ISSN 2091-2889 (Online)
ISSN 2091-2412 (Print)

Journal of Chitwan Medical College 2013; 3(6): 43-47
Available online at: www.jcmc.cmc.edu.np

ORIGINAL RESEARCH ARTICLE

# ANTENATAL CARE AND SEVERE PRE-ECLAMPSIA IN KATHMANDU VALLEY

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## ABSTRACT

Severe preeclampsia/eclampsia is one of the common cause of maternal and perinatal morbidity and mortality. So the prevention of this severe preeclampsia may prevent these complications. This study was undertaken to assess the association between antenatal care and severe pre-eclampsia/eclampsia, also to examine the role of other risk factors for severe preeclampsia/eclampsia. A case study was conducted during May to Oct 1994 in Kathmandu valley. This study failed to demonstrate that ANC could reduce the risk of severe pre-eclampsia/eclampsia. The incidence rate of ANC visits in third trimester was significantly lower among cases than among controls. Risk independently increased in women with a history of previous PET (OR 6.9, 95% CI 1.0-48.9), history of abortion (OR 4.5, 95% CI 1.1-19.3), late menarche (OR 3.7, 95% CI 1.6-8.4) and primigravidity (OR 2.9, 95% CI 1.2-7.4). Use of modern contraceptive methods decreased the risk (OR 0.21, 95% CI 0.05-0.83). Risk was also higher among the middle-income group (OR 3.6, 95% CI 1.2-10.7), manual workers (OR 13.4, 95% CI 4.5-40.3) and non-Hindu women (OR 9.9, 95% CI 3.0-32.3). This study did not demonstrate that ANC could reduce the risk of severe pre-eclampsia/eclampsia. The history of previous PET, abortion, late menarche and primigravidity status each independently increased risk. Use of modern contraceptive methods decreased the risk. Risk was higher among the middle-income group manual workers and non-Hindu women.

**Key Words:** *Ante-natal care, Risk factor, Severe-preeclampsia.*

## INTRODUCTION

Pre-eclampsia is one of the most common complications occurring during pregnancy and is common in developing countries. Its severe form is one of the major killers of mothers and foetuses though preventable.

Although pre-eclampsia is not a totally preventable, its early detection and proper treatment can prevent it from seberity. However, in Nepal ANC service is provided by various levels of health care providers, though their knowledge and skill may vary. Furthermore antenatal care itself is not widely available, especially in far and remote villages. Although no data are available, pre-eclampsia, severe pre-eclampsia and eclampsia are frequently seen in hospitals in Nepal. The previous studies as stated in literature review have shown that antenatal care can prevent severe forms of pre-eclampsia. Therefore this study aims to detect whether ANC as such has any impact on reducing risk of severe pre-eclampsia in the Nepali setting.

## MATERIAL AND METHODS

This case-control study, using hospitalized cases and community controls, was conducted in Kathmandu valley from May to October 1994. The three tertiary level hospitals situated in two large cities were included in the study.
Three hospitals are:

1. Maternity Hospital -Government hospital
2. Tribhuvan University teaching hospital
3. Patan Mission hospital - semi Government hospital.

All cases of severe pre-eclampsia/eclampsia, i.e., the pregnant women having diastolic blood pressure 110 mm Hg or more with persisting proteinuria 1+ (0.3-0.45 g per litre) or more, with or without fits, who came to the hospitals for ANC or for delivery were taken as cases.

The controls were, Postpartum women who had normal delivery within the three month period following detection of cases and were matched to cases on residential area. Here normal delivery means the delivery without any medical or obstetrical complications during ante-natal, intra-natal or post-natal period, and term delivery. The control to case ratio was 2:1.

The sample size was calculated using Epi-Info software, Prevalence of exposure (antenatal care) in control group was assumed 30 percent. For an odds ratio = 0.4, power = 80 percent, an alpha level of 0.05, and case: control ratio of 1:2, the number of cases came to 97 and controls to 194.

The subjects having following conditions were excluded from the study during sampling.

1. All cases of superimposed pre-eclampsia and eclampsia.

2. Pre-eclampsia/eclampsia with any other medical complications.
3. All cases of severe pre-eclampsia with any obstretrical complications, such as twin pregnancy, molar pregnancy etc. The reason for excluding these cases is that exposure to ANC tends to be increased in these group.
4. Preterm deliveries (deliveries before thirty seven weeks of gestational age) were also excluded from controls

## RESULTS

**Incidence of pre-eclampsia and eclampsia.**

The total number of deliveries in the three hospitals during the study period, May 1994 to Oct 1994, was 4,709 and the total number of cases of severe pre-eclampsia including eclampsia was 94. So the ratio was 20 cases of severe pre-eclampsia or eclampsia to one thousand hospital deliveries.

Among the 94 cases of severe pre-eclampsia including eclampsia nineteen of these cases, were excluded from the study for the following reasons:7 were from outside the Kathmandu Valley, 6 had heart disease, 2 had essential hypertension, 2 came from remote villages and 2 had twin pregnancy. Of the remaining 75 cases, 15 had eclampsia. Two cases of severe pre-eclampsia and four cases of eclampsia developed after delivery at home.

**Ante-natal care in each trimester and severe pre-eclampsia/ eclampsia.**

Severe pre-eclamptic patients had a higher exposure to ANC in first and second trimesters than did the normal delivery group. Exposure to ANC in the third trimester was approximately equal in both groups (Table 1).

**Table 1: The association between attendance of ANC in each trimester. SPET/EC vs ND. Crude odds ratios (OR) and 95% CI. Reference group is ND.**

| Variable | Number (percent) | | | |
|---|---|---|---|---|
| | ND N=150 | SEPT/EC N=75 | OR | 95% CI |
| Attendance of ANC: | | | | |
| First trimester | | | | |
| No | 122 (81%) | 52 (69%) | 1 | |
| Yes | 28 (19%) | 23 (31%) | 1.93 | 1.01-3.65 |
| Second trimester | | | | |
| No | 88 (59%) | 30 (40%) | 1 | |
| Yes | 62 (41%) | 45 (60%) | 2.13 | 1.21-3.74 |
| Third trimester | | | | |
| No | 83 (55%) | 43 (57%) | 1 | |
| Yes | 67 (45%) | 32 (43%) | 0.92 | 0.53-1.61 |
| * Third trimester | | | | |
| No | 83 (55%) | 43 (61%) | 1 | |
| Yes | 67 (45%) | 28 (39%) | 0.96 | 0.54-1.69 |

Note : ND = Normal deliveries, SEPT/EC = Severe pre-eclampsia and eclampsia.

* = Excluding four cases who did not have chance to do ANC in third trimester.

Four cases of severe pre-eclampsia developed between 25 and 29 weeks of pregnancy and therefore were not at risk of exposure to ANC in the third trimester. Omitting these 4 cases from the analysis failed to reveal any negative association between ANC visit and severe pre-eclampsia.

**Onset of ante-natal care and severe pre-eclampsia/ eclampsia.**

Women who subsequently developed severe preeclampsia/ eclampsia tended to attend antenatal clinic earlier than controls. Table 2. shows the proportions of women in each outcome category attending ANC before and after three different cut off points.

**Table 2. Association of onset of antenatal care using three differnt components. Crude odds ratios and 95% confidence intervals. ND is the reference group.**

| Variable | Number(percent) | | | |
|---|---|---|---|---|
| | ND N=150 | SPET/EC N=75 | OR | 95% CI |
| First trimester | 25 (17%) | 23 (31%) | | 1 |
| Second and third or none | 125(83%) | 52(69%) | 0.45 | 0.23-0.87 |
| First and second | 65 (43%) | 46 (61%) | | 1 |
| Third or none | 85 (57%) | 29 (39%) | 0.48 | 0.27-0.85 |
| First, second and third | 69 (46%) | 53 (71%) | | 1 |
| None | 81 (54%) | 22 (29%) | 0.35 | 0.19-0.64 |

**Pattern of ANC in relation to normal delivery and SPET/ EC.**

Various pattern of ANC timing were reported. Table 3 shows the relationship of the pattern to outcome, using attendance for ANC in all trimesters as the baseline. Pattern of ANC timing in which ANC was stopped before third trimester were more common among cases than among controls. Not having any ANC, however, was less common among cases than controls, but the difference was not statistically significant.

**Table 3. Pattern of timing of ANC according to outcome ND and SPET/EC. Crude odds ratios and 95% CI. ND, the reference group.**

| Variable | ND n=150 | SEPT/EC n=75 | OR | 95% CI |
|---|---|---|---|---|
| 1st+2nd+3rd | 25 | 12 | 1 | |
| 1st+3rd,2nd+3rd,3rd | 42 | 20 | 0.99 | 0.41-2.36 |
| 1st+2nd, 2nd, 1st | 2 | 21 | 21.80 | 4.30-108.9 |
| ANC not done | 81 | 22 | 0.56 | 0.24-1.30 |

**Reproductive status and socio-demographic factors as risk**

**for SPET/EC**

Risk of SPET/EC was increased in women with no education, who were manual workers, in a middle income group, non-Hindu, primigravidae and who had a history of abortion or PET and menarche after the age of 13 years. Use of modern family planning methods decreased the risk of SPET/EC Table 4.

**Table 4. Adjusted odds ratios and 95% confidence intervals of socio-economic and reproductive status factors in developing severe pre-eclampsia.**

| Variable | SPET/EC | | *$\chi^2$ | df | P value |
|---|---|---|---|---|---|
| | Adj.OR | (95% CI) | | | |
| Patient's education: | | | | | |
| None | 1 | | 14.52 | 3 | 0.002 |
| Primary | 0.16 | 0.05-0.59 | | | |
| Secondary | 0.12 | 0.03-0.42 | | | |
| Intermediate + | 0.09 | 0.02-0.53 | | | |
| Husband's education: | | | | | |
| None | 1 | | 18.86 | 3 | 0.000 |
| Primary | 0.78 | 0.17-3.57 | | | |
| Secondary | 5.24 | 1.05-26.3 | | | |
| Intermediate+ | 22.22 | 2.97-165.9 | | | |
| Occupation: | | | | | |
| Housewife | 1 | | 26.72 | 2 | 0.000 |
| Manual worker | 13.42 | 4.47-40.25 | | | |
| Others | 0.66 | 0.21-2.11 | | | |
| Income: | | | | | |
| No income | 1 | | 10.82 | 2 | 0.004 |
| Up to 3000 Rs | 3.6 | 1.2-10.7 | | | |
| 3000 Rs + | 2.5 | 0.75-8.5 | | | |
| Religion: | | | | | |
| Hindu | 1 | | 15.78 | 1 | 0.000 |
| Non-Hindu | 9.9 | 3.04-32.32 | | | |
| Gravidity: | | | | | |
| Multigravidae | 1 | | 5.7 | 1 | 0.017 |
| Primigravidae | 2.9 | 1.17-7.39 | | | |
| History of PET: | | | | | |
| No | 1 | | 4.04 | 1 | 0.044 |
| Yes | 6.9 | 0.99-48.9 | | | |
| History of abortion: | | | | | |
| No | 1 | | 4.14 | 1 | 0.042 |
| Yes | 4.5 | 1.06-19.3 | | | |
| Use of FP: | | | | | |
| No | 1 | | 6.92 | 1 | 0.009 |
| Yes | 0.21 | 0.05-0.83 | | | |
| Age of menarche: | | | | | |
| < 14 yrs | 1 | | 26.62 | 1 | 0.000 |
| >= 14 yrs | 3.72 | 1.65-8.39 | | | |

* = change in -2 log likelihood for deletion of the factor from the model.

## DISCUSSION

This study was undertaken to examine the association between exposure to antenatal care and the risk of developing severe pre-eclampsia among women living in Kathmandu Valley. No straight relationship was found. However, varied patterns of ANC visits throughout the pregnancy were reported. Subjects developing SPET/EC differed from those having normal delivery in more commonly attending ANC in the second trimester and less commonly attending in the third trimester, irrespective of their attendance for ANC at other times during the pregnancy. The odds of stopping ANC before the third trimester compared to having ANC in all 3 trimesters were higher among subjects developing severe pre-eclampsia and eclampsia than among those having a normal delivery. In another study, conducted at Aberdeen Maternity Hospital,[1] however, failure to have ANC in third trimester was shown to be a risk factor for pre-eclampsia.

An increased likelihood of 2nd trimester and the generally earlier onset of ANC among cases, suggests that the outcome of SPET/EC in our study was not associated with a disregard for ANC by these subjects during their pregnancy. It is not reasonable, however, to conclude that ANC in the 2nd-trimester itself increases the risk of developing severe pre-eclampsia. A more satisfactory explanation is that subjects who would ultimately become severely pre-eclamptic were attending ANC more commonly than were subjects who ultimately had a normal delivery, possibly because of the appearance of early symptoms ("mild" pre-eclampsia??) during this period. It is not likely that they were doing so because of the experiences of PET in a previous pregnancy, such a history had almost no effect on the association between outcome and pattern of ANC.

This would mean that ANC, in the 2nd trimester at least, was not preventing the subsequent development of severe PET. Sixty percent the cases had had second trimester ANC. This is consistent with a study conducted in South Africa, [2] which reported that improvement in ANC had no effect on the prevalence of eclampsia, although it did reduce mortality from EC.

Both reproductive history and socio-economic characteristics had significant influences on severe pre-eclampsia.

Primigravidity, history of PET, history of abortion, and late menarche independently increased the risk of PET while use of modern contraceptive method decreased the risk.

It is well accepted that the pre-eclampsia is essentially a disease of primigravidae irrespective of age. Even if the hypertensive disease does develop in a subsequent pregnancy, it tend to be less severe.[3] However, a recently (1987-1991) undertaken case-control study at New York Mt. Sinai Medical Center could not find any significant association between primigravidae and pre-eclampsia,[4] but the explanation given was that most of the multiparous patients were impregnated by new partners making them equivalent to the nulliparous or primigravidae4.

An earlier study done in North California during 1984-1985 also did identify primigravidity as a risk factor for pre-eclampsia.[5] Though since this time, many others reports have also shown primigravidity to be a risk factor for pre-eclampsia, the underlying mechanism is still not clear. Several reports[3] have assumed an immunological basis for the mechanism. This theory of immunology is strengthened by the finding that pre-eclampsia after early abortion was similar to the incidence for a first pregnancy, but after a late spontaneous abortion the risk was significantly reduced.[6] The risk attached to primigravidity could be confounded by age, as primigravidae in general tend to be younger than multigravidae.[3,7,8] However, in our study age turned out to be not a significant predictor of risk although there was a slight but non-significant increase in risk with increasing age. In the Nepali setting, an alternative explanation, related to social factors, for the increased risk associated to primigravidity might exist. Women of younger age, and/or at first pregnancy, may be unable to explain their problems to other members of the family leading to the late health-seeking practice and thus failure to detect pre-eclampsia early, with consequent risk of severe preeclampsia. It is common in Nepal for young married women to be dominated by the in-laws's family, that so they can not express their need for health examination. Social factors may indeed play more vital role in setting like Nepal where mother in-law have the dominant role in family decision-making.

Similarly to many other studies, the present study also found a positive link between history of pre-eclampsia and the severe pre-eclampsia in the index pregnancy.[4,5] Again this could be related to the immunological theory because studies have found that pre-eclampsia developing in subsequent pregnancy tends to be less severe.[3]

Perhaps this lessened severity could be due to proper management of the disease at the proper time in subsequent pregnancies as a consequence of the mother's past experience. Existing hypertension or renal diseases could lead to repeated attacks of pre-eclampsia, but would not provide an explanation for the finding of the current study as patients having essential hypertension and renal disease were specifically excluded.

Regarding history of spontaneous abortion, this study indicates that it increases the risk of severe pre-eclampsia after adjustment for socio-economic factors. Most previous studies, however, have shown spontaneous abortion to be a protective factors,[9] It is possible that differences in the timing of spontaneous abortion could be responsible for the discrepancy. Unfortunately the gestational age at the time of abortion was not asked. One study failed to show a significant association between history of abortion and pre-eclampsia.[4]

The elevated risk of SPET/EC related to late menarche shown by this study could be a new finding. No previous reports have been located which have addressed this factor, and an obvious biological explanation is lacking. Age of menarche itself is determined by a combination of hereditary, environmental and nutritional factors, so that the association between late menarche and SPET/EC could represent two outcomes of a common underlying cause. Current medical science agrees that age of menarche is decreasing and rate of this decrement is correlated with the improvement in nutritional factors.

The only protective factor for pre-eclampsia detected is the use of modern family planning methods. Among the users of family planning methods, 80% used DMPA, 8% used OC, 8% IUD and 4% condom. Whether the effect could be related to effect of progestagenic hormones is not known. A previous study reported that use of barrier contraceptive methods carries increased risk of SPET.[10]

Among the socio-economic variables, manual workers were found to be at elevated risk for severe pre-eclampsia, although there is no documented evidenced that physical activity is associated with increased incidence of pre-eclampsia. Bed-rest, however, has been an effective method of treating pre-eclampsia.[3]

The middle income group, earning up to 3000 Rs per month, were shown to be at greater risk of SPET/EC than the no income group. This is contrary to the finding of most other studies and present concepts that low socio-economic class is a risk factor for pre-eclampsia because higher socio-economic status means better access to health facilities. The data suggest that women with even higher income may be at somewhat reduced risk, although this was not statistically significant. The finding that the "no income" group may be at reduced risk could be because this group was composed mostly of students and housewives, who tend to belong to well-to-do families, and so represent a rich and educated group.

Even after adjusting for income, non-Hindu were at a considerably greater risk of SPET/EC than Hindus. Genetic differences could be involved as the religious groups in Nepal are ethnically distinct. The lifestyles of different religious groups also tend to differ and this includes differences in diets. As detailed dietary information was not obtained in this study, it was not possible to control for the differences in diet. In this connection it may be relevant that obesity has been recorded as a risk factor for severe PET.[4]

Education, especially women's education, is taken as an important contributing factor in the improvement in general health standard of a population. The association between SPET/EC and education, shown in our study, are interesting, in that SPET/EC was significantly associated with lower education in mothers, but very strongly related with higher education of the husband. While marriage between more highly educated men and lower educated women are common and reverse extremely rare, this does not seem to provide an obvious explanation for the complex relationship between education and SPET/EC. Other studies have shown PET to be common among women of low education.[9] No study has previouly reported inverse association with husband's education. The finding of the current study might be peculiar to Nepali situation.

## CONCLUSION

This case-control study did not demonstrate that ANC could reduce the risk of severe pre-eclampsia/eclampsia among women in Kathmandu valley. Rather, women who developed SPET/EC had started ANC earlier than had controls with normal delivery. On the other hand, a history of previous PET, history of abortion, late menarche and primigravidity status each independently increased risk. Use of modern contraceptive methods decreased the risk. Risk was higher among the middle-income group manual workers and non-Hindu women.

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