises from the scarcity of compatible blood for transfusion, as individuals with the Bombay blood group can only receive blood from other Bombay group donors. This rarity complicates the management of potential complications during pregnancy, labour, and delivery. To address these challenges, minimizing blood loss is essential during all stages of pregnancy, particularly during labour, Caesarean sections, and in the prevention of postpartum haemorrhage. Effective management requires a multidisciplinary approach, involving obstetricians, haematologists, and blood bank services. One potential strategy to mitigate the risk of blood shortages is autologous blood transfusion. This option can be particularly valuable during pregnancy; however, it requires careful consideration of the potential risks and benefits. The procedure should be conducted under the guidance of healthcare professionals experienced in managing such cases, ensuring the safety and well-being of both the mother and the fetus. In our case report, we present an antenatal patient with anaemia and the challenges encountered during the antenatal and postnatal periods. This case highlights the complexities of managing pregnancies involving the Bombay blood group. It underscores the importance of a well-coordinated, multidisciplinary approach to optimize outcomes for both mother and child.

Keywords: Anaemia in pregnancy, Autologous blood transfusion, Bombay blood group.

INTRODUCTION

A blood group that is rarely found is the Bombay blood group denoted as Oh type. The Oh blood type is transmitted as an autosomal recessive trait and was first described by Bhende et al. The H antigen which is necessary for synthesizing ABO groups is lacking in this blood type. Initially, all these individuals are labelled as O blood type, because of lack of A, B, and H antigens on red blood cells. There are anti-A, anti-B, and anti-H antibodies in the serum that reach all ABO phenotypes, therefore

these individuals can only receive blood from the Bombay blood type. The frequency of Oh phenotype varies globally but is commonly found in India and Europe with prevalences of 0.01% and 0.0001%, respectively.¹ As this blood type is very rare this poses a challenge for transfusion of blood. The H antigen is a precursor for both the A and B glycoproteins that constitute group A and B blood types, respectively. Blood group O has an absence of both A and B glycoproteins but still has H antigen. Based on the genetic defect, this blood type is further classified as Bombay and Para-Bombay phenotype.

Bombay Oh phenotype is due to the missense or nonsense mutation in genes coding for enzymes alpha-2 and alpha-4 fucosyltransferase leading to the inactivation of both FUT1 and FUT2 genes, resulting in a complete lack of H antigen.¹ In the Para-Bombay phenotype, either the FUT1 will be silenced and the FUT2 gene will be active or a mutated FUT1 gene encodes an enzyme with diminished activity. This leads to the presence of anti-A, anti-B, and anti-H in serum leading to a diagnosis of the Oh blood type. Hence, they require blood transfusions exclusively from Oh phenotype donors or by autologous blood transfusions.

Mutational analysis has elucidated that individuals with the Bombay blood group phenotype possess a homozygous recessive (hh) genotype, as opposed to the homozygous dominant (HH) or heterozygous (Hh) genotypes typical of the ABO blood group system. This genetic configuration leads to the absence of H antigen expression on the surfaces of red blood cells (RBCs). The h allele responsible for this absence stems from a mutation in the H gene (FUT1), which ordinarily expresses the H antigen on RBCs within the ABO blood group system. Individuals with the Bombay phenotype exhibit homozygosity (hh) for the T725G mutation in the FUT1 coding region, resulting in the substitution of leucine with arginine, alongside a gene deletion of FUT2. This mutation leads to the production of an inactive enzyme incapable of generating the H antigen. To definitively classify and diagnose a case as the typical Bombay phenotype, specialized tests such as absorption-elution studies, titration of naturally occurring antibodies at varying temperatures, inhibition of anti-H by O saliva secretor status, and determination of secretor status should be conducted, as outlined by Bhatia in 1974.² Pregnancy with such a rare blood type, poses a challenge to the obstetrician, during pregnancy, in case of anemia, postpartum hemorrhage, etc which might require a blood transfusion. and the risk of hemolytic disease in the fetus and newborn. Autologous blood donation during pregnancy is less frequently practiced compared to non-pregnant individuals due to potential maternal and fetal complications associated with the procedure.³ One concern is the exacerbation of anemia in the mother, as donating blood may further deplete her already limited blood volume and hemoglobin levels, potentially leading to increased fatigue and weakness. Furthermore, autologous blood donation in pregnancy can trigger vasovagal symptoms, such as dizziness, lightheadedness, and fainting, which can pose risks to both the mother and fetus. These symptoms are a result of the body's response to changes in blood pressure and heart rate during and after blood donation. Moreover, fetal heart rate abnormalities can occur following autologous blood donation in pregnancy. The temporary reduction in maternal blood volume and oxygen-carrying capacity may affect placental perfusion and oxygenation, influencing fetal well-being and potentially leading to fetal distress. Due to these potential risks, healthcare providers typically exercise caution and weigh the benefits and risks carefully before

recommending autologous blood donation during pregnancy. Alternative strategies to manage anemia and prepare for potential blood loss during childbirth are also applied to minimize the likelihood of complications for both the mother and the developing fetus.

CASE REPORT

A 33-year-old primigravida woman with a history of hypothyroidism was referred to our tertiary care facility upon the discovery of a rare Bombay blood group (O Rh negative) during her 25th week of pregnancy. Since her referral, she was under scheduled care at our facility. The confirmation of her unique blood type was established through forward and reverse grouping, with the O blood group serving as the control group. Upon admission, her Hemoglobin level was noted to be 9.6 g/dl, prompting consultation with specialists in transfusion medicine. Given the combination of her rare blood type and the presence of anemia, the transfusion medicine team recommended increasing her Hemoglobin levels to 11 g/dl and initiated preparations for autologous blood collection 72 hours before her anticipated delivery date. To address her anemia, she underwent a parenteral iron transfusion and was prescribed oral iron supplementation throughout her pregnancy to optimize her iron levels. Despite these challenges, her antenatal checkups remained consistent, including regular growth scans starting from 28 weeks, conducted every four weeks until delivery and fetal growth was deemed appropriate for her gestational age. Additionally, middle cerebral artery Doppler scans were performed, revealing no evidence of fetal anemia. To mitigate potential Rh incompatibility complications, she received Antenatal Anti-D immunoglobulin following a negative Indirect Coomb's Test result due to her negative Rh phenotype. This proactive measure aimed to minimize the risk of hemolytic disease of the newborn stemming from Rh factor discrepancies between mother and fetus. Additionally, robust communication between the obstetric team, transfusion medicine team, and blood bank facilitated a well-coordinated delivery plan.

Furthermore, thorough counseling of the patient and her attendant regarding the risk of bleeding and the potential need for ABO blood group transfusion under the cover of prednisolone and intravenous immunoglobulins (IVIG), to reduce the chances of hemolytic reaction, in the absence of Bombay blood group availability, along with the possible complications associated with such transfusions, was conducted. By 38 weeks, her hemoglobin level rose to 10.8 g/dl, and 350 ml of autologous blood was collected under strict monitoring. Comprehensive fetomaternal surveillance was maintained post-procedure to ensure optimal outcomes. She was planned for labor induction after 48 hours, but due to a failed induction, an Emergency Lower Segment Cesarean Section (LSCS) was performed, resulting in the birth of a live female infant weighing 2980 grams. Postoperatively, normovolemic hemodilution was initiated, and her hemoglobin was noted to be 8.3 g/dl, leading to an autologous blood transfusion under strict

monitoring. Subsequently, she recovered well and was discharged from the hospital.

DISCUSSION

The Bombay blood group is a rare blood type with a very low prevalence and is primarily found in individuals from the Indian subcontinent. In 1952, Bhende and his colleagues first identified the blood group in Bombay, which is where it received its name. The Bombay blood group is a result of a homozygous recessive gene that

prevents the formation of A, B, and H antigens. The H antigen is a precursor of A and B antigens found on all human red cells except those subject to phenotype Oh. In genotype hh (phenotype Oh), H antigen is not synthesized on red cells or in secretions, and therefore neither A nor B antigens can be synthesized.⁴ These patients can receive only autologous blood transfusions or from exclusive Bombay blood group donors after cross-matching. The clinical significance of this blood type is that mismatched blood will lead to adverse transfusion reactions. There can be also an incidence of hemolytic disease in the newborn in these blood phenotypes.

Table 1: Blood group and type and its compatibility.

Blood group	Rh type	Antigen	Antibody	Compatibility
A	Positive	A and Rh	B	A and O groups, irrespective of Rh compatibility
A	Negative	A	B	Preferrable A and O Rh negative groups, Rh positive can be considered in an emergency
B	Positive	B and Rh	A	B and O groups, irrespective of Rh compatibility
B	Negative	B	A	Preferrable B and O Rh negative groups, Rh positive can be considered in an emergency
O	Positive	Rh	A, B	O group only, irrespective of Rh compatibility
O	Negative	Nil	A, B	Preferrable O Rh negative group, Rh positive can be considered in an emergency
HH	-	Nil	A, B, H	Only HH group blood

The Bombay blood group is often mistyped as the O blood group, if it is not correctly typed, therefore cross typing and matching should be done with utmost care in this group of patients. The incidence of Bombay phenotype is usually increased in those states where consanguineous marriages are prevalent like Andhra Pradesh, Karnataka, Tamil Nadu, Maharashtra, etc. This is due to the autosomal recessive trait of this phenotype. Outside India, this blood type is usually found in South- East Asian countries. Forward and reverse blood grouping, along with the use of Anti-H reagent, can help in the detection of the Bombay blood group.⁵ Serological methods can be used to detect the presence of A, B, and H antigens in red blood cells and saliva. Molecular and genetic mechanisms can be explored to identify the Bombay blood group.⁷ Sanger sequencing and analysis of the FUT1 gene can help in identifying the genetic basis of the Bombay blood group.⁶ The genes involved in the inheritance of this Bombay blood group are present in the long arm of chromosome 19(19q13.3). Red blood cells have a surface antigen called the H antigen is a precursor molecule for the formation of A and B antigens on the red blood cells. The genes responsible for the formation of this H antigen are the FUT1 (or H) and FUT2

secretor genes, which are involved in the enzymatic activity of glycosyltransferase enzyme with adds 1-fucose to precursor substrate to form H antigen on the surface of the red blood cells.⁸ FUT 1 gene produces the H antigen only on the surface of the erythrocytes while the FUT2 gene, in addition to the erythrocytes, helps in the production of the H antigen present in saliva, gastrointestinal tract secretions, and Genitourinary secretions. Bombay phenotype occurs due to missense mutation in genes coding for enzymes alpha- 2 and alpha-4 fucosyl transferase leading to the inactivation of both FUT1 and FUT2 genes, resulting in a complete lack of H antigen on the surface of the erythrocytes and hence forming Oh blood group type.¹ General principles of managing pregnancy with Oh blood types are that there should be active management of the third stage of labor, optimizing intraoperative hemostasis, consideration of cell salvage, considering balloon tamponade or uterine artery embolization when required, considering early definitive management which might include hysterectomy in life-threatening situations and also prevention and treatment of hypothermia, acidosis and hypocalcemia. Apart from arranging blood from Bombay blood types or autologous

blood transfusion, Adjunct treatments like tranexamic acid should be available. In the event of postpartum hemorrhage, 1 gm of tranexamic acid IV stat is to be given followed by 1gm tranexamic acid every 8th hourly IV or Per oral as needed. Blood bank and transfusion medicine specialist should be informed in a close loop communication about the route and timing of delivery and 2 units of irradiated fresh red cells should be kept available along with 3 units of frozen red cells. In case of chances of hemorrhage, Fresh Frozen Plasma and cryoprecipitate should also be available. Prothrombinex should be preferred over fresh frozen plasma but it is not readily available in all centers and 2000 units single dose which is equivalent to 20 IU/kg should be given and a second dose can also be given. Fresh frozen plasma should be given at 15 ml/kg dose and should be of group O. Cryoprecipitates from group O should be given if required and a dose of 3-4 gm, with the aim to always keep levels of Fibrinogen >2g/l. Recombinant Factor VIIa can be given in case of life-threatening situations at the dose of 90 µg/kg and should be considered only if conventional measures like surgical hemostasis and blood component therapy have failed.

In case of immediate exsanguination, group O Rh compatible red cells can be used, and this has to be conveyed and counseled to the patient and party during the regular antenatal visits as there is a high risk of severe transfusion reaction with such blood transfusions. Identifying this blood type at an early stage in pregnancy is an important part of antenatal management. As soon as the pregnant woman is labelled as Oh phenotype, her hemoglobin levels should be checked and if anemia is present, further evaluation should be done to look for the cause of anemia. In the initial trimester of pregnancy, this anemia should be corrected by giving iron supplementation and can be planned for autologous blood collection in later pregnancy. Autologous blood transfusion during pregnancy is less common than in non-pregnant individuals due to potential complications for both the mother and fetus. These include exacerbation of maternal anemia, vasovagal symptoms, and fetal heart rate abnormalities. To mitigate risks, blood collection for autologous transfusion typically begins at 32 weeks of gestation. A standard protocol involves weekly phlebotomy of approximately 400 ml, allowing for a total collection of 1200-1500 ml by the time of delivery, which can then be utilized if a blood transfusion becomes necessary.³ Another challenge in this pregnancy is the risk of Hemolytic disease in neonates and newborns, as the IgG component of anti-H can cross the placental barrier. The risk of isoimmunization should be kept in mind and regular monitoring of Indirect Coomb's test should be done, and if negative Antenatal Anti D should also be given. Post-delivery also Indirect Coomb's test to be done. Future pregnancies should have to be monitored closely. Blood donation and freezing of donated blood in the interpregnancy period should help in the management of future pregnancies and if blood transfusion should be

required at any other time, as the frozen blood can be stored indefinitely.⁴

CONCLUSION

Given the rarity of the Bombay phenotype, meticulous antenatal care is paramount for patients with this blood type. Detecting and addressing potential complications early on can significantly impact the outcome of pregnancy and delivery. One crucial aspect of antenatal care is the early identification of anemia during routine visits. Anemia can be a common concern in pregnancy, but for patients with the Bombay phenotype, it takes on added importance due to potential challenges in obtaining compatible blood products. Early detection of anemia allows healthcare providers to take prompt measures to determine the type of anemia and devise appropriate interventions to improve hemoglobin levels. This may involve targeted supplementation, dietary adjustments, or specialized treatments based on the specific type of anemia identified. During labor or Cesarean section, precautions are essential to minimize blood loss. Strategies such as the use of tranexamic acid, which helps to prevent excessive bleeding by promoting blood clotting, or uterotonics to aid in uterine contractions and reduce postpartum hemorrhage risk, may be employed as needed. Planning for adequate blood reserves is crucial, typically arranged either through blood donation from compatible donors or via autologous blood transfusion, where the patient's own blood is collected and stored for potential use during delivery. This preparation should ideally be done at least 3 weeks before the anticipated delivery or Cesarean section to ensure availability and compatibility. During autologous blood transfusion, rigorous fetomaternal surveillance is necessary to monitor both the mother and the fetus closely. This includes continuous assessment of vital signs, blood parameters, and fetal well-being to detect and address any potential complications promptly. Close collaboration between obstetricians, hematologists, and transfusion medicine specialists is vital to ensure optimal outcomes for both the mother and the baby.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Pai P, Hebbar S. Navigating antenatal complexity: a case report of Bombay blood group and anaemia challenges. *Int J Reprod Contracept Obstet Gynecol* 2024;13:2179-83.