ABSTRACT

Background: Pre-eclampsia is one of the leading causes of maternal and infant morbidity and mortality worldwide. The pathogenesis of this condition involves combination of genetic predisposition and environmental factors. The aim of the study was to determine the socio demographic and other risk factors of pre-eclampsia.

Methodology: A case control study was conducted at a tertiary care hospital, Karnataka among 100 cases of pre-eclampsia and 200 controls without pre-eclampsia. Non probability purposive sampling technique was adopted to select the study subjects. Data was collected by using a pre tested semi structured questionnaire which included information related to socio demographic and other known risk factors of pre eclampsia.

RESULTS: Study subjects included 100 cases and 200 controls. Age of less than 20 y (OR=3.8), monthly income of less than Rs4000 (OR=6.8), age of menarche of less than 12 y (OR=13.1), family h/o pre eclampsia (OR=36.0), family h/o Diabetes (OR=44.9), family h/o hypertension (OR=16.7) and previous h/o PIH (OR=58.5) are found to be significant risk factors of pre eclampsia.

Conclusion: The significant risk factors may be used for screening Pre eclampsia during registration of pregnancy.

Keywords: Family history, Pre-eclampsia, Pregnancy induced hypertension, Risk factors, Women health

INTRODUCTION

Pre-eclampsia is a multi system disorder of unknown etiology characterized by development of hypertension to the extent of 140/90 mmHg or more with proteinuria after 20th week of gestation in a previously normotensive and non protein uric pregnant woman. Pre-eclampsia has been associated with intrauterine growth retardation, preterm birth, maternal and perinatal death [1]. The incidence of pre-eclampsia is 2-10%, depending on the population studied and definition of pre-eclampsia [2]. It occurs in 4-7% of pregnant women worldwide [3].

Globally, over half a million women die each year of pregnancy related causes and 99% of these deaths occur in developing countries [4]. Put another way, women in developed countries have an average life time risk of dying from pregnancy related causes of between 1 in 4000 and 1 in 10000, whereas women in developing countries have a risk that is between 1 in 15 and 1 in 50. Although rare, eclampsia which is a complication of pre-eclampsia accounts for 50,000 maternal deaths a year [5].

India is among those countries which have a very high maternal mortality rate i.e. 301 per 100,000 live births. The major causes of maternal deaths in India are haemorrhage, sepsis, hypertension, obstructed labour, abortion and other conditions. Hypertension which can be a sign of pre-eclampsia accounts for 5% of maternal deaths in India [6].

The causes of and risk factors for pre-eclampsia remain unclear, however and thus pre-eclampsia has been called a “Disease of theories” [7]. The factors that have been postulated to influence the risk of pre-eclampsia among the mothers include diabetes, obesity, multiple pregnancy, primiparity, personal or family history of pre-eclampsia, and chronic hypertension. In developing countries, evidence on the association between these factors and pre-eclampsia is scarce [8-10]. So, the study of risk factors of pre-eclampsia can be used to assess risk of pre-eclampsia at ante natal booking [11]. As there is paucity of data on risk factors of pre-eclampsia in Karnataka, India, this study was conducted to find out risk factors of pre-eclampsia.

METHODOLOGY

This matched case control study was conducted between February 2013 to October 2013 in the Department of Obstetrics and Gynaecology, Vijayanagara Institute of Medical Sciences, Bellary, Karnataka, India.

A case was defined as a woman in the ante natal period diagnosed by an Obstetrician as being pre-eclamptic. Pre-eclampsia was defined as a pregnancy induced hypertension associated with proteinuria. Pregnancy induced hypertension was defined as new hypertension with blood pressure of 140 mmHg systolic or diastolic pressure of 90 mmHg or greater arising after 20wk of gestation in a woman who was normotensive before 20wk of gestation. Proteinuria was defined as excretion of 300mg or more of protein in 24h urine sample. A control was defined as a woman in the ante natal period that did not have a diagnosis of pre-eclampsia.

Cases were selected from pre-eclamptic ward and controls from outpatient section of Obstetrics & Gynaecology department. For each case, we interviewed two controls matched on parity. Totally 100 cases and 200 controls were included for the study (1:2 ratios).

The data was collected using a pre-tested semi structured questionnaire. This questionnaire included information regarding socio-demographic characters, personal history, past history and family history of this disease related variables. Before collecting data, informed written consent was obtained from all the study participants and the subjects who did not give their consent and those who were seriously ill were excluded from the study.
RESULTS

The study subjects included 100 pre-eclamptic cases and 200 controls. Socio-demographic characters: The mean age of cases (21.16 y) was less than the controls (23.56 y). There was no much difference in proportion of illiterate among both pre-eclamptic cases (22%) and controls (20%). Similarly both the groups had almost same proportion of illiterate husband and as well as no significant difference was found in occupation status between two groups (for maternal and husband) [Table/Fig-1].

Pregnant women of age less than 20y were 3.87 times at risk of developing pre-eclampsia compared to age more than 20y (OR: 3.87, 95% CI: 2.32 – 6.44). Similarly pregnant women with household monthly income of less than Rs4000 were 6.81 times at risk of being pre-eclamptic compared to those with income more than Rs4000 [Table/Fig-1].

Obstetric characters: Women who had menarche at age of less than 12 y were at greater odds of having pre-eclampsia compared to those who had menarche after 12y of age. Women who married their first degree relative were at risk of being pre-eclamptic compared to those who did not marry their first degree relative. Among pre-eclamptic cases, 80% of them got married when they were less than 18y of age and these pre-eclamptic cases were at greater odds of having pre-eclampsia. Women who had their first conception within one year of their marriage were at risk of developing pre-eclampsia more than 10 times compared to those who had their first conception after one year of marriage. Gestational period of more than 30wk was significantly associated with pre-eclampsia compared to gestational period between 20 – 30wk [Table/Fig-2].

Family history: Family history of pre-eclampsia, diabetes and Hypertension were significantly associated with pre-eclampsia. The pregnant women with history of above mentioned parameters were at greater odds of having preeclampsia as compared to those who had no such history [Table/Fig-3].

Personal history: Previous history of pregnancy induced hypertension (PIH) was significantly associated with preeclampsia with greater odds [Table/Fig-4].

DISCUSSION

This case-control study aims to explore the risk factors of pre-eclampsia related to socio-demographic characters, gynecology and obstetrics characters, family and personal history of study subjects. It is estimated that worldwide 13% of maternal mortality is due to hypertensive disorders of pregnancy but it is much higher in developing countries where the estimates are between 20-80% in Asia [12,13].

Our study suggests that the chances of a woman having pre-eclampsia is associated with low socioeconomic status, age at pregnancy, family history of hypertension and diabetes, age of menarche, previous history of pre eclampsia and duration before

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**Socio-demographic characters**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 20 years</td>
<td>45 (45%)</td>
<td>48 (24%)</td>
<td>152 (76%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Education (maternal)</td>
<td>78 (78%)</td>
<td>40 (20%)</td>
<td>160 (80%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Husband education (maternal)</td>
<td>80 (80%)</td>
<td>42 (21%)</td>
<td>158 (79%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Occupation (maternal)</td>
<td>95 (95%)</td>
<td>62 (31%)</td>
<td>192 (96%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Personal history**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/o Diabtes mellitus</td>
<td>95 (95%)</td>
<td>00 (00%)</td>
<td>198 (99.5%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Family history**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family h/o pre-eclampsia</td>
<td>60 (60%)</td>
<td>00 (00%)</td>
<td>192 (96%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Socio-Demographic characters of Pre-eclamptic cases and controls**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 12 years</td>
<td>16 (16%)</td>
<td>57 (28.5%)</td>
<td>143 (71.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Time period b/w marriage &amp; first conception &lt; 12 months</td>
<td>20 (20%)</td>
<td>42 (21%)</td>
<td>158 (79%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Family type</td>
<td>18 (18%)</td>
<td>141 (70.5%)</td>
<td>38 (19%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Obstetric characters**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time period b/w pregnancy &lt; 12 months &gt; 30 weeks</td>
<td>02 (02%)</td>
<td>133 (66.5%)</td>
<td>67 (33.5%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Gestational period**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of menarche</td>
<td>84 (84%)</td>
<td>57 (28.5%)</td>
<td>143 (71.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Time period b/w present &amp; previous pregnancy &lt; 12 months &gt; 30 weeks</td>
<td>00 (00%)</td>
<td>12 (07.9%)</td>
<td>22.63-588.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Occupation (maternal) | 80 (80%) | 74 (37%)   | 83 (83%)           | 0.001   |

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**Monthly income < 4000 Rs | 80 (80%) | 74 (37%)   | 83 (83%)           | 0.001   |

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**Family type**

<table>
<thead>
<tr>
<th>Cases (n=100)</th>
<th>Controls (n=200)</th>
<th>Odds ratio</th>
<th>95% CI (odds ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family type</td>
<td>18 (18%)</td>
<td>141 (70.5%)</td>
<td>38 (19%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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**Table/Fig-1**: Socio-Demographic characters of Pre-eclamptic cases and controls

**Table/Fig-2**: Obstetric characters of Pre-eclamptic cases and controls

**Table/Fig-3**: Family history of pre-eclamptic cases and controls

**Table/Fig-4**: Personal history of pre-eclamptic cases and controls

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conception after marriage. Most significant and important risk factor is -previous history of pre-eclampsia.

Historically, the first correlation identified as a risk factor for pre-eclampsia has been a history of pre-eclampsia in the previous pregnancy. Various studies have already established a relation between these two factors [14-17] but our study showed an even stronger association between these two factors with an odds ratio of 58.5. We also found that there was significant number of mother with pre eclampsia with family history of Diabetes. Studies done during pregnancy suggest that insulin resistance predate the development of pre-eclampsia, implying that insulin resistance may play a role in its aetiology [18,19]. Although this association has been known [20], the stronger association found in our study, stresses the importance of screening this factor during regular ante natal care for prevention and early diagnosis of Pre eclampsia. The incidence of pre eclampsia/eclampsia in India is high and is associated with high maternal morbidity and mortality.

Increased age of women is an important risk factor due to increased vilious reaction leading to pre eclampsia in a woman greater than 30y. This has been conclusively found in various studies [13,15], but the incidence of pre-eclampsia in women less than 20y of age is an area that has not been given much importance. Nulliparity is associated with increased risk of pre - eclampsia and eclampsia by two folds. Many studies have reported nulliparity as a risk factor for severe pre eclampsia [21-23] cite as (Table/Fig 5). This is because nulliparity is due to initial trophoblastic invasion and how the mother reacts to it. The failure of the normal invasion of trophoblastic cells leads to mal adaptation of the spiral arterioles, which are related to the causation of pre-eclampsia [24]. We found that pre eclampsia is 4 times likely if a woman was pregnant before 20y of age. A similar retrospective study done in Finland also concluded with the same result [13]. This might either be due to the age itself or may be due to inadequate antenatal care given to a teenage pregnant girl.

Age of menarche was also found to have a significantly strong association with pre eclampsia. Previously, early menarche (<12 y) has been associated with increased risk of CVD events [25] investigators observed associations are potentially mediated by increased adiposity mediated with early menarche [25]. In the current study, we found an inverse relationship between age at menarche and increased risk of pre-eclampsia with OR 13.7. In a case-control study, conducted in Seattle, USA [26] reported no significant 3-fold increase in risk of pre-eclampsia among overweight women with longer menstrual cycle length (OR: 3.11, 95%). The evidence from the current study is stronger since it is based on a study population from a prospective cohort study. However, its role in the relationships of age at menarche and cycle length with risk of pre-eclampsia has not been well investigated [26].

Our study showed that the chances of pre eclampsia in women who conceived within a year of marriage were high. In a similar study done in Nigeria [27] long birth interval of more than sixty months was associated with seven fold risk of developing pre-eclampsia. The reason for prolonged birth interval and pre - eclampsia was not quite clear but prolonged period could be due to factors such as change of paternity and possibly sub fecundity, which predispose to pre – eclampsia [28]. It remains too studied if this association is simply because women who conceive early in marriage are usually nulliparous, which is an independent risk factor [29].

Low Socio economic factors act as multiple risk factors for pre eclampsia. Low socio economic factors are associated with Nutritional issues, reduced ante-natal care and unsanitary hygienic conditions. In Mexico low socio-economic status of women doubled the risk of pre-eclampsia and eclampsia[30]. A study in Australia found working women compared to non working ones had a higher risk of developing pre-eclampsia and eclampsia [31]. This may be related to the stress that women get during work. Our study similar to a study done in a semi urban setting [32] showed significant association between maternal education, income and pre-eclampsia.

CONCLUSION

The risk factors that we have identified can be used to assess risk at the booking visit, so that a suitable surveillance routine to detect pre-eclampsia can be planned for the rest of the pregnancy.

REFERENCES

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Community Medicine, Vijayanagara Institute of Medical Sciences, Bellary, Karnataka, India.
2. Junior Resident, Department of Community Medicine, Vijayanagara Institute of Medical Sciences, Bellary, Karnataka, India.
3. Junior Resident, Department of Community Medicine, Vijayanagara Institute of Medical Sciences, Bellary, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Ramesh.K, Assistant Professor, Department of Community Medicine, Vijayanagara Institute of Medical Sciences and Research centre, Bellary, Karnataka- 583104, India .
Phone : 9481181291, E-mail : ramspsm@yahoo.co.in

FINANCIAL OR OTHER COMPETING INTERESTS: None.