Introduction:

Clinical manifestation of haemolytic disease of newborn (HDN) range from asymptomatic mild anemia to hydrops fetalis or still birth[1]. Guidelines for blood grouping and red blood cell antibody testing during pregnancy has been well established in Caucasian Population[2]. Anti-D, anti-c and anti-Kell are the most alloantibodies often implicated in causing moderate to severe HDN in this group[3]. Introduction of anti-D immunoglobulins prophylaxis for potential sensitization episodes and routine antenatal anti-D prophylaxis has significantly reduced the anti-D alloimmunizaiton[4].

Racial differences in frequency of Rh-D negative blood is well known, for instance it is approximately 15-20% in whites, 5-10% in African American and less than 1% in Chinese[5]. The frequency of RhD negative-subject among pregnant women in Saudi Arabia has been reported 8-10% but the incidence of anti-D alloimmunization and clinical outcome of this patient group is lacking. Majority of the severe HDN cases referred to specialist fetal medicine units are associated with anti-D. At present there are no national guidelines on antenatal screening and anti-D Ig prophylaxis in Saudi Arabia. This has prompted us to conduct this retrospective review of HDN cases in our hospital.

Aim:

The aim of this study is to document the frequency and significance of anti-D alloantibodies detected during antenatal visit at King Abdulaziz University Hospital – Jeddah and to look at the current implemented guidelines. Recommendations for the prevention, identification and management of women and fetuses at risk of developing anti-D alloantibodies and associated HDN, will be addressed.

Materials and Methods:

The Blood Bank records from year January 2000 – December 2004 were reviewed retrospectively to identify all pregnant women found to have allo-antibodies and anti-D in their sera during antenatal visits. Clinical data were collected from antenatal and delivery records. Blood samples were collected from pregnant women during their first antenatal visit. All samples were tested for ABO and Rh blood groups. All samples were tested also for antibody screening (three-cell screening panel at 37oC by indirect antiglobulin test IAT (Diamed gel technique) and antibody identification (ten panel testing cells IAT), Diamed gel technique at 37oC. The results were documented in the patients' medical files and blood bank records.

Results:

Of the 20,743 pregnant women attended the antenatal clinic, about 366 (1.8%) had alloantibodies. Anti-D was found in 161 (44%) of the cases which accounts 0.8% of total pregnant ladies. Twenty eight (17.4%) of the cases with anti-D have also other alloantibodies in their sera, mostly anti-D+C. Majority of the women were Saudi 100 (62.1%). Most of our pregnant ladies with anti-D alloantibodies are multiparas 139 (86.3%). Seventeen (10.6%) of the women with anti-D alloantibodies in their sera gave a history of blood transfusion. Whereas only twenty two (13.7%) were primigravida. Characteristic features of the obstetric cases with anti-D are shown in ***Table-1***. Anti-D+C accounted for 21 of cases as it shown in ***Table-2.*** Twenty nine (18%) of the cases with anti-D had bad obstetric history. Five (17.2%) of them required intra-uterine transfusion, 11 (37.9%) ended up in intra-uterine fetal death, whereas 13 (44.8%) cases had babies with HDN. The details of the obstetric complications, neonatal outcome with the antibody specificities are summarized in *Table-3*.

Discussion:

Red cell alloimmunization cause important implications for blood transfusion practice and pregnancy outcome[6]. During pregnancy, maternal alloimmunization to Rh-D is a major factor in perinatal morbidity and may result in the compromise of the women's obstetric career[7]. In Saudi Arabia accurate population based studies to determine

Table1: Characteristics Featares of Obsterris Patients

Characteristic	Number	%
Race:		
Saudi	100	62.1
Non-Saudi	61	37.9
Parity:		
Primigravida	22	13.7
Multigravida	139	86.3
Transfusion history:		
Positive	17	10.6
Negative	144	89.4

Table2 : Anti-D and other alloantibodies

Alloantibodies	Number	%
Anti-D + C	21	75
Anti-D + E	4	14.3
Anti-D + C + Lea	1	3.6
Anti-D + fya + c + S	1	3.6
Anti-D + c	1	3.6
Total	28	100

Table3 : Obstetric and neonatal outcome in anti-D maternal allo-immunization.

Antibody specificities	Intra-uterine fetal death	Intra-uterine transfusion	HDN
Anti-D	10	2	6
Anti-D + C	1	2	7
Anti-D + C + Lea	-	1	-
Total	11 (37.9%)	5 (17.2%)	13 (44.8%)

the prevalence of Rh-D negative women and the incidence of alloimmunization are lacking, and the available studies describe the frequency of Rh-D negative blood group among obstetric patients which ranged between 8-10%[10-8].

During the 5-years period, from 2000 through 2004, 20,743 pregnant ladies were reviewed and 366 of them (1.8%) were found to possess irregular antibodies during their antenatal visits. The finding is higher than those in the Western and the Chinese population who reported a prevalence of irregular antibodies of 0.2% and 0.79% respectively[2,5,11].

In this hospital-based study, anti-D alloantibodies were identified in 161 (44%) out of the total alloimunized women (around 0.8% of total pregnancy). Transfusion history was obtained in 17 (10.6%) women which may explain the development of alloantibodies in few cases. Twenty-two (13.7%) were primigravida while the rest had two or more pregnancies. We are very much concerned about this high anti-D sensitization rate among the primigravida in our region. Prophylactic anti-D can suppress primary Rh-D immunization[12]. Introduction of routine post-partum anti-D immunoprophylaxis was introduced in the United Kingdom in 1969[13]. Prophylaxis was extended in the 1976 to include abortions and spontaneous miscarriages[14], and in 1981 to include a number of other potentially sensitizing events[15]. Studies have shown that this programme has significantly reduced the sensitization rate to 0.9% and 1.12% respectively[16,17]. Despite the success of the prophylactic anti-D program, a number of women 0.2-0.79% still become allo-immunized, for various reasons, including inefficient administration of anti-D immunoglobulin immunoprophylaxis, unrecognized abortion and leakage of fetal red blood cells into the mother's circulation during the third trimester[18,19]. In our study, out of the 22 primigravida women, only three (13.6%) gave history of miscarriages, the rest appear to have no identifiable risk events (silent sensitization)[13]. Administration of anti-D immunoprophylaxis was documented in 18 of them. Thirteen received single injection and anti-D dose was not recorded. This finding is not entirely surprising as there is no local guidelines regarding anti-D prophylaxis in our region. Introduction of routine antenatal anti-D prophylaxis further reduce the risk of immunization from 1.5% to 0.2%, without any adverse effects and it is estimated to reduce sensitization by a factor of 10[14].

In this study, we found that the anti-D alloantibody was a significant cause of fetal morbidity and mortality in 29 (18%). Intra-uterine fetal death was diagnosed in 11 (37.9%) of our patients and the reason was related directly to anti-D allo-antibodies as no other causes were found. Few of these cases presented late during pregnancy or at time of delivery. Intrauterine fetal blood transfusion was required in 5 patients (17.2%) for whom the fetal investigations and blood samples were compatible with intrauterine fetal haemolysis and anaemia, two of them had good outcome. Haemolytic disease of newborn, in form of neonatal jaundice and anaemia with positive laboratory tests of HDN, was found in 13 (44.8%).

These complications are mainly related to improper anti-D immunoglobulin prophylaxis doses and timing and also a direct influence of the lack of strict guidelines.
Our data demonstrated that red blood cell alloimmunization among women during antenatal care is commoner than those of the Chinese and Western population. We have documented that the HDN caused by anti-D antibodies was a significant cause of perinatal mortality and morbidity in our region. This serious outcome needs more care and attention from our health care authorities to introduce anti-D immunoprophylaxis programme in Saudi Arabia which should be followed strictly throughout the country.

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ANTI-D ALLOIMUNIZATION AMONG PREGNANT WOMEN AT KAUH JEDDAH, SAUDI ARABIA

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ABSTRACT:

Background: In the western population the incidence of clinically significant antibodies has been reported to 0.09-0.24% in pregnant women and anti-D alloantibodies remain a major cause of haemolytic disease of the fetus and newborn. However, use of anti-D immunoprophylaxis reduced significantly the incidence of this complication.

Aim: There is no data on prevalence, specificity and clinical outcome of clinically significant red cell alloantibodies in Saudi women during pregnancy.

The frequency of Rh-D negative subject among pregnant women in Saudi Arabia has been reported 8-10% but the incidence of anti-D alloimmunization and clinical outcome of this patient group is lacking.

This study was to document the frequency and clinical outcome of anti-D and to review the anti-D prophylaxis programme.

Study Design and Methods:

Retrospectively, we studied 20,743 pregnant ladies during their antenatal visits from January 2000 to December 2004 antibody screening and identification were done by using indirect antiglobulin (Diamed gel) techniques.

Result: Three hundred sixty six (1.8%) women were found to have irregular alloantibodies. Anti-D was found in 161 (44%) of the cases, most of them were multiparus 139 (86.3%). Twenty nine (18%) of pregnant ladies with anti-D alloantibodies had bad obstetric history. Five ladies (17.2%) required intrauterine blood transfusion, 11 (37.9%) ended up in intrauterine fetal death and 13 (44.8%) had babies with evidence of haemolytic disease of newborn.

Conclusion: The most common identified alloantibody in our pregnant ladies is anti-D. Therefore, development of national guidelines and proper implementation of it are highly recommended to decrease the magnitude of this problem.

Keywords: Alloantibodies, Pregnancy, Anti-D, Haemolytic Disease of Newborn, Guidelines.

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