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### Original Article

## ABO blood group - a risk factor for pregnancy induced hypertension

Rwitusmita Bharali

Wasima Jahan, Horshajyoti Chutia, Pranjal Bhuyan, Department of Physiology, Assam medical college, Dibrugarh-786002

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#### ABSTRACT

Hypertension is one of the most common medical problem encountered in pregnancy and is a major cause of maternal, fetal and neonatal morbidity and mortality in both developing and developed countries. Pregnancy induced hypertension (PIH) complicates approximately 15% of all pregnancies. In India, its incidence ranges from 5–15 % (In primiparous- 16% and in multiparous- 7%). The exact cause of PIH is not known and is thought to be multifactorial. Since ABO blood groups are known to be associated with various pathological conditions, so the present study was undertaken to assess any association between ABO blood group with PIH. 1000 cases of PIH and 1000 primi women with normal blood-pressure were included in the study. PIH cases were divided into four groups depending on their severity of PIH. Using blood group O as a reference, odds ratios was calculated and the association of different groups of ABO blood group in the categories of PIH were assessed. Compared with blood group O, all non-O blood groups had modest but statistically significant higher odds of pre-eclampsia. Blood group AB had the highest risk for PIH (OR =21.132, 95% CI-15.344-29.105). The association of blood group AB was also higher than all blood groups in all categories of PIH. The present study suggests that AB blood group is a risk factor for PIH

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### 1. Introduction

Approximately 800 women die from pregnancy or childbirth-related complications around the world every day<sup>1</sup>. More women die due to pregnancy-related causes in India than anywhere else in the world. In India, roughly one maternal death occurs every five minutes.<sup>2</sup> According to the government, these deaths account for 15% of all deaths of women of reproductive age.<sup>3</sup> The most common direct medical causes of maternal death around the world are haemorrhage, obstructed labour, infection (sepsis) and hypertensive disorders related to pregnancy, such as eclampsia.<sup>4</sup> Preeclampsia complications do arise in about 3 % of pregnancies, and all hypertensive disorders affect about 5–10 % of pregnancies.<sup>5</sup>

Globally, preeclampsia and eclampsia account for 10–15 % of maternal deaths. A majority of deaths in developing countries result from eclampsia, while in developed countries, complications of preeclampsia are more often the cause.<sup>6</sup> PIH is a multisystem disorder of unknown etiology.

ABO blood-group antigens are oligosaccharides conjugated to cell-surface glycoproteins and glycolipids or secreted into body fluids by "secretor" individuals<sup>7</sup>. ABO antigens may alter the presentation of cell-surface glycans and modulate their interactions with pathogens<sup>8</sup> or may provide receptors for pathogen attachment, hence ABO antigen is associated with various diseases. ABO antigens may play a major role in the interaction of the immune and coagulation systems by influencing gene-environment interactions. As the current view on preeclampsia suggests that it has a exaggerated maternal systemic immune response component and characteristic changes in coagulation systems, differences in ABO blood groups may increase the risk of disease according to the inherited antigens.

### 2. Materials and methods

The present study was a cross-sectional study which included 1000 cases of PIH and 1000 primiparous women with normal blood pressure, who were selected from antenatal clinic, labour room and indoor patients of obstetrics and gynaecology department of Assam medical college, Dibrugarh, Assam. The ethical committee clearance and an informed consent of the subjects were taken. Only Rh positive primi cases were included in the study. All multiparous pregnant women and women having any other medical and surgical complication and women having history of any drug use, multi-fetal pregnancy, smoking, erythroblastosis fetalis, were excluded from the study. Hypertensive disorder of pregnancy was classified as:-

\* Corresponding Author: **Rwitusmita Bharali**,

Post graduate trainee,  
Department of Physiology,  
Assam medical college,  
Dibrugarh-786002,  
Email:- [rwitu.smita@gmail.com](mailto:rwitu.smita@gmail.com)  
Mobile no- +91-9435410006

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1. Gestational hypertension-blood pressure more than 140/90mmHg without proteinuria and oedema.

2. Mild pre-eclampsia:- blood pressure more than 140/90mmHg but less than 160 systolic or 110 diastolic without significant proteinuria.

3. Severe pre-eclampsia:- Severe preeclampsia was diagnosed when one of the following criteria were met in association with hypertension and proteinuria:

a) blood pressure of 160 mmHg systolic, or 110 mmHg diastolic, recorded on at least two occasions at least 6 h apart, with the patient at bed rest;

b) proteinuria of 5 g or more in 24 h, and/or 3+ or 4+ (=300 mg/dL) on dipstick testing obtained on at least two occasions;

c) elevated serum creatinine (>1.3 mg/dL);

d) pulmonary edema;

e) oliguria (500 mL or less in 24 h);

f) microangiopathic hemolysis confirmed either by increased lactate dehydrogenase (LDH) level of >180 IU/L or total bilirubin >1.5 mg/dL;

g) thrombocytopenia (platelet count <150 × 10<sup>9</sup>/L);

h) hepatocellular dysfunction confirmed by elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels of >40 IU/L;

i) symptoms suggesting significant end-organ involvement: headache, visual disturbances, or epigastric or right-upper quadrant pain.

4. Eclampsia:-Pre-eclampsia complicated with convulsion or coma.

A detailed history of all the subjects was taken. Relevant past history, family history, any drug history, personal history like smoking, alcoholism and occupational history was taken. General physical examination, vital signs were recorded. The blood samples were collected by finger prick with sterile lancet and after cleaning the puncture site with 70% ethyl alcohol. A drop of monoclonal Anti A, Anti B, Anti D was added to a drop of finger prick blood on clear slide and mixed well. Results of agglutination were recorded immediately for ABO blood group and after 2 minutes for Rh. The proteinuria was measured by urine dipsticks.

The subjects were categorised into five groups- controls, gestational PIH, mild pre-eclampsia, severe pre-eclampsia.

The data were analyzed by using Microsoft Excel and Statistical Package of Social Sciences (SPSS version 20.0). Categorical data analysis for comparison of percentages was performed with chi-square contingency table analysis. The association of blood group with PIH, and the association of blood group with different categories of PIH, was estimated by calculating odds ratio from logistic regression models using blood group O and controls respectively as reference group after adjustment for various covariates. A p-value of < 0.05 was considered as statistically significant.

#### RESULTS AND OBSERVATION:-

The study population consist of 1000 cases and 1000 controls. The distribution of the different ABO blood group in the categories of PIH is shown in table 1. The number of cases as well as percentages of cases of blood group AB is highest in all the categories of PIH as shown in table 1 and figure 1,2,3 and 4

Using blood group O as the reference group, the association between blood group and PIH was estimated using odds ratios and 95% confidence intervals from logistic regression models. The results as shown in table 2 indicated that AB has the highest risk (OR 21.132, 95% CI 15.344–29.105) among the ABO blood group.

Using women who had no diagnosis of any gestational hypertensive disorders as the reference group, we estimated the association between blood group and the different categories of PIH (gestational hypertension, mild pre-eclampsia, severe- pre-eclampsia, eclampsia) using odds ratios and 95% confidence intervals from logistic regression models (table 3). When compared with blood group O, women of blood group AB had an increased risk of gestational hypertensive disorders (OR 20.036, 95% CI 14.017–28.639), mild pre-eclampsia (OR 21.577, 95% CI 14.430–32.264), severe pre-eclampsia (OR 27.228, 95% CI 17.248–42.982) and eclampsia. (OR 15.797, 95% CI 9.040–27.607)

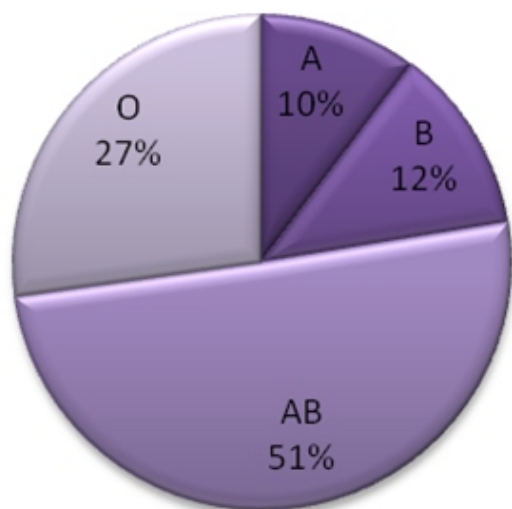
**TABLE 1:-Showing the distribution of different blood groups in different categories of PIH**

CATEGORIES OF PIH		BLOOD GROUPS				Total
		A	B	AB	O	
Control	Number of case	152	235	52	561	1000
	% of case	15.2%	23.5%	5.2%	56.1%	100%
G_PIH	Number of case	48	56	234	126	464
	% of case	10.3%	12.1%	50.4%	27.2%	100%
Mild ecl	Number of case	39	33	142	71	285
	% of case	13.7%	11.6%	49.8%	24.9%	100%
Severe ecl	Number of case	8	17	106	42	173
	% of case	4.6%	9.8%	61.3%	24.3%	100%
ecl	Number of case	2	7	41	28	78
	% of case	2.6%	9.0%	52.6%	35.9%	100%

{G\_PIH=gestational hypertension, Mild ecl=mild pre-eclampsia, Severe ecl=severe- pre-eclampsia, ecl=eclampsia.

The reference category is: control group. p value > 0.05 was non-significant (NS); p value < 0.05 was as significant (S)}

**Figure 1: DISTRIBUTION OF BLOOD GROUP IN GESTATIONAL HYPERTENSION**

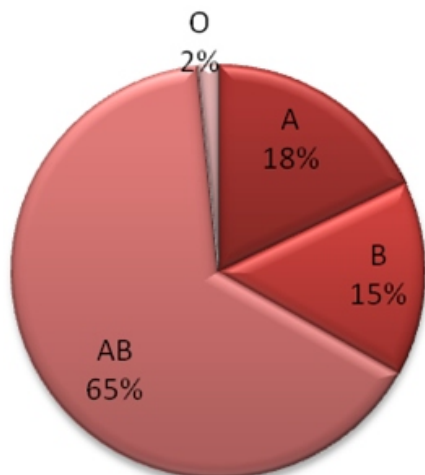


**TABLE 2: SHOWING THE ASSOCIATION BETWEEN ABO BLOOD GROUP AND PIH.**

BLOOD GROUPS	ODDS RATIO	95% Confidence Interval		Significance(p-value)	
		Lower Bound	Upper Bound		
A	1.341	1.000	1.798	0.05	NS
B	1.010	.773	1.320	0.94	NS
AB	21.132	15.344	29.105	<0.05	S

The reference category is: blood group O, p value > 0.05 was non-significant (NS); p value < 0.05 was significant (S)

**Figure 2: DISTRIBUTION OF BLOOD GROUP IN MILD PRE-ECLAMPSIA**



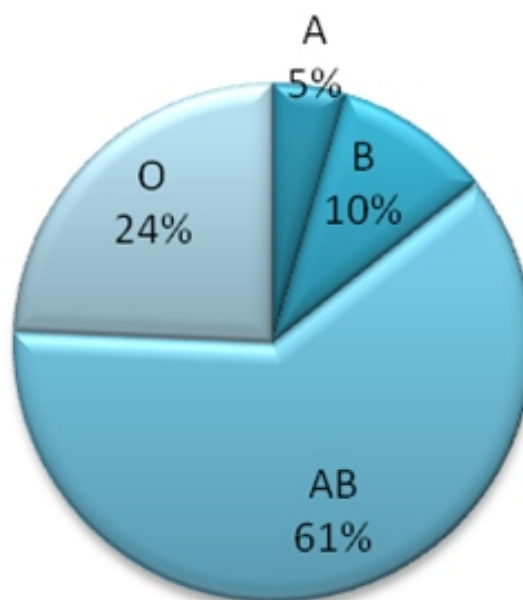
**TABLE 3: SHOWING THE ASSOCIATION BETWEEN ABO BLOOD GROUP AND DIFFERENT CATEGORIES OF PIH.**

CATEGORIES OF PIH	OF	ODDS ratio	95% Confidence Interval		Significance(p-value)	
			Lower Bound	Upper Bound		
G_PIH	A	1.406	.964	2.051	0.077	NS
	B	1.061	.748	1.505	0.740	NS
	AB	20.036	14.017	28.639	<0.05	S
Mild - ecl	A	2.027	1.319	3.116	<0.05	S
	B	1.110	.715	1.723	0.643	NS
	AB	21.577	14.430	32.264	<0.05	S
Severe - ecl	A	.703	.323	1.529	0.374	S
	B	.966	.539	1.732	0.908	NS
	AB	27.228	17.248	42.982	<0.05	S
Ecl	A	.264	.062	1.119	0.071	NS
	B	.597	.257	1.385	0.23	NS
	AB	15.797	9.040	27.607	<0.05	S

{G\_PIH=gestational hypertension, Mild ecl=mild pre-eclampsia, Severe ecl=severe- pre-eclampsia, ecl=eclampsia.

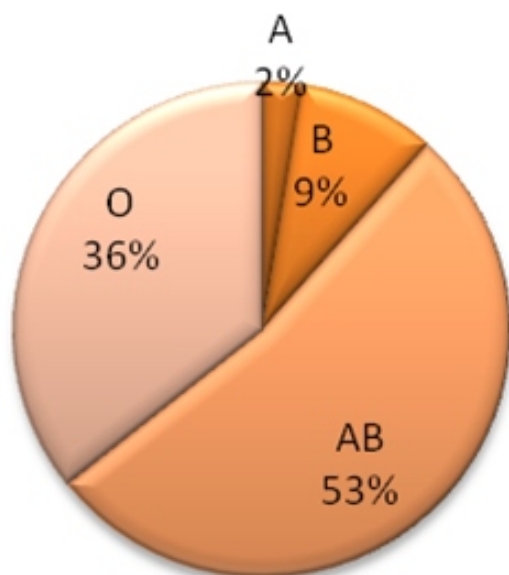
The reference category is: control group. p value > 0.05 was non-significant (NS); p value < 0.05 was as significant (S)}

**Figure 3: DISTRIBUTION OF BLOOD GROUP IN SEVERE PRE-ECLAMPSIA**



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Figure 4: DISTRIBUTION OF BLOOD GROUP IN ECLAMPSIA

**DISCUSSION:-**

The results of the present study indicated that AB blood group had the highest risk of developing PIH and the risk increases as the severity of PIH increases. This finding is in consistent with the findings of Hiltunen LM et al<sup>10</sup> and Spinillo A et al<sup>11</sup>. BK Lee et al<sup>12</sup> study on 641 926 singleton deliveries of Sweden showed that AB blood group have the highest risks of gestational hypertensive disorders, pre-eclampsia, and severe pre-eclampsia, whereas women with O blood group have the lowest risks of developing these disorders. However, a study by Lawoyin TO et al<sup>13</sup> found that blood group O Rh-positive were found to be more than twice as likely as others to develop preeclampsia. But , that study included only 20 preeclamptic women. One suggested mechanism of association of blood group with PIH

is through the maternal immune response. A study concluded that placental protein 13 (PP13), an early biomarker of pre-eclampsia with suspected function in the maternal-fetal immune interface, differentially binds to erythrocytes from distinct ABO groups, with strongest binding to blood group AB.<sup>14</sup> In addition, compared with O group, A, B, and AB groups are associated with an increased risk of thrombotic events, although this relationship

is not confirmed.<sup>15</sup> Also, ABO blood groups may differ in the occurrence of known vascular risk factors for preeclampsia, such as endothelial dysfunction,<sup>16</sup> insulin resistance, <sup>17</sup> and hypercholesterolemia. ABO blood groups display differences in levels of endothelial cell markers, including von Willebrand factor, E-selectin, and thrombomodulin. <sup>16</sup>Recent genome-wide association studies indicate that genetic variants at the ABO locus are associated with soluble E-selectin,<sup>18,19</sup>P-selectin, and ICAM-1,<sup>20</sup> vascular inflammatory agents that are associated with hypertension and type-2 diabetes.<sup>21</sup> However, of a diverse panel of inflammatory biomarkers, including E-selectin, P-selectin, and ICAM-1, a recent study found that only E-selectin levels were higher in pre-eclampsia cases versus controls.<sup>22</sup>

**CONCLUSION:-**

In conclusion, the results of this study suggest an association between ABO blood group systems and PIH in our population. Considering the role of ABO blood groups on the hemostatic process and thrombus formation, special attention should be given to pregnant patients carrying the AB blood group in order to prevent the PIH and improve prognosis.

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