Original Research Article

A case control study to evaluate correlation of anemia with severe preeclampsia

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ABSTRACT

Background: Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality worldwide. This study aims to evaluate correlation of anemia with severe preeclampsia.

Methods: It is a prospective case control study conducted in Sultania Zanana Hospital, Bhopal over one year period. Patients were grouped as cases (severe preeclampsia with severe anemia, n=180) and controls (severe preeclampsia with no/mild/moderate anemia, n=180). Collecting data were compared using the Pearson chi square, fisher's exact test and the independent t-test as appropriate. Logistic regression analysis was performed. Odds ratio (OR) and their corresponding 95% confidence intervals were calculated.

Results: Higher incidence of maternal complications abruption (8.88% v/s 0.5%), ARF (2.2% v/s 0.5%), PPH (2.8%), pulmonary edema (5%), CCF (3.3%), HELLP (1.6%), CVA (1.1%), pulmonary embolism and DIC in 0.5% and maternal mortality seen in cases. Perinatal complications like pregnancy wastage (22.8% v/s 7.8%), IUGR (55.8% v/s 32%), early neonatal death (7.5% v/s 2.4%), NICU admission (31.3% v/s 20.7%) were more in cases.

Conclusions: Perinatal and maternal complications are significantly associated with severity of anemia in preeclampsia women. Anemia being a easily detectable and modifiable risk factor, detection of anemia in early gestation can be a key to prevent or decrease the severity of preeclampsia.

Keywords: Acute renal failure, Anemia, Preeclampsia, Small for date

INTRODUCTION

Hypertensive disorders of pregnancy and their complications rank as one of the major cause of maternal mortality and morbidity in the world. Amongst them, preeclampsia is emerging as one of the most common complication of pregnancy.

Pre-eclampsia is a multi-system disorder of unknown aetiology, unique to pregnancy, with onset after 20 weeks of gestation.

Although, the exact aetiology of preeclampsia is not yet known, many factors such as low education, prim parity, family history of hypertension, obesity, younger and advanced maternal age and malnourishment are proven as its risk factors and evidence suggests that various other factors like severe anemia could also be a risk factor for development of preeclampsia and that cannot be ignored.

The uncertainty of cause of a disease of such common occurrence worldwide, make it to be more studied. Several studies have shown the association between severe anemia and preeclampsia and thus considers anemia as one of the main and treatable risk factor for preeclampsia.

Anemia during pregnancy is a major public health problem especially in developing countries which itself increases the maternal mortality, in addition it further

adds to the maternal and perinatal morbidity associated with preeclampsia, being a risk factor. It affects 41.8% women globally. In India overall prevalence of anemia is 65-70% and it contributes to 40 % maternal deaths.

Although preeclampsia is not a preventable disease but by putting light on the modifiable risk factors which play a role in its aetiology and which are amenable to get treated, the incidence of preeclampsia can be decreased. Thus identification of reversible factors such as anemia in pregnancy which is a treatable condition will be of great help for policy making and clinical purpose such as prioritization of interventions so that more intensive observation and improvement of risk management strategies can be done.

METHODS

The present study is a prospective case-control study conducted among pregnant women admitted in Sultania Zanana Hospital, Bhopal. Data were collected from all Antenatal cases with gestational age ≥20 weeks between 18yrs and 40yrs of age as per the inclusion and exclusion criteria admitted under OBG department, SZH Bhopal.

Inclusion criteria were all severe preeclampsia women of age between 18-40 years were enrolled in this study and divided into following groups:

- Group 1- severe preeclampsia with severe anemia (Cases)
- Group-2- severe preeclampsia with no/mild/moderate anemia (Controls)

The two groups were matched according to parity. All women were followed until delivery and early postpartum period and babies till early neonatal period.

Exclusion criteria included pregnant women with- essential hypertension/hypertension <20 weeks gestation/ pre-existing diabetes mellitus/renal disease/liver disorder/ thyroid disorder.

Sampling was done using case-control incidence density sampling i.e. cases were enrolled consecutively as they were diagnosed to have severe preeclampsia with severe anemia until the required sample size was obtained. For each case, one control was selected as soon as the case was diagnosed.

Data retrieved included socio-demographic characteristic (age, residence, education), maternal outcome (eclampsia, heart failure, DIC, pulmonary embolism, pulmonary edema, haemorrhage), and neonatal outcome (preterm birth, still birth, low birth weight).

Collected data were entered into Microsoft excel spreadsheet and were analysed by using SPSS20.0 Software. Comparison between categorical variable were made using the Pearson chi square and Fisher's exact test

as appropriate, and between quantitative variable using the independent t-test. Logistic regression analysis was performed. Odds ratio (OR) and their corresponding 95% confidence intervals were calculated. P value <0.05 was regarded as significant.

RESULTS

The present study was carried out in Department of Obstetrics and Gynaecology, Sultania Zanana Hospital during the period 1st March 2015 to 29th February 2016. Total no. of deliveries in SZH during this period was 14029. Number of preeclampsia cases admitted during this period 818. Thus incidence of Preeclampsia comes about 5.8%.

Most of the cases as well as controls were found to be of age group 21-30 yrs. Mean age of women among the cases was 24.98years (SD 4.155) and of control was 25.57 years (SD 3.871) . Out of the 180 cases maximum i.e.42% were illiterate while among 180 controls, 30% were illiterate. In present study, among the cases 81% presented at term pregnancy while 19% were preterm pregnancies. In controls, 78% presented at term and 22% were preterm .There is no significant difference between the gestational age among the cases and control, at which they presented.

Table 1: Mode of delivery.

Mode of delivery	Case	Control	Chi square
FTVD	117 (65%)	117 (65%)	2.154, P=0.341, NS
PTVD	35 (19.5%)	43 (24%)	
LSCS	28 (15.5%)	20 (11%)	
Total	180 (100%)	180 (100%)	

As observed in Table 1, out of 180 cases 65% had full term vaginal delivery, 19.5% had preterm vaginal delivery, and 15.5 % landed up in caesarean section. Most common indication of caesarean was fetal distress f/b previous LSCS f/b malpresentation. In controls maximum had vaginal deliveries, 65% had full term while 24% had pre term vaginal deliveries while 11% had caesarean section. Most common indication of caesarean was fetal distress. There is no much difference in the mode of delivery among cases and controls.

Table 2: Maternal outcome.

Maternal outcome	Case	Control	Fisher's exact test
Discharged	156 (86.7%)	179 (99.44%)	24.815, P=<0.001, S
Mortality	9 (5%)	0	
Transferred	15 (8.3%)	1 (0.56%)	
Total	180 (100%)	180 (100%)	

Table 2 shows the maternal outcome. In this study maternal outcome was significantly poor among the cases. 5% mortality reported in case group and none in the control group.

All mortalities were due to complications contributed to severity of preeclampsia.15 patients of 180 cases were transferred to other department due to adverse outcome.

Table 3: Maternal complications.

Complication	Case	Control	P value
Abruption	16 (8.88%)	1 (0.5%)	<0.001, S
Pulmonary edema	9 (5%)	0	0.002, S
PPH	5 (2.8%)	0	0.024, S
CCF	6 (3.3%)	0	0.013, S
ARF	4 (2.2%)	1 (0.5%)	0.176, NS
HELLP	3 (1.6%)	0	0.081, NS
Eclampsia	3 (1.6%)	12 (6.6%)	0.017, S
CVA	2 (1.1%)	0	0.156, NS
Pulmonary embolism	1 (0.5%)	0	0.316, NS
DIC	1 (0.5%)	0	0.316, NS

Table 3 shows that all maternal complications were significantly higher among the cases, except eclampsia which was surprisingly more seen among the controls.

The odds ratio calculated for maternal complication (OR=3.836, 95% CI: 2.017-7.295) suggest that odds of maternal complication in women with severe preeclampsia with severe anemia is 3.83 times more than controls, and the result is significant (p<0.001). However, the effect of mild/moderate anemia cannot be ignored.

Table 4: Fetal outcome.

Viability	Case	Control	Chi square
Alive	147 (78.2%)	169 (92.3%)	14.721, P= <0.001, S
SB/IUD	41 (21.8%)	14 (7.7%)	
Total	188 (100%)	183 (100%)	

Table 4 shows the fetal outcome in cases and controls. Pregnancy wastage in cases were 22.8% while in controls were 7.8%. This suggests poor fetal outcome among the cases which was statistically significant. OR=3.3669 (95% CI, 1.765-6.421).

Odds of having still birth is 3.3 times higher in cases than controls and the result is significant (p<0.001). The majority of deaths were due to abruptio placenta. Other causes were non-viable pregnancy, severe IUGR, and prematurity.

Table 5: Perinatal outcome.

Perinatal outcome	Case	Control	Chi square
Term appropriate for date	64 (43.5%)	103 (60.9%)	
Term small for date	71 (48.3%)	34 (20.1%)	
Pre term appropriate for date	1 (0.7%)	12 (7.1%)	32.6933, P<0.001, S
Pre term small for date	11 (7.5%)	20 (11.9%)	
Total	147 (100%)	169 (100%)	

Table 6: Neonatal mortality.

Early neonatal death	Case	Control	Chi square
Present	11 (7.5%)	4 (2.4%)	
Absent	136 (92.5%)	165 (97.6%)	P=0.032, S
Total	147 (100%)	169 (100%)	

Table 5 shows that in our study, out of total live births in cases 43.5%% were term appropriate for date, 48.3%% term small for date, and 7.5%% were preterm SFD, while among the controls maximum i.e. 60.9% were TAFD, which shows that chances of IUGR are more among the cases which is statistically significant.

As observed in Table 6, In this study, out of total 147 live births among cases, 11(7.5%) succumb to early neonatal death that was significantly more than the controls i.e.4 (2.4%) out of 169 live births. Most common cause of death was perinatal asphyxia.

The odds of early neonatal death for cases is 3.33 times higher than controls (OR 3.336, 95% CI (1.038-10.714) the result is significant (p=0.03).

DISCUSSION

Thus incidence of preeclampsia in Sultania Zanana Hospital is 5.8%. Jaiprakash et al found the similar result of incidence i.e. 5.8%, 5.8% reported from a study in Scotland.[1] Mudaliar and Menon has noted incidence of preeclampsia between 7-9% in Indian studies.[2] Pre-eclampsia affects approximately 2–8% of all pregnancies worldwide.[3]

In this study the mean age of study population is 25.28 years. Advanced maternal age has been found to be an independent risk factor for preeclampsia, while in this study most of the cases and controls were in the age

group 21–30 years, which is probably because in our population early marriage is more common. Jaiprakash et al found the mean age of patients was 26.6±5 years.[1] Enaruna et al found 30 years (range: 19 to 41) and Assis et al found that age above 30 years was associated with a risk for preeclampsia.[4,5] Andhra Pradesh found the highest prevalence of anaemia (68.4%) in the age group 20-24 years . There has been increased risk of anaemia among pregnant adolescents (teenage pregnancy) due to depleted iron stores that occurred during the adolescent growth spurt.

This study shows that out of 180 cases 42% had no formal education as compare to controls in which 30% were illiterate. It suggests that women with lower education level were more likely to develop preeclampsia as well as severe anemia as compared to controls. Tebeu et al found that illiteracy was associated with about 2-fold risk for presenting hypertensive disorder in pregnancy (OR: 1.7; 95% CI: 1.1-2.4).[6]

Out of 180 cases 94.4% were referred from other hospital, 3.9% were not referred and 1.7% were booked at SZH. Among controls 81.7% were referred, 13.3% were not referred and 5% were booked at SZH .Boniface et al reported that obstetric risks were more in un-booked pregnant women compared to booked ones.[7] The booked patient benefits from focused antenatal care objectives, which have obvious benefits in terms of risk assessment, active management, correction of modifiable conditions, and boosting the psychological support and family preparedness for a new child.

These result shows that compared with control significantly higher numbers of cases were resident of rural area, had lower level of education and were referred from other hospitals. This indicates that women from rural area may not afford or have access to good maternal health care services because of lack of education or financial constraints.

In our study, maximum no. of cases i.e. 81% as well as controls i.e. 78% presented at term pregnancies. While 8% cases and 7% controls presented at 28-32 weeks of gestation. And 11% cases and 14 % cases presented at 33-36 wks of gestation, which shows no statistical significance. Cheema et al observed higher prevalence of anemia in 3rd trimester.[8] Jaiprakash et al found approximately half of 47. 16% of the preeclamptic women were at 32-36 wks of gestation period, 15.09% were at <32 weeks and 26.41% were at >36 weeks.[1] Anemia leads to increased synthesis of corticotrophin-releasing hormone (CRH) as a result of tissue hypoxia. These raised levels can induce maternal and fetal stress, and thus produce a risk factor for preterm labour.

Present study shows that, 84.5% cases undergone vaginal deliveries and 15.5% cases were resorted to LSCS, 63.9% patients went in spontaneous labour while rest were induced While among controls rate of vaginal deliveries

was 89% and of LSCS was 11% and 77.8% went in spontaneous labour while 22.2% were induced. Aabidha et al observed 58% of the patients were induced and 45% needed caesarean section due to obstetric indication in severe preeclampsia patients.[9]

Present study shows, out of 180 cases, 8 were twin pregnancy and among 180 controls, 3 were twins. Proportion of dead fetus was more in cases as compare to controls i.e.21.8% versus 7.7%. This suggests poor fetal outcome in cases.

Aabidha et al, found 10% stillbirths in patients with severe preeclampsia.[9] The higher proportion of SB in our study shows impact of severe anemia on severe preeclampsia. Severe preeclampsia represents significant risk factor for intrauterine fetal demise, with estimated stillbirth rate of 21 per 1000.[10]

Present study shows that Women with severe anemia delivered infants with a significantly lower birth weight than women in control group. In cases the proportion of extremely low birth weight, very LBW and LBW is significantly higher than controls (13.3% versus 3.3%, 10.1% versus 8.2% and 58.5% versus 50.3%). Low birth weight, i.e. 2.5 Kg is widely used as an indicator of newborn health. Jones et al also found an increased incidence of low birth weight babies in anaemic mothers, however the difference from the non anaemic group in their study was non significant (p=0.11)

Present study shows, 55.8% of 147 live birth babies in cases were IUGR as compare to 31.9% of 169 live birth in controls. Of 147 live born in cases, 46 (31.3%) were admitted in NICU whereas NICU admission rate was 20.7% in controls.

Among the cases 11 (7.5%) neonate succumb to early neonatal death as compared to controls (2.4%). Nirmala Devi et al found IUGR in 12.77% patients of severe anemia.[11] Swamy et al observed perinatal and neonatal mortality rates were 13.83 and 6.49%, respectively in severe preeclampsia cases.[12] Enaruna et al observed stillbirth (32.8% more) and ENND (13.8% more) were significantly associated with severe anemia in severe preeclampsia cases.[4] Liu et al observed the proportion of babies who stayed alive up to 7 days after delivery was significantly reduced by the presence of severe anemia.[13]

The increased incidence of perinatal morbidity and mortality seen in pregnancies complicated by preeclampsia, is due to the need for premature delivery and utero-placental insufficiency resulting in compromised blood supply to the fetus but presence of severe anemia contribute to adverse outcome of severe preeclampsia .

In this study the maternal outcome in majority of patients in control group was normal i.e. the patient was

discharged in a satisfactory condition However outcome was significantly poor among the cases.

Out of 180 cases, 9 (5%) deaths were recorded in this study and 15 patients (8.3%) were transferred to other department due to adverse outcome. 3 deaths were due to pulmonary edema, 2 due to CCF, 1 due to pulmonary embolism, 1 due to PPH, 1 due to CVA and 1 due to HELLP leading to ARF. Enaruna et al observed that Severe anemia was 7.7-fold more associated with maternal mortality in severe preeclampsia cases than no anemia.[4]

Abruption was seen in 8.88% cases than 0.5% controls, ARF was seen in 2.2% cases than in 0.5% control. Pulmonary edema seen in 5% cases, PPH occurred in 2.8% cases, CCF in 3.3%, HELLP in 1.6%, CVA 1.1%, Pulmonary embolism and DIC in 0.5% cases. Whereas none of these complications reported in controls. Singhal et al reported maternal complication as PPH 31%, abruption 11%, renal dysfunction 4%, pulmonary edema 8%, pulmonary embolism 8%, HELLP %, DIC 2%, and maternal mortality in 8% cases of severe preeclampsia which was comparable with this study.[14]

Ndoni et al observed eclampsia 7.1%, HELLP syndrome 11.0%, stroke 1.9%, pulmonary edema 1.3%, renal failure 2.6%, placental abruption 7.8%, and severe postpartum hemorrhage 3.9% in severe preeclampsia.[15].

CONCLUSION

Anemia and preeclampsia per se causes increased perinatal and maternal morbidity and mortality. Present study analysed the association of anemia with severe preeclampsia it was observed that the risk of perinatal and maternal morbidity and mortality increases with severity of anemia, when associated with preeclampsia. Thus analyzing the obtained result of this study and considering the previous studies, it can be concluded that detection of anemia in early gestation can be a key to prevention of preeclampsia.

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