# DETERMINA NTS OF PRE-ECLAMPSIA AND GESTATIONAL HYPERTENSION

Asnake Hailu*,M.D. and Derege Kebede**,M.D.

**ABSTRACT:** To examine the determinant factors for pre- eclampsia and gestational hypertension, a total of 567 pregnant women were randomly selected from 13 urban sub-districts and 13 rural villages from a central region in Ethiopia and included in the study. Albuminuria was detected in 11.5% and abnormal diastolic blood pressure in 12.2%. 2.9% and 9.2% were classified as pre-eclamptic and gestational hypertensive, respectively. Younger educated women, in a higher income category, and in their first pregnancy were found to be at a higher risk of pre- eclampsia and gestational hypertension. Strenuous physical exertion and low dietary protein intake during the early months of pregnancy also increased the risk of both pre-eclampsia and gestational hypertension. A high dietary calcium intake during the early months of pregnancy increased the risk of pre-eclampsia but not gestational hypertension.

## INTRODUCTION

Globally, an estimated 500,000 maternal deaths occur each year. Nearly all of these deaths occur in developing countries where women's health is poor and maternal health care is scarce (1). The estimates for maternal mortality in Ethiopia are 5.66 per 1000 live births (2), and 9.6 per 1000 patients (3).

Pre-eclampsia or eclampsia are recognized as one of the major complications of pregnancy. Hypertension is the commonest disorder of pregnancy (4).

Dietary factors are now suspected of being associated with the development of pre- eclampsia. Low protein content in the diet has been correlated to pre-eclampsia (5). Another observation was the inverse relation between calcium and the incidence of pre-eclampsia and gestational hypertension. Calcium has been also implicated in the pathogenesis of essential hypertension (6).

Physical activity has also been implicated in the development of pre-eclampsia and/or gestational hypertension (7), and has also been shown to affect fetal growth (8).

Population-based studies on the determinant factors for pre-eclampsia and gestational hypertension have not been reported from Ethiopia. The purpose of this study was to quantitate whether dietary protein and calcium intake and physical activity are risk factors for pre-eclampsia and gestational hypertension.

* Ada-a District Health Office, Debre Zeit Health Center, Debre Zeit.
** Dept. of Community Health, Faculty of Medicine, Addis Ababa University, P.O.Box 1176, Addis Ababa, Ethiopia

**METHODS**

The study was conducted in urban and rural communities of Ada-a district in the central part of the country in 1990/91. Ada-a district is administratively and geographically divided into 15 urban sub-districts and 293 rural peasant associations. It has a population of 294,171 (from the district administrative office in 1989). All the 15 sub-districts in the urban and 57 accessible villages in the rural were included as our sampling frame. Simple random selection was adopted for both urban and rural villages to obtain 13 urban and 13 rural villages from which all pregnant women (n=567) were included in the study.

The questionnaire comprised the following items: demographic, socio-economic and other characteristics of the pregnant woman. The total monthly family income were categorized into 0-99 Birr, 100-249 Birr, 250-449 Birr and above 500 Birr to be designated as very low, low, medium, and high respectively for use in the text. Past and current obstetric and medical history; recordings of height, blood pressure measurements and the presence of albumin in the urine were noted.

A semi-quantitative food frequency questionnaire was used which consisted of a list of 57 food items with portion sizes and a set of frequency response options to indicate how often each food is consumed during the first 20 weeks of pregnancy. The nutrient content of the food items were calculated using an Ethiopian Food Composition Table (9). Daily dietary intakes as expressed in terms of percent of caloric intake were used for grouping the pregnant women into three categories of relative nutrient intake levels: low, moderate and high intake.

The assessment of physical activity consisting of leisure time, occupational and household activities was done by use of a recall of specific physical activity during the first 20 weeks of the current pregnancy. The questionnaire had 20 physical activity items and a set of frequency response options to indicate how often a specific physical activity was carried out. Daily activity scores were developed by classifying tasks into one of the three (light, moderate, heavy) based on values for total energy expenditure reported from other studies (8). Thus light work requires $\leq$3.5 KCal/min, while moderate work involves an expenditure between 3.5-5.5 KCal/min and heavy $\geq$6 KCal/min. Examples of physical activity in each class are:- Light - walking and sweeping floor, moderate - washing cloths and carrying water from a distance and heavy - grinding grain and farm activities. The maximal intensity of physical activity performed by a subject was determined by the intensity level of the activity with the highest intensity code. Daily energy expenditure was obtained by multiplying the intensity code of each activity by its corresponding duration, and by summing up the values of all activities reported. Daily energy expenditure was then categorized into low, medium and high to divide subjects into groups based on the habitual activity to measure the relationship between physical activity and pre-eclampsia and/or gestational hypertension.

Blood pressure was measured, the mother sitting comfortably, the sphygmomanometer cuff tied on the right arm at the same level as the heart. Diastolic blood pressure was taken at the point of muffling (Phase IV) of the korotkoff sound. This measure corresponds closely to the true values in pregnancy (10). Two blood pressure measurements were taken at the mid and end of the interview by the enumerator and the supervisor respectively. Measurements done by supervisors (health assistants) were used in the analysis. Diastolic blood pressure $\geq$90 mm Hg were considered abnormal.

Random midstream urine was then collected at the end of the interview. Reading was made visually by comparing the reagent areas to the corresponding color chart on the bottle in 60 seconds. The results were recorded as negative, trace, +, ++, and +++ on the space provided. Because of the possibility of false positive results a high cutoff point, therefore, $2^+$ or more was considered as significant proteinuria.

The following operational definition of pre-eclampsia was used: diastolic blood pressure $\geq$90 mm Hg with albuminuria $\geq 2^+$.

A pre-test was carried out in Dukem clinic. Data collection was conducted twice, the first survey took six weeks, four weeks for urban and two weeks for rural. After a period of two months the second reassessment of those pregnant women who were on their first 20 weeks of gestation and were negative during the first survey was conducted and required a period of four weeks. A six day training was given for enumerators (12th grade female students) and supervisors (health assistants). The two supervisors conducted a 10% repeatability check of the pregnant women in each sub-district/village on daily basis.

Data entry was carried out via a visible screen terminal into a disc file, using a data entry program. After computer input was complete, a 2% check of all the questionnaires in the completed computer information was carried out. The analysis was done using SPSS (PC) program (11). The EPI-INFO program (12) was additionally used to assess the strength of the associations.

**RESULTS**

A total of 48,546 people were surveyed. This was 90% of the estimated total population for the study area. Of the 567 pregnant women studied, 60% were urban, and 40% rural inhabitants. 14.3% were with in the age group of 15-19, 71.4% with in 20-34 and the rest 14.3% were with in 35- 49 years of age during the survey.

21.7% were nulliparous women and those who had 1-4 live births were 56.1%. 22.2% had 5-10 live births. 60.2% were in their 3rd trimester, 30.6% in their 2nd trimester and 7.4% were in their first trimester (Table 1).

Table 1. Socio-demographic and other characteristics of pregnant women in Ada-a District, Ethiopia, 1990.

| Characterstics | | Total No. % |
|---|---|---|
| Maternal age in years | 15-19 | 81(14.3) |
| | 20-34 | 403(71.4) |
| | 35-49 | 81(14.3) |
| Parity | 0 | 123(21.7) |
| | 1-4 | 318(56.1) |
| | 5-10 | 126(22.2) |
| Period of gestation in months | 1st Trimester | 42(7.4) |
| | 2nd " | 173(30.5) |
| | 3rd " | 340(60.0) |
| | Unknown | 12(2.2) |
| Occupation | Home maker | 513(91.8) |
| | Non home maker | 46(8.2) |
| Education | Illiterate | 222(39.2) |
| | Elementary | 258(45.6) |
| | >Secondary | 86(15.2) |
| Total Family monthly income in Birr | 0-99 | 243(42.9) |
| | 100-249 | 152(26.8) |
| | 250-499 | 63(11.1) |
| | 500+ | 28(4.9) |

1 Birr = 0.48 USD

92% of the total pregnant women were homemakers. 39.2% were illiterate. 42.9% of the pregnant women had a total family monthly income of 0-99 Birr, 26.8% had 100-249 Birr, 11.1% had 250-499 Birr, and 4.9% earned 500 Birr and above.

11.5% had albuminuria. 12.2% had a diastolic blood pressure $\geq$90 mm Hg and 2.9% had pre-eclampsia. The relative risk of pre-eclampsia decreased with increasing age of mothers although this trend was not statistically significant, P>0.05 (Table 2). Pre-eclampsia was also associated with education. The lowest relative risk was among the pregnant women attended elementary school. The observed differences was however not

statistically significant. Pre- eclampsia was associated with income. The relative risk decreased with a decrease in monthly family income. The trend was statistically significant ($P<.05$).

Nulliparous women had a 6 times higher risk of developing pre-eclampsia than the rest of the study group. The difference was statistically significant ($P<.01$). Cases of pre-eclampsia tended to engaged in physical activities which require high energy expenditure during their first 20 weeks of gestation. The group of pregnant women who had a high level of energy expenditure were at risk 3 times higher than those with low level of energy expenditure. However the difference was not statistically significant.

High dietary protein intake during the first 20 weeks of gestation is observed to have a protective effect against the development of pre-eclampsia. The relative risk decreased with an increase in a daily dietary protein intake. However, the trend was not statistically significant.

In this study, low dietary calcium intake during the first 20 weeks of gestation was found to have a protective effect for pre-eclampsia. The relative risk decreased with a reduced daily dietary calcium intake. The observed trend, however, was not statistically significant.

Pregnant women in the age group of 15-19 had a 2 times higher risk of having gestational hypertension than those in the age group of 35-49. However, the difference was not statistically significant (Table 3). No association was observed between educational status and gestational hypertension.

Table 2. Distribution of Cases of Pre-eclampsia Among Pregnant Women in Ada-a District by Different Maternal Characteristics.

| CHARACTERISTICS | CASES | CONTROL | RR (95% CI) | CHI-SQUARE |
|---|---|---|---|---|
| | No (%) | No(%) | | |
| Maternal age in years | | | | |
| 15-19 | 4(23.5) | 77(14.1) | 1.0[a] | |
| 20-34 | 12(70.6) | 391(71.3) | 0.59(0.17,.6) | 1.9 |
| 35-49 | 1(5.9) | 80(14.6) | 0.24(0.01,2.72) | |
| Education | | | | |
| Illiterate | 5(29.4) | 217(39.5) | 0.5(0.14,1.65) | |
| Elementary | 1(5.9) | 85(15.5) | 0.26(0.01,1.87) | 1.7 |
| >Secondary | 11(64.7) | 247(45.0) | 1.0[a] | |
| Total family monthly income in Birr | | | | |
| 0-99 | 5(29.4) | 270(49.2) | 0.3(0.06,1.07) | 12.78 |
| 100-249 | 6(35.3) | 194(35.3) | 0.4(0.11,1.7) | (4.7)** |
| 250+ | 6(35.3) | 85(15.5) | 1.0[a] | |
| Parity | | | | |
| Primi | 10(58.8) | 112(20.4) | 5.6(1.83,15.92) | 0.0008*** |
| Others | 7(41.2) | 437(79.6) | 1.0[a] | |
| Total energy expenditure | | | | |
| Low | 1(5.9) | 89(16.2) | 1.0[a] | |
| High | 16(94.1) | 460(83.8) | 3.0(0.47,131) | 0.22*** |
| Daily protein intake | | | | |
| Low | 1(5.9) | 14(2.5) | 5.1(0.06,403.5) | |
| Moderate | 15(88.2) | 464(84.5) | 2.3(0.34,97.9) | 1.2 |
| High | 1(5.9) | 71(13.0) | 1.0[a] | |
| Daily calcium intake | | | | |
| Low | 1(5.9) | 47(8.6) | 0.42(0.01,5.44) | |
| Moderate | 13(76.5) | 443(80.7) | 0.58(0.15,3.25) | 0.48 |
| High | 3(17.6) | 59(10.7) | 1.0[a] | |

[a] Referent category * 1 Birr=0.48 USD ** P<0.05 (trend test) *** P-Value for Fischer's exact test

Gestational hypertension was associated with income. The relative risk decreased with a decrease in the monthly family income. However, the trend was not statistically significant.

Parity was also associated with gestational hypertension. The relative risk for primiparous women was two times higher than the others. The observed difference was however not statistically significant.

Physical activities which required high energy expenditure during their first 20 weeks of gestation were associated with gestational hypertension. The group of pregnant women who had a high level of energy expenditure had five fold higher risk than those with low level of energy expenditure. The observed difference was statistically significant ($P<.05$).

Distribution of cases of gestational hypertension have little or no variation in the three categories of protein intake. The relative risk was lower in the group with moderate daily dietary protein intake. However, the difference was not statistically significant.

Low dietary calcium intake during the first 20 weeks of gestation was associated with gestational hypertension. The relative risk increased with the reduced dietary calcium intake. The observed trend was however not statistically significant.

**DISCUSSION**

The risk of pre-eclampsia decreased with increasing age. A "J shaped" curve have been reported for the relationship between maternal age and the incidence of pre-eclampsia in nulliparous women (13).

Cases of pre-eclampsia tended to be among the group who attended secondary school or more. This is in general agreement to other reports where pre-eclampsia was more common among the highly educated group (14).

Table 2. Distribution of Cases of Pre-eclampsia Among Pregnant Women in Ada-a District by Different Maternal Characteristics.

| CHARACTERISTICS | CASES | CONTROL | RR (95% CI) | CHI-SQUARE |
|---|---|---|---|---|
| | No (%) | No(%) | | |
| Maternal age in years | | | | |
| 15-19 | 11(21.2) | 66(13.3) | 1.5(01.51,4.57) | |
| 20-34 | 33(63.5) | 358(72.2) | 0.83(0.36,2.17) | 0.79 |
| 35-49 | 8(15.3) | 72(14.5) | 1.0[a] | |
| Education | | | | |
| Illiterate | 24(46.2) | 193(48.6) | 1.0[a] | |
| Elementary | 19(36.5) | 131(33.0) | 1.2(0.58,2.32) | 1.66 |
| >Secondary | 9(17.3) | 73(18.4) | 0.99(0.39,2.34) | |
| Total family monthly income in Birr | | | | |
| 0-99 | 19(44.2) | 221(51.6) | 1.0[a] | |
| 100-249 | 13(30.2) | 133(31.1) | 1.14(0.5,2.52) | 1.6 |
| 250+ | 11(25.6) | 74(17.3) | 1.7(0.71,4.03) | |
| Parity | | | | |
| Primi | 17(32.7) | 95(19.1) | 2.1(1.03,3.95) | |
| Others | 35(67.3) | 402(80.9) | 1.0[a] | 5.4 |
| Total energy expenditure | | | | |
| Low | 2(3.8) | 87(17.5) | 1.0[a] | |
| High | 50(96.2) | 410(82.5) | 5.3(1.35,45.77) | 7.3** |
| Daily protein intake | | | | |
| Low | 11(21.2) | 60(12.1) | 1.1(0.20,11.46) | |
| Moderate | 39(75.0) | 425(85.5) | 0.55(0.12,5.25) | 1.9 |
| High | 2(3.8) | 12(2.4) | 1.0[a] | |
| Daily calcium intake | | | | |
| Low | 5(9.6) | 42(8.5) | 1.6(0.33,8.74) | |
| Moderate | 43(82.7) | 400(80.5) | 1.5(0.51,5.88) | 0.5 |
| High | 4(7.7) | 55(11.0) | 1.0[a] | |

[a] Referent category * 1 Birr=0.48 USD ** P<0.05 (trend test) *** P-Value for Fischer's exact test

Pre-eclampsia was significantly more common among the group with a relatively higher income. Most studies on risk factors for pre-eclampsia were conducted in developed countries within homogeneous income groups and were unable to measure the relationship between income and pre-eclampsia.

A significant association was observed between pre-eclampsia and parity. Nulliparous women had a higher risk of pre-eclampsia. This finding is in agreement with those of some other studies, where pre-eclampsia was considered predominantly a disease of nulliparous women (10,15). Hypertensive disorders of pregnancy are taken to be essentially diseases of primigravidae. Even if hypertensive disorders recur in a subsequent pregnancy it tends to be less severe. The combination of age 35 or more and being a primigravida leads to a particularly high risk of severe pre-eclampsia (16). Other study considered relative proportion of primigravidae of 1.3 or more as a test for a valid definition of pre-eclampsia (15). In our case the relative proportion is 1.4.

The result from this study suggests that women who had physical activities which require high energy expenditure during the first 20 weeks of their pregnancy are at a higher risk of pre-eclampsia. Another report suggested a protective effect of leisure time physical activity on pre-eclampsia (7). However, their report focused mainly on leisure time activities in affluent communities. The non significant results observed might be the reflection of the smaller sample size.

Low dietary protein intake in the first 20 weeks of gestation was observed to be a risk factor for the development of pre-eclampsia. This was in agreement with another study (4).

Low dietary calcium intake was negatively associated with pre-eclampsia. This is in contrast to other findings where calcium has been shown to be protective (6). It is likely that this is a chance finding as the association was not statistically significant.

Gestational hypertensive women were also observed to be younger than the controls. This however is in contrast to other reports where a "J" shaped curve for the relationship between maternal age and gestational hypertension which was probably attributed to the unmasking of latent hypertension in these older women is seen (16).

Education was observed to have no significant effect on the development of gestational hypertension. However, the effect of education on the development of gestational hypertension cannot be differentiated from that of the socio-economic status. Gestational hypertension was significantly more common among the group with a relative higher income. Most studies on risk factors for gestational hypertension were done in developed countries with homogenous income groups and did not measure the relationship between gestational hypertension and income. Nulliparity was also observed to be a risk factor for gestational hypertension. The finding is also in agreement with those of some other studies where gestational hypertension was accepted as essentially a disease of nulliparous women (10,15,16).

The result of this study suggests that women who had physical activity which require high energy expenditure during the first 20 weeks of gestation are at a higher risk of developing gestational hypertension. However, a study from Europe suggested a protective effect of leisure time physical activity on gestational hypertension (7). However, this study was based on a high socio-economic group where the extent of physical activity is different from ours. Thus similar studies on a similar population base are required for comparison.

In this study it was observed that dietary protein intake has no influence on the development of gestational hypertension. This is in agreement with suggestion from other reports where protein diet was considered not to influence the occurrence of gestational hypertension (16).

Higher levels of dietary calcium intake in early pregnancy is observed to be protective against the development of gestational hypertension. This finding is in agreement with those of other findings where a negative

dose- response relationship was observed between calcium supplementation and blood pressure levels (6). The observed non-significant difference might be due to the smaller sample size used in the study.

The results from this study are unlikely to be biased. Exposure data that was collected (diet, physical activity, etc.) was on the first 20 weeks of gestation prior to the occurrence of outcome measures. This assumed an appropriate temporal sequence between the exposure and the disease. The information collected was prior to the classification of cases and controls. The enumerators being non-health professionals making them unaware of the objective of the study was possible. The place and circumstance of interview and measurements were similar.
Because of the gender similarity of enumerators, the cooperation from the study group was very high.

The problem of differentiating secondary hypertension from that of gestational hyper-tension is problematic since it requires post partum evaluation. Random misclassification as a result of the inherent variability of blood pressure, the use of questionnaires for the assessment of diet and physical activity, is likely to occur in our results. Our use of the second measurement of two BP measurements and a cut-off point to classify hypertensive is likely to reduce this misclassification. Moreover, the misclassification will be non directional with a tendency to decrease the relative risk. Because of the small number of cases the confounding effect of several variables were also not controlled.

In conclusion, pre-eclamptic women tended to be younger, attended secondary school or higher and earn a relatively high monthly income. Nulliparity was observed to be a risk factor for the development of pre-eclampsia. Strenuous physical activity during the early periods of gestation is observed to be a risk factor for pre-eclampsia. A protective effect of high dietary protein intake in early pregnancy was also observed. No association between dietary calcium intake in early pregnancy and preeclampsia was found.

Gestational hypertensive women also tended to be younger, and earn a relatively higher monthly income. Education showed no influence in the occurrence of gestational hypertension. Nulliparity was observed to be a risk factor for gestational hypertension. Physical activity which requires high energy expenditure during the first 20 weeks of gestation was observed to be a risk factor for gestational hypertension. Differences in dietary protein intake showed no influence on the occurrence of gestational hypertension. High dietary calcium intake was observed to have a protective effect against the development of gestational hypertension.

Pregnant women normally have lower total serum proteins, reduced albumin-globulin ratio and reduced oncotic pressure of the plasma. These are further decreased in pre-eclampsia or eclampsia. Animal experiments show that the lower albumin concentration is accentuated if the maternal diet is low in protein (4,5). Thus a low dietary protein intake in early pregnancy will likely increase the risk of pre- eclampsia.

A higher dietary calcium reduces the level of parathyroid hormone which in turn reduces the cytosolic calcium ion resulting in reduced muscular reactivity and eventually in reduced blood pressure. A low dietary calcium has the opposite effect (6). Thus a low dietary calcium intake in early pregnancy will likely increase the risk of developing hypertension.

Further research on the magnitude and determinants of high risk pregnancies should be encouraged. Until such a time when conclusive evidence is obtained on the protective effect of a high protein and calcium diet and moderate physical activity, specific nutrition education to encourage a high dietary protein and calcium rich intake and advice on physical activity during pregnancy should probably be part of the strategies in the health care services for pregnant women.

**ACKNOWLEDGEMENTS**
The study was supported by a grant from the International Development Research Center, Canada (IDRC). We gratefully acknowledge the cooperation given by the Peasant Associations in Ada-a district, the City

Council of Debre-zeit town, the districts, sub-districts and rural villages involved in the survey, the enumerators and supervisors, the pregnant women enrolled in this study, the Ministry of Health for allowing use of existing resources in the respective health service units.

We also thank Dr.Francis Aboud for her assistance in data processing, Dr.Adanetch KidaneMariam for her kind help and advice in the preparation of the protocol, W/O Woudie Fikre, for her help in the training programme, and W/t Manyaheleshal Kebede for typing the manuscript.

**REFERENCES**

1. Population reports, September. *Maternal Health in the Community,* Series L, 1988; No.7, pp 1-26.
2. Kwast BE, W Kidanemariam, EM Seid and FGR Fowkes. Epidemiology of maternal mortality in Addis Ababa, A community based study. *Ethiop. Med. J.* 1985; 23:7-16.
3. S Yoseph and G Kifle. A six year review of maternal mortality in a teaching hospital, Addis Ababa, Hospital based study. *Ethiop. Med. J.* 1988; 26:(3):115-119.
4. Charles P. MC Cartney. *Toxemia of pregnancy in obstetrics* (eds. Greenhill), W.B.Sounders Company, Philadelphia and London, 13th edition, chapter 31, 1965; 501-34.
5. Briend A, C Carles. Protein deficiency and pregnancy toxemia in Africa, *Lancet,* 1978; 8056:146.
6. Belizan JM, J Villar, J Repke. The relationship between calcium intake and pregnancy induced hypertension. *Am. J. Obstet. Gynecol,* April 1988; 158(4): 898-902.
7. Marcoux S, J Brisson, J Fabia. The effect of leisure time physical activity on the risk of pre-eclampsia and gestational hypertension, *Journal of Epidemiology and Community Health,* 1989; 43:147- 152.
8. N. Tafari, RL Naeye, A Gobezie. Effects of maternal undernutrition and heavy physical work during pregnancy on birth weight, *British Journal of Obstetrics and Gynecology,* March 1980; 87:222-226.
9. Agren G, R Gibson. *Food Composition Table for use in Ethiopia*. The food analytical department, children's nutrition unit, Addis Ababa, 1968.
10. Davey DA, I MacGillivary. The classification and definition of hypertensive disorders of pregnancy. *Am. J. Obst. Gynecol*. 1988; 158(4):893-898.
11. Statistical package for social sciences (SPSS) Version II, 1989.
12. EPI-INFO Version V, June 1990 Georgia.
13. Chesly LC, BM Sibai. Clinical significance of elevated mean arterial pressure in the second trimester, *American Journal of Obstetrics and Gynecology,* 1988; 159(2): 257-259.
14. Klebanoff MA, PH Shiano, GG Rhoads. Outcomes of pregnancy in a national sample of resident physicians, *The New England Journal of Medicine,* 1990; 323(15): 1040-1045.
15. Redman CWG, M Jefferies. Revised definition of pre-eclampsia. *Lancet,* April 9, 1988; 809-812.
16. World Health Organization. The hypertensive disorders of pregnancy. Genva, *Technical report series,* 1987; 758:20-29.