

# Rhesus alloimmunization in pregnancy

## *A tertiary care center experience in the Western region of Saudi Arabia*

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### ABSTRACT

**الأهداف:** تحديد توزيع فصائل الدم والعامل الريصي لدى النساء الحوامل، وتقدير مدى انتشار الأجسام المضادة لهذا العامل (تطوير أجسام مضادة ضد أنواع معينة من المستضدات) ومن ثم دراسة نتائج الفترة المحيطة بالولادة لجميع الحالات التي عويئت في مستشفى الملك عبدالعزيز الجامعي.

**الطريقة:** لقد قمنا باسترجاع سجلات جميع الحوامل اللاتي ترددن على عيادات الحمل والولادة ووضعن في مستشفى جامعة الملك عبد العزيز، جدة، المملكة العربية السعودية وذلك خلال الفترة من يناير 2004م إلى ديسمبر 2009م. وتمت مراجعة سجلات المرضى اللاتي كانت فصيلة دمهن سالبة العامل الريصي واستعراضها فيما يتعلق بوجود الأجسام المضادة، ونسبة الأجسام المضادة، ومدى الزيادة في مستواها. ولقد قمنا أيضاً بتسجيل نتائج المرضى أثناء الحمل وبعد الولادة وحالة الأجنة.

**النتائج:** شملت الدراسة 24005 من النساء الحوامل، وكانت مجموعة الدم O الموجبة هي الأكثر شيوعاً وتلتها مجاميع الدم الموجبة A و B و AB على التوالي. وتم تسجيل فصيلة الدم موجبة العامل الريصي في 7.5% من الحوامل المشاركات في الدراسة. وبلغ عدد الحالات التي تحمل الأجسام المضادة 424 حالة ونسبة 1.8% من عدد الحالات المدرجة في الدراسة و23.6% بين النساء ذوات فصيلة الدم سالبة العامل الريصي. لقد كان معدل الوفيات في الفترة المحيطة بالولادة 250 لكل 1000 في النساء الحوامل للأجسام المضادة وذلك بالمقارنة مع 17 لكل 1000 في كافة المشاركات بالدراسة.

**خاتمة:** أظهرت هذه الدراسة بأن فصيلة الدم O الموجبة قد كانت من أكثر فصائل الدم انتشاراً بين النساء الحوامل اللاتي ترددن على عيادات الحمل والولادة في العينة التي شملتها الدراسة، وقد بلغت نسبة الحوامل اللاتي حملن فصيلة الدم سالبة العامل الريصي 7.5%. وبلغ معدل انتشار تكون الأجسام المضادة للعامل الريصي في مجتمع الدراسة عشرة أضعاف المعدل المسجل في البلدان المتقدمة التي تطبق برنامج الوقاية من هذا المرض.

**Objectives:** To determine the distribution of ABO blood group and rhesus (RH) factor among pregnant women, to estimate the prevalence of Rh

alloimmunization, and report the perinatal outcome of all cases of Rh alloimmunization at King Abdul-Aziz University Hospital (KAUH).

**Methods:** This is a retrospective study of pregnant women attending the antenatal clinics in KAUH, Jeddah, Saudi Arabia between January 2004 and December 2009. Records of patient diagnosed as Rh negative blood group were reviewed for the presence of antibodies, antibodies titer, and progress in the level of antibodies. Maternal and neonatal outcomes were reported.

**Results:** Twenty-four thousand and five pregnant women were included in this study. The most common blood group was O followed by A, B and AB positive. Rhesus negativity blood group was reported in 7.5%. Four hundred and twenty-four cases were reported as Rh antibody positive with a prevalence of alloimmunization of 1.8% in the studied population, and 23.6% among Rh negative women. The perinatal mortality rate was 250 per 1000 in alloimmunized women compared to 17 per 1000 in the study population.

**Conclusions:** Blood group O positive is the most prevalent blood group among pregnant women attending our antenatal clinics and the prevalence of Rh negativity was 7.5%. The prevalence of Rh alloimmunization in the present study was 10-folds higher than that reported in the developed countries. Rhesus alloimmunization represent an avoidable direct cause for perinatal morbidity and mortality in our population.

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The prevalence of rhesus (Rh) negativity in different populations varies by race and ethnicity. Approximately 15% of Caucasians are Rh negative, compared to 5-8% of African American and 1-2% of Asians and native American.<sup>1</sup> Local population based studies from Saudi Arabia on males and females volunteers showed that the prevalence of Rh negative blood group in the Eastern region of Saudi Arabia is 8% and in Southwest Saudi Arabia is 7.2%.<sup>2,3</sup> There is a major paucity in the literature regarding the estimated prevalence of Rh negativity among pregnant women in Saudi Arabia particularly in the western region. The recognition of the prevalence of Rh negativity will allow different health authorities to develop prevention programs for Rh alloimmunization on evidence based facts, thus one of the main objectives is to determine the prevalence of Rh negative blood group among pregnant women in the western region. Rhesus alloimmunization is a serious preventable disease that develops in Rh negative pregnant women and carries major impact in the prenatal outcome including major morbidity and mortality.<sup>4</sup> In recent years, major advances in the prevention and treatment of Rh alloimmunization have developed. The development and implementation of antenatal Rh (D) immune globulin prophylaxis in the 1960's led to a significant reduction in the frequency of maternal alloimmunization with anti-D antibodies.<sup>5,6</sup> The most important task in the management of this disease is the prevention through the introduction of nationwide prevention programs, such programs proved to be effective and successfully reduced the rate of antibodies development, hence reducing the rate of maternal sensitization in the developed countries.<sup>1</sup> Most of the local reports on the ABO and Rh blood grouping in pregnant women are lacking the determination of the prevalence and the perinatal outcome of Rh alloimmunization, on reviewing the medical literature through PubMed we could not identify any local study published in an indexed journal reporting the management and the outcome of Rh alloimmunization in Saudi Arabia, likewise the prevalence of Rh alloimmunization in the local area is not well documented. The current study was designed to estimate the prevalence of Rh alloimmunization in a local population and evaluate the perinatal outcome of patients with Rh alloimmunization to determine the need for prevention program.

**Methods.** All pregnant women attending the antenatal clinics at King Abdul-Aziz University

Hospital, Jeddah, Saudi Arabia between January 2004 and December 2009 were tested for the blood group and Rh factor in their first visit as part of their antenatal care. Samples were tested for ABO and Rh blood groups and antibody screening (3-cell screening panel at 37°C by indirect antiglobulin test (IAT) (Diamed Gel Technique, Cressier, Switzerland) and antibody identification (ten panel testing cells IAT), Diamed gel technique at 37°C.

The study group included all women followed in the antenatal clinics and gave birth in King Abdul-Aziz University Hospital, and women who delivered in another institution were excluded. Data were collected based on the blood group and the Rh factor positivity and negativity to determine the frequency of blood groups (ABO) and estimate the prevalence of Rh negative blood group in our population. Out of all pregnant women tested for Rh factor, patients who showed Rh negative results were further screened for the presence of anti D, E, e, C, and c antibodies. Women who are tested positive for anti D antibodies had Anti D antibodies titer performed by testing serial dilutions of the serum against selected cell from Diamed. The result was expressed as the reciprocal of the highest serum dilution that causes macroscopically apparent agglutination. Anti-D antibodies titer of 1:16 is considered as the critical level for invasive testing including cordocentesis with possibility of intrauterine intravascular blood transfusion.

All Rh negative patients who had positive antibodies were divided into 2 groups. Group I (high risk patients) and group II (low risk patients) based on their past obstetrical history and their antibodies titer. The low risk patients group II were followed up by their primary physician with repeated antibodies titer in 2-4 weeks until delivery or any change in the antibodies level, patient then will be referred to the Feto-Maternal Medicine Unit for further management. The high risk patients (group I) are directly referred to the fetal medicine unit and managed according to a standardized protocol related to their clinical and laboratory tests findings. The Feto-Maternal Medicine at King Abdul-Aziz University Hospital was established 1992 and is operated by board certified specialist in Feto-Maternal Medicine. The unit deals with high risk pregnancy including maternal and fetal disease.

High risk patients were managed utilizing invasive fetal testing including amniocentesis and cordocentesis before 2007, cases after 2007 were followed up by Middle Cerebral Artery Doppler (MCA) after its introduction to the unit and becoming a standard of practice in managing such cases. The ultimate treatment by fetal intrauterine intravascular blood transfusion or delivery was carried out based on the results of the tests, ultrasound

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findings, and the fetal gestational age. Medical record of all cases tested positive for Rh antibodies were reviewed, and data collected regarding the gravidity, parity past obstetrical history, blood transfusion, antibodies titter, and progress in the antibodies titter level.

In high risks patients (Group I) the perinatal outcome of the pregnancy was reported including the need for intervention in utero (intrauterine intravascular fetal blood transfusion), mode of delivery, gestational age, birth weight, and intrapartum complication. The neonatal outcome is also reported including exchange transfusion, simple blood transfusion, neonatal jaundice, NICU admission, and Apgar score. The perinatal outcome of the alloimmunized women was compared to the perinatal outcome of the studied population and the statistical differences were calculated and reported.

The study was approved by the Research Committee, Faculty of Medicine, King Abdul-Aziz University, after fulfilling the criteria of medical research involving human subject based on good practice guidelines.

Data were collected using the statistical analysis SPSS Version 16. The statistical analysis was performed using Chi-square tests, and a *p* value of less than 0.05 was considered significant.

**Results.** During the study period, 24005 pregnant women were included in the study. Of these, 22210 (92.5%) women had Rh positive blood group and 1795 (7.5%) had Rh negative. The most common ABO blood group encountered was O followed by blood group A, B and AB. The distribution pattern of ABO blood groups and their respected Rh in our population is shown in Table 1.

Out of the 1795 Rh negative women, 424 were Rh antibodies positive with a detection rate of Rh antibodies of 23.6% (424/1795) among Rh negative women. On the other hand, the detection rate among

all women delivered at KAUH during the same study period was 1.8% (424/24005). Of the 424 cases with positive red blood cells antibodies, the Rh antibody pattern was as follows: 3 cases of c antibodies, one case of C antibodies, 2 cases with e, no case reported with E, 2 cases with anti D combined with c, and one case of combined anti D and anti e. All the remaining cases had only anti D antibodies detected.

Reviewing the past medical history of the 424 antibodies positive cases, we found that the vast majority of cases were multiparous women (92.6%) and only 8.4% were primigravidas. Nineteen patients out of the 424 (4.5%) reported history of blood transfusion, one patient had previous ectopic pregnancy, and 170 (40%) had history of previous miscarriage.

Analysis of the data obtained from the medical record of the 424 patients with positive antibodies showed that 91 patients (21.5%) had a significant level of antibody titter (>1:16) and managed as high risk patients (Group I). The remaining 333 patients had antibodies titter below the critical level (low risk patients Group II). Out of the 333 cases, 215 (50.7%) were followed up with repeated titer and no significant change in their titer level was observed, 70 women (16.5%) had no repeated follow up antibodies testing and 48 women (11.3%) had lost their follow up.

Pregnant women with significant Rh alloimmunization (Group I) were followed up in the Fetal Medicine Unit with routine ultrasound, amniocentesis for bilirubin level before the year 2007 and repeated regular Middle Cerebral Artery Doppler testing the years after. Of the 91 cases with positive antibodies, 7 were lost to follow up in our unit; therefore, they were excluded from further analysis. In the remaining 84 cases, 10 fetuses presented with advanced immune hydrops fetalis with positive cardiac pulsation, 6 cases presented with intrauterine fetal death secondary to severe Rh alloimmunization, 5 fetuses had intrauterine intravascular blood transfusion because of either poor past obstetric history or abnormal fetal testing results, and the remaining cases had close follow up in the Fetal-Medicine Unit. The perinatal outcome in group I was as follows: out of the 10 fetuses with advanced immune hydrops fetalis and positive cardiac pulsation, 8 had intrauterine fetal death before intervention, 2 had intrauterine fetal blood transfusion of which one ended with fetal death 12 hours after the procedure while the other one was delivered prematurely and ended with early neonatal death. In fetuses that had intrauterine blood transfusion, 3 survived and needed neonatal exchange transfusion, the other 2 were hydropic and ended with intrauterine fetal death and neonatal death.

The number of perinatal deaths among all women delivered at KAUH during the study period

**Table 1** - Distribution of different blood groups and rhesus status at King Abdul-Aziz University Hospital for the years 2004-2009 (N=24,005).

Blood groups	n	(%)
O Positive	10698	(44.6)
O Negative	838	(3.5)
<b>Total</b>	<b>11536</b>	<b>(48.1)</b>
A Positive	6744	(28.0)
A Negative	536	(2.1)
<b>Total</b>	<b>7280</b>	<b>(30.1)</b>
B Positive	3745	(15.6)
B Negative	326	(1.5)
<b>Total</b>	<b>4071</b>	<b>(17.1)</b>
AB Positive	1023	(4.3)
AB Negative	95	(0.4)
<b>Total</b>	<b>1118</b>	<b>(4.7)</b>

was 408 with a perinatal mortality rate of 17 per thousand (408/24005). The perinatal deaths in the 84 alloimmunized women were as follows: 16 cases of intrauterine fetal deaths and 5 early neonatal deaths giving a perinatal mortality rate of 250 per thousand (21/84). This difference in the perinatal mortality rate among the 2 groups is statistically significant ( $p=0.003$ ) (Table 2). Cesarean section rate was 36%; nevertheless, further analysis showed that most of the cases were carried out for repeat cesarean and malpresentation; when these cases were excluded for the above mentioned indications the cesarean section rate was not different from the studied population. Nineteen women delivered prematurely giving an incidence of 22.6% for preterm delivery, while the incidence of preterm delivery in women delivered at KAUH in the same period of time was 6.7%, the calculated difference was statistically significant ( $p=0.01$ ) (Table 2).

The neonatal birth weight ranged between 850 grams to 3600 grams, the average weight was 1600 g  $\pm$  945 g. The birth weight was significantly lower in the study group compared to the average birth weight in the study population with a  $p$  value of 0.01 Table 2.

Reviewing the neonatal outcome revealed that 51 (60.1%) out of the 84 patients in group I needed NICU admission, 19 (22.6%) newborns delivered prematurely, 5 (6%) newborns had early neonatal death, 11 (13%) needed neonatal blood exchange transfusion, 17 (20%) had simple blood transfusion, 43 (51%) newborns had phototherapy to treat significant jaundice, 56 (66%) had low 5 minutes Apgar score, and 35 had no intervention. Note that most of the newborns' had more than one complication (Table 3). Comparing the above mentioned figures with the rest of the 24,005 women delivered at KAUH during the study period revealed statistically significant difference in the rate of NICU admission, neonatal jaundice, and low Apgar score (Table 2).

**Discussion.** The nomenclature for designating human blood type is the ABO type with Rh (D) positive or Rh (D) negative subtypes depending on the presence or absence of the Rh (D) antigen on their RBCs. However, this nomenclature is not technically correct because the Rh blood system consists of the C, c, D, E, and e antigens (there is no d antigen). Maternal alloimmunization is by far the most common cause of erythroblastosis fetalis and hemolytic disease of the newborn.<sup>7</sup> Determining the prevalence of Rh negativity among pregnant women is an essential step in recognizing the magnitude of Rh alloimmunization complications in pregnant women; hence, the development of screening, preventive, and management programs nationwide based on the calculated prevalence and the complications rate. The prevalence of Rh negative blood group among pregnant women in Saudi Arabia was reported in limited number of series from different regions except the western region where the current study is conducted. Published reports from the central region of Saudi Arabia on the frequency of ABO and Rh phenotypes showed that the

**Table 3** -The neonatal complication among rhesus alloimmunized pregnancies.

Neonatal complications	Number of cases (%)	
Exchange transfusion	11	(13.0)
Simple transfusion	17	(20.0)
Neonatal death	5	(6.0)
Jaundiced needed phototherapy	43	(51.0)
Five minute APGAR score <5	56	(66.0)
NICU admission cases	51	(61.0)
Preterm delivery	19	(22.6)
NICU - neonatal intensive care unit		

**Table 2** - The perinatal outcome of rhesus alloimmunized pregnant women compared to none immunized at King Abdul-Aziz University Hospital (KAUH).

Variable	Patients with significant alloimmunization (n=84 cases)	All pregnant women delivered at KAUH 2004-2009 (24005)	P-value	Statistical significance
PNR	250:1000	17:1000	0.003	Significant
CS rate	36% corrected 20%	19%	0.2	Non-significant
Preterm delivery	22.6%	6.7%	0.01	Significant
Average birth weight	1600 grams $\pm$ 2SD	2900 grams $\pm$ 2SD	0.03	Significant
NICU admission	60.7%	3.1%	0.001	Significant
Phototherapy for NN jaundice	51%	2.0%	0.004	Significant
Neonatal blood transfusion	33%	1.1%	0.0002	Significant
APGAR Score in 5 minute less than 5	66%	3.0%	0.002	Significant
PNR - perinatal mortality rate, CS - cesarian section, NICU - neonatal intensive care unit, NN - neonatal				

highest frequency was that of blood group O followed by A, B and AB blood group subsequently.<sup>8,9</sup> Similar results were reported from other parts of Saudi Arabia including Tabuk, Madina Munawwara and Eastern Province of Saudi Arabia<sup>10,11</sup> indicating that blood group O is the most prevalent and AB is the least frequent blood group among pregnant women in these parts of Saudi Arabia. The current study is describing the pattern of distribution of ABO blood groups among pregnant women in the western region of Saudi Arabia and confirming the findings of other regions with blood group O being the most frequent blood group (48%) followed by A (30.1%), B (17.1%), and AB (4.7%) in decreasing order of frequency. The sample size in the current study is different from the previously published reports being the largest among all the studies performed to determine the ABO blood group and the Rh status in pregnant women in Saudi Arabia with a total number of 24,005 cases. The prevalence of Rh positive blood group was 92.5% and the Rh negative was 7.5% in pregnant women delivered at KAUH in the western part of Saudi Arabia. These findings are in concordance with what was reported in the Central region by Talib et al,<sup>8</sup> where Rh positivity was 91.5% and Rh negativity was 8.5%, and marginally different from that reported by Al-Ibrahim and AlSaeed<sup>9</sup> with a prevalence of 85.9% for Rh positive women and 14.1% Rh negative. The prevalence of Rh negative blood group in Madina Munawwara was 11% and in Tabuk was 8%,<sup>10</sup> these findings are similar to the current study.

In the Eastern region, the prevalence of Rh negative pregnant women was noticeably lower than what was reported from the other regions being only 1.9%,<sup>11</sup> the low prevalence of Rh negative pregnant women in the Eastern region needs further studies to explain the reasons for this low prevalence compared to what was reported in the rest of Saudi Arabia. Table 4 shows the distribution pattern of ABO blood group and

indicating the low prevalence of Rh negative pregnant women in the eastern part of Saudi Arabia. The rate of allimmunization in Rh negative women was estimated to be 16% after 2 deliveries of Rh positive and ABO compatible neonates in the era before anti-D immunoglobulin was introduced to the clinical practice.<sup>12</sup> There was a dramatic reduction in the rate to 2% with routine postpartum administration of a single dose of anti-D immune globulin and further reduction to as low as 0.1% with the addition of routine antenatal administration in the third trimester.<sup>13</sup> However, Rh (D) alloimmunization has not been completely eliminated particularly in the developing countries. The recognized causes for continued emergence of sensitized pregnancies include both failure to administer anti-D immune globulin in accordance with published guidelines and sensitization in early gestation before routine third trimester antenatal anti-D prophylaxis.<sup>14,15</sup> The development of screening and prevention program may reduce the rate of alloimmunization by a 90% as reported by Freda et al.<sup>16</sup> The implementation of Rh prevention programs in the developed countries was based on understanding the estimated risks of Rh alloimmunization by determining the prevalence of sensitization among pregnant women in their local population. Unfortunately, there is a major deficiency in our knowledge regarding the rate of alloimmunization in our local pregnant population, only one study from the central province of Saudi Arabia reported an incidence of 1.84% for maternal alloimmunization during pregnancy.<sup>9</sup>

In the current study, 424 patients were tested positive for antibodies during pregnancy with alloimmunization rate of 1.8% of the total number of deliveries during the study period, and 23.6% of women with Rh negative blood group indicating that one in every 5 women with Rh negative is sensitized. This figure alertly exceeds the reported figures in the developed countries who applied the Rh prevention programs by 18-folds being 1.8% in our population compared to 0.1-0.4% in the developed countries.<sup>14,17,18</sup> However, further studies are needed from different regions of Saudi Arabia to confirm this findings. The development and implementation of Rh alloimmunization prevention program nationwide will reduce the prevalence of such preventable disease. The prevention program should be supported by organized nationwide screening program, utilizing anti-D immunoglobulin in the appropriate time and dosages as described in the literature. Informative national data base on Rh negative pregnant women is an important applicable tool in implementing of such programs and has to be developed hand in hand with the prevention and screening programs. Traditionally, the literature describe the outcome among Rh D-alloimmunized pregnancies

**Table 4 -** Prevalence of rhesus (Rh) negative and sensitization rates among pregnant women reported in different regions of Saudi Arabia.

Study	Place	Number of patients	Rh positive n (%)	Rh negative n (%)
Current study	Western region	24005	22210 (92.5)	1795 (7.5)
Talib et al <sup>8</sup>	Central region	859	786 (91.5)	73 (8.5)
Al-Ibrahim and AlSaeed <sup>9</sup>	Central region	1195	1026 (85.9)	169 (14.1)
Ozoylu and Alhejaily <sup>10</sup>	Tabook and Madinah	166	153 (90.0)	13 (10)
AlSaeed et al <sup>11</sup>	Eastern region	567	556 (98.1)	11 (1.9)



to the following categories, mild to moderate hemolytic anemia, and hyperbilirubinemia occurs in 25-30% and hydrops fetalis occurs in 25%.<sup>19</sup> The current study showed the same findings with an incidence of hydrops fetalis of 19% and mild to moderate anemia in 50% of the cases, the remaining 31% had no major effect of the disease. The current study shows a significant increase in the perinatal mortality and morbidity in alloimmunized patients, the perinatal mortality was 250 per 1000 among the alloimmunized women compared to 17 per 1000 among all women who delivered at KAUH at the same period of time. This increase in the perinatal mortality can be explained by the lack of organized screening and prevention programs in addition to the late reporting of the patients to specialized centers with facilities to perform intrauterine intravascular blood transfusion. Reports from other countries showed high perinatal mortality among alloimmunized pregnant women. In a study by Nardoza et al<sup>20</sup> from Brazil they reported the outcome of 291 consecutive Rh-negative pregnancies, the perinatal mortality was significantly higher in the 99 Rh-negative alloimmunized patients than in the 192 unimmunized patients 12.1% versus 1% ( $p=0.0001$ ). Matijevic et al<sup>21</sup> from Croatia reported a perinatal mortality of 13%. In 23 patients with Rh alloimmunization, they concluded that despite the precise diagnostic criteria and modern therapeutic options, alloimmunization remains a problem and still associated with a high perinatal mortality and morbidity, these reports confirms our findings of high perinatal mortality rate among Rh alloimmunized patients. The rate of prematurity was significantly higher among the alloimmunized mother; this high rate of preterm delivery may be explained by iatrogenic deliveries for fetal indications. The neonatal outcome in this series was also poor with the high neonatal deaths, high rate of NICU admission, excessive demands for blood transfusion, low Apgar score and high incidence of neonatal jaundice (Table 3). The difference between the reported neonatal outcome for the alloimmunized women and the outcome among all women delivered in the same institution at the same period of time was statistically significant, Table 2.

Gobalakichenane et al<sup>22</sup> from France reported 42 cases of Rh alloimmunization in 6 years,<sup>28</sup> newborns (67%) were admitted for NICU, 16/28 (57%) were preterm, 6 fetuses received intrauterine intravascular blood transfusion, 22 did not receive intrauterine fetal blood transfusion of those 6/22 (27%) had neonatal exchange blood transfusion and 18/22 (82%) of them received 1-4 blood transfusions. Three perinatal deaths were reported, one due to necrotizing enterocolitis and the other 2 due to sudden infant death and fulminant meningococemia. There was no direct mortality related to Rh alloimmunization and no cases of hydrops fetalis.

The neonatal morbidity reported in Gobalakichenane et al study is comparable to the morbidity in our study, but the mortality rate related to Rh disease is remarkably higher in our series, this is most probably explained by the late referral of our cases to specialized centers, either because of the under estimation of the risks encountered with such disease or patients were overlooked by the primary care giver. There is no local experience to compare our results with as the literature is lacking the description of local experience in such an important fetal and neonatal disease. Further studies are needed to explore the experience and the outcome of Rh alloimmunization in different regions of Saudi Arabia.

Our data also showed that 70 patients (16.5%) had no repeated antibodies titer despite the fact that they showed positive antibodies testing, in addition 48 patients (11.3%) had lost the follow up. These obstacles can be improved by designated part of the prevention programs for patients counseling regarding their clinical problem and the introduction of clinical protocols for screening and prevention of Rh alloimmunization to all care giver in the field of Obstetrics & Gynecology and Family Medicine particularly the junior staff including interns and residents.<sup>23</sup> In a Dutch case control study of 42 Rh alloimmunized women Koelewijn et al<sup>24</sup> concluded that Rh alloimmunisation may be further reduced by strict compliance to guidelines which support the above mentioned recommendations.

There are some limitations to this study. For example, small number of patients who actually received the appropriate care in the appropriate time, the high number of patients who lost the follow up, and lastly that this is a retrospective study, which can be improved by developing a nationwide registry that follow the patients prospectively in order to obtain a stronger conclusions.

In conclusions, blood group O is the most common blood group in the studied population followed by A, B and AB subsequently. The Rh negative blood group is 7.5% among pregnant women in the western region of Saudi Arabia. The prevalence of Rh alloimmunization in the present study is ten times higher than figures reported in many developed countries that adopted and implemented Rh prevention programs Rh alloimmunization in pregnancy still represent an avoidable direct cause of high perinatal morbidity and mortality in the developing countries. The development of a nationwide program is the best strategy in the management of such perinatal disease.

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