

# Comparison of Hemoglobin and Hematocrit Concentration between Rh- Hydropic, Non-Hydropic and Control Group; Severe Vs Mild Hydropic Group

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## Abstract

**Introduction:** Maternal RBC alloimmunization results from exposure and response to a foreign RBC antigen. Transplacental fetal to maternal hemorrhage is the most common cause of alloimmunization. Rh incompatibility can lead to either fetuses with hydropic features or non hydropic. The precise mechanism leading to the development of hydrops is not certain. All direct fetal sequelae of hemolytic disease relate to the development of anemia. In general, the fetus tolerates mild to moderate anemia well. However, metabolic complications develop as the anemia worsens. Because the RBC is the principal fetal buffer, a metabolic acidemia with hyperlactatemia develops in fetuses with severe anemia.

**Objective:** To compare the difference in mean hemoglobin and hematocrit concentration between Rh-hydropic, non hydropic and control group and further based on severity of hydrops. **Methods:** A Total of 40 pregnant patients were enrolled which included 10 hydropic fetuses of Rh isoimmunised mothers, 10 non hydropic fetuses of Rh isoimmunized mothers. Control group included 18 Rh positive women without any fetal complication and 2 fetuses in women undergoing cordocentesis. Blood sampling was done at time of intrauterine transfusion and sent for estimation of hemoglobin and hematocrit in fetal blood. Pregnancies were followed up till delivery and fetal outcome noted. **Result:** Mean values of haemoglobin in hydrops group are 4.54g %, as compared to 6.65g % and 14.26 g % in non-hydrops and control group. Mean haematocrit in hydropic group is 13.91% as compared to 20.25% and 43.51% in non hydropic and control group. The mean haemoglobin concentration in mild hydrops was 5.17g % as compared to 2.7g % in severe hydrops. **Conclusion:** There was severe hemoglobin and hematocrit deficit in hydropic fetuses as compared to non hydropic and normal fetuses matched for the gestation age. Thus severity of anemia can be considered a strong marker for development of hydrops in Rh isoimmunized fetuses.

**Keywords:** Hemoglobin Hematocrit Mild Hydropic Group isoimmunized.

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## INTRODUCTION

Rh incompatibility refers to a condition developing in an Rh negative mother carrying an Rh positive fetus, due to maternal anti Rh antibodies; resulting in serious, sometimes life-threatening condition in the fetus- anemia, jaundice, leading to kernicterus and even death. Rh sensitization occurs in approximately 1 per 1000 births to women who are Rh negative [1]. Levine and coworkers identified that the rhesus (Rh) antibodies on the RBCs of affected but not unaffected neonates was the cause of the anemia [2]. In 1961, hemolytic anemia became the first treatable fetal disease after Sir William Liley characterized its natural

history and then successfully transfused affected fetuses intraperitoneally with adult RBCs [3]. The incidence of Rh-negative individuals varies by race [4]. The vast majority (85%) of individuals are considered Rh positive. Rh sensitization occurs in approximately 1 per 1000 births to women who are Rh negative [5].

All direct fetal sequelae of hemolytic disease relate to the development of anemia. However, metabolic complications develop as the anemia worsens [6]. Presently ultrasound is the only tool being used for finding the severity of hydrops and cardiac failure [7]. If MCA PSV value is >1.55 MoM intrauterine

transfusion is done, also intrauterine transfusion is done in a hydropic fetus at the time of detection [8].

All direct fetal sequelae of hemolytic disease relate to the development of anemia [9]. The present study has therefore been planned to find the hemoglobin and hematocrit deficit based on severity of Rh-isoimmunization.

## MATERIALS AND METHODS

### Study population

This prospective study was conducted in the Department of Obstetrics and Gynecology at AIIMS, DELHI from June 2014 to July 2016. Exclusion criteria were. Multiple pregnancy, patients with medical disorders, fetuses in whom cordocentesis for genetic indication detected chromosomal anomaly. Ethical Clearance was obtained from the institutional ethical committee. Informed written Consent was taken from the women.

### Examination and procedure

Rh isoimmunized patients whose MCA PSV values were  $>1.5$  MoM were given intrauterine transfusion of doubly irradiated and centrifuged blood. They were followed up by ultrasound and MCA-PSV, and subsequent intrauterine transfusions performed when indicated as per Institute protocol of management of Rh-isoimmunised pregnancies. Severity of hydrops was quantitated based on Ascitic rim measured at level of hepatic vein in transverse view into 4-6 mm (mild) and  $\geq 6$  mm (severe).

## STATISTICAL ANALYSIS

The data were entered in Microsoft Excel spread sheet and analysed using statistical product service solutions (SPSS) software IBM version 19.0. Mean values compared using analysis of variance (ANOVA). Frequency distributions were compared using Chi-square/Fisher's exact test as appropriate. A probability value of p value of  $<0.05$  was considered for statistical significance.

## RESULTS

A total of forty pregnant women attending the outpatient department of department of Obstetrics and Gynaecology, All India Institute of Medical Sciences (AIIMS) New Delhi, were enrolled in the study it included 10 hydropic fetuses of Rh isoimmunised mothers, 10 non hydropic fetuses of Rh isoimmunized mothers, Control group included 18 Rh positive women without any fetal complication or anomaly who came with preterm labor and delivered, and 2 fetuses in women undergoing cordocentesis for genetic indication at 23 and 26 weeks period of gestation but were normal.

The mean age group of the patients was 29.60 years and was similar in non hydropic, hydropic group and in control Group. There was significant difference

between hydrops, non-hydrops and control groups with respect to parity. All the patients in hydropic and non hydropic group were multigravida. mean gestation age was 26.01 weeks (SD 3.59, range 21.2-32.4) in hydropic group as compared to 28.3 weeks (SD3.6,range 23.7-34.8) in non hydropic and 31.7 weeks (SD 3.2,range 23.8-36.5) in control group and was comparable.

There were 2 with fetal ascitic rim more than 6 mm (severe hydrops), whereas 8 patients had fetal ascitic rim between 4-6 mm (mild hydrops).number of patient based on severity of hydrops in table 1.

Mean total number of IUTs received by hydrops and non-hydrops was 4.90 and 3.20 respectively. P value was significant ( $p=0.024$ )

Mean values of haemoglobin in hydrops group are 4.54g %, as compared to 6.65g % and 14.26 g % in non-hydrops and control group. p value was significant  $<0.01$ . Mean hemoglobin and hematocrit concentration in cord blood at first intrauterine transfusion in relation to presence/absence of fetal hydrops given in table 2.

Mean haematocrit in hydropic group is 13.91% as compared to 20.25% and 43.51% in non hydropic and control group. Hemoglobin and hematocrit concentration in cord blood at first intrauterine transfusion in relation to period of gestation and presence/absence of fetal hydrops in table 3 and table 4. Severity of hydrops was quantitated based on ascitic rim into 4-6 mm (mild) and  $\geq 6$  mm(severe). The mean haemoglobin concentration in mild hydrops was 5.17g % as compared to 2.7g % in severe hydrops. p value was significant  $<0.01$ .

The mean haematocrit concentration in mild hydrops was 15.37 % as compared to 7.6 % in severe hydrops. There was significant difference in mean haemoglobin and haematocrit concentration between two groups. P value was significant  $<0.01$ . Mean hemoglobin and hematocrit in cord blood sampling at first intrauterine transfusion in relation to severity of fetal hydrops in table 5. In the present study 90% of non hydropic fetuses delivered after 34 weeks POG whereas 30 % and 50% of control and hydropic fetuses delivered after 34 weeks POG. It was statistically significant.

In the present study in control group 14 women in preterm labor delivered vaginally as compared to 2/10 in hydropic and 3/10 in non hydropic group. 6 in control group underwent caesarean section for maternal/ fetal indication most common being fetal distress. 8/10 in hydropic group and 7/10 in non hydropic group underwent cesarean section, most common indication being fetal anemia with poor biophysical profile. 3/10 in non hydropic group, 1/10 in hydropic group delivered after 36 weeks POG.

There was no significant difference in mean cord blood PCV between hydropic and non hydropic group according to period of gestation at delivery. Mean cord blood PCV in hydropic group was 42.75 % as compared to 50% in non hydropic group.

One case with severe hydrops died in utero 2 days after IUT. All the fetuses in non hydropic group had favourable outcome

**Table-1: Number of patients according to severity of hydrops**

Ascitic rim (mm) at time of first IUT	Number of fetuses
4 -6 (mild hydrops)	8
≥6 (severe hydrops)	2

**Table-2: Mean hemoglobin and hematocrit concentration in cord blood at first intrauterine transfusion in relation to presence/absence of fetal hydrops**

Mean (SD)	Hydrops (n=10)	Non hydrops (n=10)	Controls (n=20)
Hb (g/dl)	4.54 (1.24)	6.65 (1.47)	14.26 (1.26)
Hct (%)	13.91 (3.58)	20.25 (4.50)	43.51 (3.98)

**Table-3: Hemoglobin concentration in cord blood at first intrauterine transfusion in relation to period of gestation and presence/absence of fetal hydrops**

Period of gestation (weeks)	Hydrops Mean hb (SD) (g/dl)	Non hydrops Mean hb (SD) (g/dl)	Control Mean hb (SD) (g/dl)	P value
20-26WK	4.81(1.23)	5.90(1.25)	16.40	<0.01
26 <sup>+1</sup> -32WK	3.90(1.25)	6.76(1.56)	14.68(0.99)	<0.01
32 <sup>+1</sup> -38WK	5.80	8.20	13.66(1.18)	<0.01

**Table-4: Hematocrit in cord blood sampling at first intrauterine transfusion in relation to period of gestation and presence/ absence of fetal hydrops**

Period of gestation (weeks)	Hydrops Mean hct (SD) (%)	Non hydrops Mean hct (SD) (%)	Control Mean hct (SD) (%)	P value
20-26WK	14.38(3.87)	17.53(3.25)	49.20	< 0.01
26 <sup>+1</sup> -32WK	11.93(2.99)	20.85(4.83)	44.33(3.22)	<0.01
32 <sup>+1</sup> -38WK	17.0	24.80	42.20(4.24)	<0.01

**Table-5: Mean hemoglobin and hematocrit in cord blood sampling at first intrauterine transfusion in relation to severity of fetal hydrops**

Ascitic rim (MM)	Hb (g/dl) Mean (SD)	Hct (%) Mean (SD)	P value
4-6 (n=8)	5.12 (1.20)	15.37 (3.42)	
≥6 (n=2)	2.7 (0.98)	7.6 (2.64)	P <0.05 sig

## DISCUSSION

Rh incompatibility is a condition developing in a Rh negative mother carrying a Rh positive fetus due to maternal anti Rh antibodies resulting in a serious, sometimes life-threatening reaction in the fetus. Current concepts on the pathophysiology of hydrops in fetal anemia include myocardial failure, high output cardiac failure, reduced plasma colloid oncotic pressure, increased capillary permeability and obstruction of venous and lymphatic flow [10]. Very often hydrops fetalis resolve after varying range of time or even remain unresolved [11].

There remains lacunae and need for knowing biochemical abnormalities in relation to severity of anemia leading to cardiac failure and late or non-

resolution of hydrops. Comparing the difference in hemoglobin and hematocrit will help in predicting the development of hydrops/prognosis of hydrops/resolution of hydrops, or even change in fetal therapy

The present study attempted to investigate the deficit in hemoglobin and hematocrit concentration in Rh isoimmunized fetus and based on severity of hydrops.

In a study by Nicolaidis KH *et al.* the haemoglobin was measured in fetal blood from 154 red cell isoimmunised pregnancies from 17 to 36 weeks' gestation. In 48 fetuses with ultrasound features of hydrops the haemoglobin was 7-10 g/dl below the

normal mean for gestation. Into mild (haemoglobin deficit less than 2 g/dl), moderate (deficit 2-7 g/dl), and severe (deficit greater than 7 g/dl)[12].

In another study done by Warenski JC *et al.* all fetuses with sonographic evidence of hydrops had hemoglobin of 3.8 gm/dl or less, whereas all but one of those without hydrops had a haemoglobin greater than 4.0 gm/dl[13].

Strength of our study was that we categorized severity of hydrops based on ascitic rim and compared the difference in hemoglobin and hematocrit concentration between these two groups. We found a significant difference in hemoglobin and hematocrit concentration between the Rh isoimmunized and hydrops group and the difference was significant even between mild and severe hydrops. Limitation of our study was small sample size.

## CONCLUSION

This study is one of the few studies which compared the hemoglobin and hematocrit concentration between Rh isoimmunized non hydropic and hydropic group when compared with controls. There was significant difference between mild and severe hydrops. There was severe hemoglobin and hematocrit deficit in hydropic fetuses as compared to non hydropic and normal fetuses matched for the gestation age.

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