# Exchange transfusion in neonatal hyperbilirubinaemia: experience in Isfahan, Iran

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## ABSTRACT

**Introduction: This study aims to determine the aetiology and complications of exchange transfusion (ET) performed for neonatal hyperbilirubinaemia in Isfahan, Iran.**

**Methods: A retrospective chart review of 68 term and near-term newborns who underwent ET at two perinatal centres in Isfahan, Iran between January 2001 and January 2004, was performed.**

**Results: Of the 68 patients who underwent ET, nine (13.2 percent) required more than one ET. The most common causes of ET overall were ABO incompatibility (22.1 percent) and glucose-6-phosphate dehydrogenase deficiency (19.1 percent). The maximum total serum bilirubin concentration was 25.9 +/- 7.5 mg/dL. ET complications occurred in 14 neonates (20.9 percent), the most common being thrombocytopenia (6 percent). One (1.5 percent) of the 68 patients died of complications, probably attributable to ET.**

**Conclusion: ET causes high morbidity, even in term and near-term newborns. Therefore, it should be initiated only when the benefit of preventing kernicterus outweighs the complications associated with the procedure.**


**Keywords: blood transfusion, exchange transfusion, hyperbilirubinaemia, neonate hyperbilirubinaemia, thrombocytopenia**

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## INTRODUCTION

Jaundice is a common neonatal problem. This may be due to the limited ability of a neonate to metabolise indirect bilirubin, which leads to hyperbilirubinaemia and predisposes to the risk of encephalopathy and long-term sequela if not managed promptly.[1] Administration of anti-D immunoglobulin to prevent erythroblastosis foetalis, and the use of phototherapy to treat neonatal jaundice, have resulted in a decline in the rates of significant neonatal hyperbilirubinaemia.[2,3] The bilirubin level at which exchange transfusion (ET) is indicated remains controversial; the recommendations attempt to balance the benefits of preventing bilirubin toxicity with the risks of ET.[4-6]

Mortality rates attributable to ET ranged from 0.7% to 3.2% in studies performed in the 1960s, and from 0.4% to 3.2% during the 1970s and 1980s.[7-13]

In the study of Keenan et al, among 190 infants who underwent 331 ET, adverse clinical problems were observed in 6.7%, and the observed rate of serious morbidity was 5.2%.[14] Information concerning the risk of adverse events from neonatal ET in the past decade is sparse,[6,15] and we did not find any report of ET aetiology and complication in Iran. This study was undertaken to determine the aetiology and complications of ET at two perinatal referral centres in Isfahan, Iran.

## METHODS

The study included all infants below 30 days of age who were admitted to the neonatal intensive care units of Alzahra and Shahid Beheshti Hospitals, Isfahan, Iran. During the three-year period from January 2001 to January 2004, infants were selected if they had discharge diagnosis of ET in their medical record. After excluding records for patients who underwent only partial ET for polycythaemia and severe anaemia, the medical records of the 68 remaining patients were reviewed in detail. The cause of jaundice reported in the records was classified in the following way: Rh disease was defined as jaundice in Rh-positive newborns from Rh-negative mothers and evidence of haemolysis, and ABO disease was defined as jaundice in newborns with positive Coombs test against the A or B antigens from type O mothers.

Either whole blood ABO compatible with both the baby and mother, or group O red cells resuspended in compatible plasma (usually AB), was used. ET was performed by a paediatric resident. The double volume exchange procedure was generally completed in about 60–90 minutes by repeatedly removing and replacing small aliquots of blood (5 ml/kg) according to standard published guidelines.[6] The following investigations

were performed on all neonates as a baseline: complete blood count, total and direct serum bilirubin, erythrocyte glucose-6-phosphate dehydrogenase (G6PD) level, direct Coombs test, blood culture and pre- and post-exchange haemoglobin, bilirubin, calcium and blood glucose. Double volume ET was performed in every case using a single line (umbilical vein). 1 ml of calcium gluconate 10% was given after exchange of every 100 ml of blood.

An adverse event was defined as any complication that occurred within three days of an ET. The following definitions were used: hypoglycaemia: serum glucose < 40 mg/dL; hypocalcaemia: total serum calcium < 8 mg/dL; thrombocytopenia: platelet count < 100,000/mm$^3$; bradycardia: heart rate dropping to < 80 beats per minute; apnoea: cessation of respirations for > 20 seconds; seizure: any tonic and/or clonic movement; necrotising enterocolitis: defined according to Bell et al's criteria.[16]

## RESULTS

During the three-year study period, 68 patients underwent ET. The infants had a mean birth weight of 2,812.6 ± 531.1 g and a mean gestational age of 38.6 ± 1.8 weeks. Overall, eight infants had two ET and one had four ET. The most common cause of jaundice was ABO incompatibility (22.1%), G6PD deficiency (19.1%), and Rh incompatibility (11.7%). The mean maximum total serum bilirubin level was 25.9 ± 7.5 mg/dL. The mean age at presentation was 4.4 ± 2.1 days. Table I shows the causes of jaundice, maximum total serum bilirubin level before ET and the age of presentation. 19 infants had total serum bilirubin of more than 30 mg/dL at admission. The most common causes of extreme hyperbilirubinaemia (bilirubin > 30 mg/dL) were ABO incompatibility (11.7%), and G6PD deficiency (8.8%).

Of the 68 infants, five (7.3%) had abnormal neurological examination at the time of ET. This included hypotonia in two infants (2.9%), hypertonia in two (2.9%), and a high pitch cry in one (1.4%) infant. All five infants who developed kernicterus had a serum bilirubin greater than 30 mg/dL.

Complications occurred in 14 (20.9%) infants (Table II). The most common adverse event was related to thrombocytopenia. Only one infant had suspected disseminated intravascular coagulation (DIC) after ET. Four infants experienced severe complications attributable to ET. These complications included cardiorespiratory arrest (1.5%), apnoea with cyanosis requiring resuscitation during or immediately after ET (1.5%), limb colour change (1.5%), and necrotising enterocolitis (1.5%). One infant expired within 24 hours after ET.

**Table I. Causes of jaundice, maximal total serum bilirubin level before exchange transfusion and age of presentation.**

| Causes of jaundice | Value |
|---|---|
| Rh disease, n(%) | 8 (11.7) |
| ABO incompatibility, n(%) | 15 (22.05) |
| G6PD deficiency, n(%) | 13 (19.1) |
| Maximum mean bilirubin (mg/dL ± SD) | 25.9 ± 7.5 |
| Presenting age (mean days ± SD) | 4.4 ± 2.1 |

**Table II. Complications of exchange transfusion.**

| Complication | n (%) |
|---|---|
| Death | 1 (1.5) |
| Seizure | 1 (1.5) |
| Platelet < 100,000/mm$^3$ | 4 (6) |
| Calcium < 8 mg/dL | 2 (2.9) |
| Blood glucose < 50 mg/dL | 0 |
| Bradycardia < 100 | 1 (1.5) |
| Suspected DIC | 1 (1.5) |
| Cardiorespiratory arrest | 1 (1.5) |
| Hypoxia | 1 (1.5) |
| Limb colour change | 1 (1.5) |
| Necrotising enterocolitis | 1 (1.5) |

## DISCUSSION

This study shows a high rate of adverse events associated with ET for neonatal hyperbilirubinaemia. However, most of these complications were asymptomatic and transient, such as thrombocytopenia. Exchange blood transfusion remains the gold standard for effective treatment of neonatal hyperbilirubinaemia. Although reports show a progressive decline over the years in the number of neonates needing ET, it is still required in up to 7% of neonates admitted to nurseries.[17] This reduction in the number of ET may be due to the development of anti-Rh globin for Rh-negative mothers and the widespread use of phototherapy for neonatal jaundice.[18,19] In this study, the most common cause of ET was ABO immunisation, which is similar to the finding in some other series. Dikshit and Gupta, and Sanpavat reported that ABO haemolytic disease of newborns is the most common cause of ET in term neonates (35.9% and 21.3%, respectively).[12, 20]

G6PD deficiency accounted for 19% of all causes of ET in our study. This figure is higher than the estimated 10% prevalence of G6PD deficiency in the Jordanian population.[21] Abu-Ekteish et al showed that G6PD deficiency, alone and concomitant with ABO haemolysis, accounted for 38% of all causes of ET.[1] A possible explanation for these differences may be the racial differences in the prevalence of G6PD deficiency. Multiple ET was required in 12.3% of our neonates. This is similar to findings of Abu-Ekteish et al, but is lower than some other studies.[1, 12, 22]

The most common morbidities included seizure (1.5%), cardiorespiratory arrest (1.5%), bradycardia

(1.5%), hypoxia (1.5%), limb colour change (1.5%) and necrotising enterocolitis (1.5%). In Jackson's study, permanent serious sequela was observed in 1% of healthy newborns who underwent ET.[6] Serious transient complications occurred in 17% and asymptomatic complications in 27% of infants. Patra et al showed that the most common adverse events following ET were thrombocytopenia (44%) and hypocalcaemia (29%), none of which were symptomatic.[23]

In our study, the mortality rate was 1.5%. Panagopoulos et al in Greece examined 606 exchanges performed on 502 neonates between 1962 to 1966 and reported a mortality rate of 0.66 % per patient and 0.79% per procedure; Keenan et al reported a mortality rate of 0.5%; but Chima et al reported no serious adverse event or death in 22 term infants who underwent 26 ET between 1990 and 1998.[9,14-15] However, complications are common enough that ET, even in healthy newborns, should be performed only in nurseries prepared to respond to these adverse events. Although apnoea, bradycardia and cyanosis rarely occur during ET of healthy infants, cardiorespiratory and oxygen saturation monitoring should be considered during ET.

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## REFERENCES

1. Abu-Ekteish F, Daoud A, Rimawi H, Kakish K, Abu-Heija A. Neonatal exchange transfusion: a Jordanian experience. Ann Trop Paediatr 2000; 20:57-60.
2. Stockman JA 3rd. Overview of the state of the art of Rh disease: history, current clinical management, and recent progress. J Pediatr Hematol Oncol 2001; 23:385-93. Erratum in: J Pediatr Hematol Oncol 2001; 23:549.
3. Dennery PA, Seidman PS, Stevenson DK. Neonatal hyperbilirubinemia. N Engl J Med 2001; 344:581-90.
4. Watchko JF, Oski FA. Bilirubin 20 mg/dL = vigintiphobia. Pediatrics 1983; 71:660-3.
5. Newman TB, Maisels MJ. Evaluation and treatment of jaundice in the term newborn: a kinder, gentler approach. Pediatrics 1992; 89:809-18. Comment in: Pediatrics 1992; 89:819-31. Pediatrics 1993; 91:166-7; author reply 168. Pediatrics 1993; 91:1218-9.
6. Jackson JC. Adverse events associated with exchange transfusion in healthy and ill newborns. Pediatrics 1997; 99:E7.
7. Boggs TR, Westphal MC. Mortality of exchange transfusion. Pediatrics 1960; 26:745-55.
8. Weldon VV, Odell GB. Mortality risk of exchange transfusion. Pediatrics 1968; 41:797-801.
9. Panagopoulos G, Valaes T, Doxiadis SA. Morbidity and mortality related to exchange transfusions. J Pediatr 1969; 74:247-54.
10. Kitchen WH. Neonatal mortality in infants receiving an exchange transfusion. Aust Paediatr J 1970; 6:30-40.
11. Hovi L, Siimes MA. Exchange transfusion with fresh heparinized blood is a safe procedure. Experiences from 1 069 newborns. Acta Paediatr Scand 1985; 74:360-5.
12. Dikshit SK, Gupta PK. Exchange transfusion in neonatal hyperbilirubinemia. Indian Pediatr 1989; 26:1139-45.
13. Guaran RL, Drew JH, Watkins AM. Jaundice: clinical practice in 88,000 liveborn infants. Aust N Z J Obstet Gynaecol 1992; 32:186-92.
14. Keenan WJ, Novak KK, Sutherland JM, Bryla DA, Fetterly KL. Morbidity and mortality associated with exchange transfusion. Pediatrics 1985; 75:417-21.
15. Chima RS, Johnson LH, Bhutani VK. Evaluation of adverse events due to exchange transfusion in term and near-term newborns. Pediatr Res 2001; 49:324A.
16. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg 1978; 187:1-7.
17. Funato M, Tamai H, Shimada S. Trends in neonatal exchange transfusions at Yodogawa Christian Hospital. Acta Pediatr Jpn 1997; 39:305-8.
18. Lucey JF. Neonatal jaundice and phototherapy. Pediatr Clin North Am 1972; 19:827-39.
19. Woodrow JC. Effectiveness of Rh prophylaxis. Haematologica (Budap) 1974; 8:281-90.
20. Sanpavat S. Exchange transfusion and its morbidity in ten-year period at King Chulalongkorn Hospital. J Med Assoc Thai 2005; 88:588-92.
21. Madanat F, Karadsheh N, Shamayleh A, et al. Glucose-6-phosphate dehydrogenase deficiency in male newborns. Jordan Med J 1986; 21:205-12.
22. Tan KL. Glucose-6-phosphate dehydrogenase status and neonatal jaundice. Arch Dis Child 1981; 56:874-7.
23. Patra K, Storfer-Isser A, Siner B, Moore J, Hack M. Adverse events associated with neonatal exchange transfusion in the 1990s. J Pediatr 2004; 144:626-31.