Prevalence of weak D in northern hilly areas of Uttarakhand, India

Sir,

The Rh blood group system is the next most important to the ABO system in term of its clinical significance in blood transfusion. Rh blood group system, with 49 distinct antigens is the most polymorphic blood group system. The Rh gene lies on chromosome number 1 and is carried in groups of three.[1] The Rh locus is composed of two highly homologous genes; the RHD gene, which encodes the D protein, and the RHCE gene, which encodes the C, c, E, and e proteins.[2]

Stratton in 1946 coined the term Du to describe red cells with a weakened form of the D antigen.[3] Race, *et al*. in 1948 and Renton and Stratton in 1950 found that Du red cells were not agglutinated directly by anti-Rh(D) serum, but required subsequent antiglobulin addition to show the presence of this antigen.[4] With the use of more potent anti-sera (monoclonal reagents) certain previously Du labelled persons now classified as D-positive.

The number of D antigen sites on the Rh(D)-positive red blood cell is normally in the range of 9900 to 33000. The weak D phenotype appears to be a quantitative variation in the number of D antigen sites on the red blood cell (i.e. 110 to 9000 per red blood cell).[5] The difference between 'D' and weak D antigen is that the latter is weakly immunogenic and difficult to detect. RBCs with a partial D antigen usually are agglutinated by some but not all – monoclonal anti-D reagents in a distinct pattern. For this reason, RBCs with a weak D antigen may type as D+ with one anti-D reagent (containing a reactive clone) but D– with another (containing a non-reactive clone). The significance of weak D lies in the fact that transfusion of red cells from a weak D person to a D– person may result in alloimmunization and subsequent exposure to such red cell can lead to fatal hemolytic reaction or hemolytic disease of newborn in a sensitized pregnant female. The aim of the present study is to find out the prevalence of weak D in the northern hilly region of Uttarakhand, India.

This study was done in the largest stand alone blood bank of the state with 100% voluntary donations through mobile vans and camps organized in various areas of Uttarakhand. The study period was 3 years from January 2008 to December 2010. A total of 58,614 blood donors were screened and bled during this period. ABO and Rh blood grouping was performed as a routine protocol in micro plates using two antisera (one IgM and one IgM+IgG blend), from 2 different companies (Ortho clinical diagnostics and J. Mitra) on an automated blood grouping machine (MITIS II, Ortho Clinical Diagnostics, Rochester, US). Samples that were not agglutinated in routine test were subjected to further testing the sample by IAT method using monoclonal anti IgG anti D (ID-Diaclon, DiaMed, Switzerland) with DiaMedgel cards for weak D containing anti-IgG.

Out of a total of 58,614 donors tested, 55566 (94.8%) donors were found to be RhD positive and only 3048 (5.2%) donors were RhD negative. On testing of these Rh negative samples by IAT method, 3 samples (0.09% of Rh negative and 0.005% of total population) came to be positive (i.e. weak D).

Our study shows that the prevalence of 'D' antigen in the Uttarakhand region is around 94.8%, which is similar to other studies from India.[6] The incidence of weak D varies worldwide. We found in our study, that the prevalence of weak D is 0.005% of total population and 0.09% of Rh negative population in Uttarakhand region. This is low as compared to other studies published from India.[7-9] There may be two reasons for this difference. First of all, there may be an actual difference in frequency of weak D in different geographical areas of India. Other valid reason for lower prevalence of weak D in our study could be that all other studies have used conventional tube technology for their routine 'D' testing, whereas we have screened our sample using automated microplate technology using two anti-D (one IgM and one IgM+IgG blend), therefore with increased chances of detecting weakly reacting cells with lower number of 'D' antigen and therefore these cells were already termed Rh D positive.

Though there are lesser number of antigens present on the red cells of a person with weak D, still there are fair chances of sensitization of Rh D negative person transfused with weak D cells (or a hemolytic reaction, in case a person is already sensitized). Alloimmunization of females with weak-D during the child-bearing age may results in hemolytic disease of the newborn. This contention is however debated, as there are not enough cases recorded in literature to give conclusive evidence. Many transfusion centres have advocated dropping testing for weak D, but Ministry of Health and Family welfare, Government of India still recommends searching for weak D in Rh D negative persons. The current opinion of the majority, albeit debatable is that weak D persons should be termed as Rh D negative when they are recipients of blood and D positive when they are donating blood.

Due to the paucity of infrastructural support, genotype of the subjects could not be performed and that is the main limitation of the study. Though the low prevalence of weak D that has been found to be very low in our study (0.005%), it is a prudent strategy to routinely screen the donor for weak D, keeping in mind the theoretical risk of hemolysis. An elaborative study on the real chances of D negative persons forming an antibody when exposed to weak D blood has to be performed to further enhance our knowledge on the matter.

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