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GENERAL INTRODUCTION

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1.1 Background

The phenomenon of alloimmunization is an important adverse effect that follows transfusions with allogeneic blood (Walker *et al.*, 1989; Heddle *et al.*, 1995) and pregnancy (Moise, 1993; Moise, 2005). It results from an immune response due to genetic differences between the blood donor and recipient of the same species on the one hand, and the mother and fetus on the other. Immune alloantibodies against red blood cell (RBC) antigens are generally formed early in the course of multiple transfusions, usually before the 10th transfusion (Blumberg *et al.*, 1983; Fluit *et al.*, 1990). Upon further transfusion exposures, patients who have formed antibodies showed a 4 - 5 times increased risk for developing additional alloantibodies (Schonewille *et al.*, 2006; Schonewille *et al.*, 2009). Antibodies may also be formed against class I human leucocyte antigens (HLA) and human platelet antigens (HPA) when whole blood, platelets and granulocytes are transfused. Sickle cell disease (SCD) patients and other multiply transfused (OMT) blood recipients are at high risk of being alloimmunized. Once immunized, obtaining compatible blood for their future transfusions can pose complex serological problems and the need for an RBC typed donor inventory. The antibodies can cause alloimmune haemolysis presenting as haemolytic disease of the fetus and newborn (HDFN) or acute and delayed haemolytic transfusion reactions (HTRs), with potentially serious morbidity and mortality.

No data were available on the frequency of post-transfusion and maternal RBC alloimmunization in Uganda before the commencement of this research project. In the well-resourced parts of the world, the incidence and prevalence of RBC alloantibody formation are reported to be less than 1% up to more than 40% respectively. The frequency of post-transfusion RBC alloimmunization is generally high in patients with haemoglobinopathies, ranging up to 37% in thalassaemia and to 65% in sickle cell anaemia (Wang *et al.*, 2006; Ameen *et al.*, 2009). Factors assumed to influence the rate of alloimmunization are antigen immunogenicity, duration of transfusion therapy, and genetic and environmental factors, but their individual contribution is unknown.

In Uganda, pre-transfusion testing is currently limited to ABO/D typing plus room temperature (RT) saline cross-matches, and most of the patients are given whole blood transfusions instead of blood components. No screening for immune RBC alloantibodies is carried out in antenatal and pre-transfusion settings. Also, Rh immune globulin (RhIG) prophylaxis is not routinely administered to RhD negative mothers who deliver RhD positive babies. Therefore, there was a need to determine the magnitude of the problem of post-transfusion and maternal RBC

alloimmunization in Uganda. In this thesis, recommendations are given on the prevention of RBC alloimmunization and the delivery of improved blood transfusion and related obstetric services in Uganda. The proposed changes in policy and practice are aimed at reducing the morbidity and mortality associated with the consequences of RBC alloimmunization.

1.2 Outline of the thesis

This thesis provides results of a series of studies on the occurrence of RBC alloantibodies in blood transfusion recipients and pregnant women in Uganda.

We tried to answer the following research questions:

- Is there sufficient documentation on the clinical transfusion process and on post-transfusion complications related to RBC alloimmunization in Ugandan hospitals? (Chapter 3)
- What is the frequency and nature of RBC alloimmunization in SCD patients in Uganda? (Chapter 4)
- Does the rate of RBC alloimmunization differ among SCD patients compared to OMT Ugandan blood recipients? (Chapter 5)
- What is the prevalence of RhD negativity and maternal RBC alloimmunization in Ugandan pregnant women? (Chapter 6)
- Is it cost-effective to introduce RBC alloantibody screening as part of pre-transfusion testing in Uganda? (Chapter 7)

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