Dietary intake of Ca^{2+} and Mg^{2+} in subjects with Pregnancy Induced Hypertension

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DECLARATION

I hereby humbly declare that this Thesis entitled '**Dietary intake of Ca^{2+} and Mg^{2+} in subjects with Pregnancy Induced Hypertension**' is based on works carried out by me. No part of it has been presented previously for any higher degree.

The research work carried out in:

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetrics and Gynecology
ADA	American Diabetic Association
AVP	Arginine Vasopressin
BIRDEM	Bangladesh Institute of Research and Rehabilitations in Diabetes, Endocrine and Metabolic Disorders
BIHS	Bangladesh Institute of Health sciences
BMI	Body Mass Index
BMRG	Biomedical Research Group
BP	Blood Pressure
Ca^{2+}	Calcium
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
EASD	European Association for the study of diabetes
ESR	Erythrocyte Sedimentation Rate
ELISA	Enzyme Linked Immunosorbent Assay
FAO	Food and Agriculture Organization
g	Gram
GH	Gestational Hypertension
GFR	Glomerular Filtration Rate
INFS	Institute of Nutrition and Food Science
IU	International Unit
IUGR	Intra Uterine growth Retardation
Kg/m^2	Kilogram per miter square

L	Liter
Mg^{2+}	Magnesium
MBP	Mean Blood Pressure
M	Mean
Mg/day	Milligram per day
MM	Maternal Mortality
Mmol/l	Milimole per liter
mmHg	millimeter mercury
MMR	Maternal Mortality Rate
mg	Miligram
Nacl	Sodium Clorlde
OPD	Out Patient Department
PE	Preeclampsia
PIH	Pregnancy Induced Hypertension
PM	Perinatal Mortality
PP	Postprandial
RDA	Recommended Dietary Allowances
RDI	Recommended Dietary Intake
SBP	Systolic Blood Pressure
SPSS	Software Statistical Package for Social Science
SD	Standard deviation
SE	Standard error
μg	Microgram
US	United States
Vit B_2	Riboflavin

Vit B_6	Pyridoxine
WHO	World Health Organization

ABSTRACT

Pregnancy Induced Hypertension (PIH), comprising of both proteinuric (preeclampsia or PE) and nonproteinuric (gestational hypertension or GH), is one of the major complications of pregnancy which, if uncontrolled, may lead to eclampsia with potentially life threatening consequences for the mother as well as for the child. The incidence of PIH is particularly high in developing countries due to lack of proper antenatal care and it is thought to be nearly 20% among Bangladeshi pregnant women. Hypocalcemia and hypomagnesemia have been implicated in the pathophysiology of PIH and Mg supplementation to pregnant mothers has already been started as a routine practice in some of the hospitals in Bangladesh. However, a balanced diet during pregnancy with adequate Ca and Mg should be the ideal solution and to proceed in this direction evidence is required on the nature and extent of Ca and Mg deficiency in the diet of the PIH mothers in a specific society. In the context of the lack of such evidence the present study was undertaken to assess the dietary intake (along with sources) of Ca and Mg in PIH (compared to Non-PIH) mothers and to explore the factors affecting the intake of those nutrients in the two groups.

Under an observational Case-control design 150 pregnant mothers with PIH (PIH Group), along with 150 mothers without PIH (Non-PIH Group), aged between 20-40 yrs, were purposively recruited (from 3 tertiary hospitals in Dhaka) at the 3rd trimester of their pregnancy. PIH was diagnosed by hypertension, with or without proteinuria and/or edema. *Hypertension* was defined following the criteria of the American College of Obstetrics and Gynecology BP equal to or greater than 140/90 mm of Hg, rise of systolic BP 30 mm/Hg or more and rise of diastolic BP 15 mm of Hg or more. *Edema* was

defined as: Dependent edema greater than 1+ pitting edema after 12 hour of rest in bed /or weight gain in excess of 2 pound per week, or particularly sudden weight gain over 1or2 days. Proteinuria was defined as two random clean catch urine specimens with 2+ or more on reagent strip and with urinary albumin-creatinine ratio (ACR) cut of value > 0.35.

The dietary Ca intake [(mg/day), Median (Range)] was significantly lower [265(111-487)] in the PIH as compared to the Non-PIH [350(201-984); ($p<0.001$)] group. Dietary intake Mg (mg/day), was also found to be significantly lower in the PIH [235(122-391)] compared to the Non-PIH [309(306-497);($p<0.001$)] group]. On bivariate analysis, the dietary Ca and Mg intakes had significantly negative correlation with mean blood pressure (MBP) which is used an indicator of the severity of PIH ($r=-0.276$;$p<0.001$) and ($r=-940$;$p=021$) for Ca and Mg respectively . On logistic regression analysis, PIH was found to be significantly associated with lower intake of Ca ($\beta=-0.009$; $p<0.001$) and Mg ($\beta=-0.016$; $p<0.001$) when the effects of age, family history of HTN and family income were adjusted. On multiple regression analysis, dietary Ca and Mg intake was found to be significantly associated with HTN ($p<0.001$). The main sources of dietary Ca and Mg were found to be fish, meat and dairy products and those were significantly lower ($p<0.001$) in the diet of the PIH compared to the Non-PIH group. In conclusion, the present data indicate that, dietary consumption of Ca and Mg during pregnancy are much lower than those recommended in our population, PIH seems to have an association with dietary deficiency of Ca and Mg in our pregnant women and inadequate of Ca and Mg are related to low intake of fish, meat and dairy products which, in turn, may have a linkage with family income of a woman.

Chapter 1

INTRODUCTION

1. INTRODUCTION

Pregnancy induced hypertension (PIH) is one of the major complications of pregnancy which includes both gestational hypertension (GH) and preeclampsia (PE). Gestational hypertension is characterized by an abnormal rise in blood pressure that usually develops after the 20^{th} week of pregnancy.

Preeclampsia is defined as the combination of high blood pressure (hypertension), swelling of the face and hands (oedema), and protein in the urine (albuminuria, proteinuria) (Solomon, 2001). Woman with PE, of seizures that cannot be attributed to other causes with potentially life threatening consequences for both mother and child. If the condition progresses to eclampsia, life-threatening convulsions and coma can occur.

PIH can also result in preterm labor and delivery and low-birth-weight infants. Preeclampsia ranges in severity from mild to severe; the mild form is sometimes called proteinuric pregnancy-induced hypertension or proteinuric gestational hypertension. It complicates 3-5% first pregnancies and 1% of subsequent pregnancies with around 5-10% cases being severe (Robson 1999).

The incidence of PIH in developing countries is particularly high due to lack of proper care of the mother during pregnancy. Geographic, social, economic and racial differences are responsible for an incidence that is up to three times higher in some populations (Lopez Jaramilleo, 2001). The worldwide incidence of the disease is still high in spite of the significant improvement of mother and childcare over the last decades. Mortality from hypertensive disorders is much higher reaching rates of 70-120 per 100 thousand maternities (Robson, 1999). It is the main cause of maternal mortality in these countries and is associated with a 5-fold increase in perinatal mortality (Lopez Jaramilleo 2001). PE and GH (together

considered as pregnancy induced hypertension or PIH) are thus highly important public health problems.

PIH is a multi system syndrome characterized by vasoconstriction, metabolic changes, and endothelial dysfunction, activation of coagulation cascade and increase inflammatory response. PIH contributes to (MMR) Maternal Mortality Rate, Prenatal mortality rate and still birth with variations to geographical location and race (Duckitt, 2005).

Hypertensive disorders of pregnancy are frequent cause of maternal and fetal morbidity and mortality, the most common being preeclampsia and eclampsia. Pregnant mothers should be screened routinely. Early recognition and prompt care form a multidisciplinary service, including obstetrics, cardiology, and hypertensive disorders of pregnancy reflect endometrial endothelial dysfunction and abnormalities and systematic endothelial dysfunction, which might predict future cardiovascular disease in these young women, prompting early preventive measures (Duley, 2003).

In a study it was stated that in most of the countries, PIH is the single largest cause of maternal mortality. WHO (2000), stated that maternal mortality is said to be an indicator of social inequity and discrimination against women. The Goal of national health policy was to reduce maternal mortality rate to 100 / 1, 00,000 like births by 2010 (Chang, 2003).

In Global, Pre-eclampsia or PIH is a condition that affects up to 80% of pregnancies every year and is among the leading cause of maternal and fetal illness worldwide .The incidence of pre-eclampsia and eclampsia was higher in the developing countries with the highest rate reported for pre-eclampsia as 7.1% in Zimbabwe and for eclampsia as 0.81% deliveries in Columbia. The Maternal and fetal mortality rate was 0.4% for pre-eclampsia reported in Magpies and as 6.1%

for eclampsia reported from Columbia. Hypertension disorders of the pregnancy are the common and direct cause of maternal deaths in South Africa. 19.1% of maternai deaths in a three year period (2002-2004) were associated with hypertensive disorders of pregnancy (Lopa Banerje, 2010).

A study was conducted in US, stated that pregnancy associated hypertension is a leading cause of maternai death. The study reported Maternal death rate in 2005 was 9.8/1, 00,000 (Berg, 2010).

In national level, the developing countries like India, the maternal and prenatal mortality rates are still high. It is of great concern to suggest mothers to improve the health status of the Mother and the child. It is well accepted that only a healthy mother can give birth to a healthy baby. In 2003, Maternal mortality has declined to 301/1, 00,000 live births. A study was conducted on comprehensive antenatal care and prevention of pregnancy induced hypertension. Hypertensive disorders in pregnancy are a universally common disease. How pregnancy induces and aggravates hypertension is still not understood fully. The incidence of pregnancy induced hypertension (PIH) in India ranges from 5-15%. In Primi mothers 16% and Multi mothers 7%.

It causes IUGR leading to low birth weights. It increases the maternal mortality by 10-15% and the prenatal mortality and morbidity by 15 to 25%. PIH can be detected early during regular prenatal visits, which is one of the reasons they are so very important. PIH can be result in preterm baby, a stillborn baby and a baby who has growth retardation (IUGR) (Dutta, 2001).

A study was conducted on incidence of pregnancy induced hypertension and the effects of mother and fetus in Shangai. There were 158,790 deliveries in ten years. The total numbers of PIH were 8,852 cases. The incidence of PIH was 5.57%. The rate of mild, moderate and severe PIH was 55.83%, 29.39%, and

14.78% respectively. There were 114 cases (1.29%) complicated with preeclampsia. The rate if caesarean section of placenta 0.52%, heart failure 0.34%, renal failure 0.20%, DIC 0.03%, maternal death one cases. The prenatal death 66 occurred in cases (7.18@1000) in which fetal death 48 cases, still birth 12 and neonatal death. The incidence of PIH and the rate of prenatal infant death can be reduced by strengthen antenatal monitoring, prevention, early diagnosis and treatment of PIH (Huang, 2001)

A study was conducted in Ohio, to compare the frequency of the adverse fetal outcome in women who developed PIH with or without Proteinuria. The findings revealed that in women who have pre-eclampsia has increased the rate of preterm delivery (25%) and delivery of small for gestational age (20.8%) infant (Buchbinder, 2002)

Although a fairly good degree of knowledge has now been accumulated on the etiopathogenesis of PIH, the exact biochemical events leading to the disorder remain still unclear. The disease is known to have genetic, environmental and nutritional basis (Lopez et al, 2001). Many different factors, i.e. lack of nutrients, poverty, dietary habit, and lack of exercise or many other lifestyle changes might play an important role in the development of this disease. The cause of PIH is unknown, although several factors have been shown to contribute. PIH is more common in women during their first pregnancy, as well as in women who are obese, who have diabetes, or who have gestational hypertension. Women who have had preeclampsia during a previous pregnancy are also at increased risk.

Preeclampsia has also been associated with calcium deficiencies, antioxidant deficiencies, older maternal age, and job stress. Women with even mild preeclampsia must be monitored carefully by a healthcare professional. Hospitalization may be necessary to enable close observation.

Recent studies have emphasized that possible role of general nutritional deficiency or imbalance of several specific nutrients in the etiology of the disease. Prescription medications to reduce high blood pressure may be used. The categories of prescription drugs known as diuretics are commonly used to treat hypertension. Other treatment for preeclampsia includes strict bed rest, maintenance of normal salt intake, intravenous magnesium sulphate, and possibly hospitalization for observation. The definitive conventional treatment of preeclampsia is induced delivery or caesarean section.

Dietary changes that may be helpful for preventing PIH. Unlike the conditions that cause high blood pressure, salt restriction and use of diuretics can worsen PIH by reducing blood flow to the kidneys and placenta (Franx, 1999) In preeclampsia, unrestricted use of salt and an increased consumption of water are needed to maintain normal blood volume and circulation to the placenta (Moutquin, 1997) Data from one preliminary study suggest that diets high in Tran's fatty acids are associated with an increased risk of PIH (Williams, 1998) Tran's fatty acids are found in foods that contain partially hydrogenated vegetable oils, such as margarine. Foods that have been deep-fried (eg, French fries) are also rich sources of Trans fatty acids.

Lifestyle changes also may be helpful. Regular prenatal care is essential for the prevention and early detection of PIH. Job stress (lack of control over work pace and the timing and frequency of breaks) may be detrimental, and reducing job stress may be beneficial in the prevention of PIH (Wergeland, 1998). In a preliminary study, women exposed to high job stress were found to be at greater risk of developing PIH and, to a lesser extent, gestational hypertension than were women exposed to low job stress. In this study, evaluation of job stress was based on scores assessing on-the-job psychological demand and decision-making latitude. High stress was defined as high psychological demand with low decision

latitude, and low stress was defined as low-demand, high-latitude (Marcoux, 1999). For women with PIH, obstetricians and midwives often recommend bed rest and lying on the left side; this position helps reduce oedema and lower blood pressure by increasing urinary output (Katz, 1990). However, a review of clinical trials concluded that bed rest can significantly worsen pregnancy-induced hypertension (Allen, 1999).

Nutritional supplements may be helpful. In one preliminary trial, women with a previous pregnancy complicated by PIH and high homocysteine supplemented with 5 mg of folic acid and 250 mg of vitamin B_6 per day, successfully lowering homocysteine levels (Leeda, 1998). In another trial studying the effect of vitamin B_6 on PIH incidence, supplementation with 5 mg of vitamin B_6 twice per day significantly reduced the incidence of PIH. Women in that study were not, however, evaluated for homocysteine levels (Wachstein, 1956). In fact; no studies have yet determined whether lowering elevated homocysteine reduces the incidence or severity of PIH. Nevertheless, despite a lack of proof that elevated homocysteine levels cause PIH. Lycopene is a carotenoid found in tomatoes, watermelon, and several other foods. The concentration of lycopene in the blood has been found to be significantly lower in women with PIH than in healthy pregnant women. In a double-blind trial, supplementation of pregnant women with lycopene significantly reduced the incidence of PIH by 51.4%, compared with a placebo (Sharma, 2003). The amount of lycopene used was 2 mg twice a day; treatment was begun between the sixteenth and twentieth week of pregnancy and was continued until delivery.

A marginal zinc deficiency has been reported in some women with PIH (Lazebnik, 1989; Cherry, 1981). The common practice of prescribing iron and folic acid supplements to pregnant women can lead to reduced zinc absorption (Simmer,1987). Trials studying the relationship between zinc supplementation and

PIH incidence have produced conflicting results. In one double-blind trial, the incidence of PIH was significantly lower in women receiving a multivitamin-mineral supplement, which provided 20 mg of zinc per day, than in women who received the same supplement without zinc (Hunt, 1984). However, in another double-blind trial, a higher incidence of PIH was reported in pregnant women given 20 mg of zinc per day than was reported in women given a placebo (Mahomed, 1989). In yet another trial, zinc supplementation failed to prevent PIH (Jonsson, 1996).. Therefore, current evidence does not sufficiently support the use of zinc as a way to protect against PIH.

Women with PIH have been found to be depleted in antioxidants (Tabacova, 1997; Mutlu-Turkoglu, 1998). Some (Valsecchi, 1995) but not all studies (Schiff, 1996) have reported deficiencies in vitamin C, vitamin E, and beta-carotene in PIH patients. In a double-blind trial, supplementation of vitamin C (1g/day) and vitamin E (400 IU per day) reduced the incidence of preeclampsia by 76% in women at high risk (Chappell, 1996). However, for those already suffering from this condition, supplementation with these same vitamins has led to only in significant effects (Gulmezoglu, 1997).

Deficiency of a variety of nutrients like Ca and Mg has been reported in patients with PIH. Ca and Mg are known to play major roles in modulating insulin secretion and sensitivity. Ionized Ca plays a central role in the secretion of insulin from pancreatic β cells (Grapengiesser et al, 1993). On the other hand, Ca as well Mg has critical roles in mediating insulin action in peripheral tissues. Thus the relationship of these ions with the distal process of insulin secretion and action are linear. There are reports of decreased Mg and Ca in the serum of PIH patients and it has been claimed that serum calcium deficiency and increased intracellular Ca

concentration during late pregnancy contributes to the pathogenesis of PE (Hojo, 1999). There is correlation between intracellular Ca and arterial tension (Pereyra, 1991). Some authors reported an inverse association between Ca intake and maternal BP and the incidence of PE (Paolisso, 1990).

Regular nutrient intake for adequate maternal reservoir is needed to meet foetal nutritional requirements, without imposing any negative health effects to the mother.

Inadequate intake of calcium is a public health concern among pregnant women in several societies. The importance of calcium during human pregnancy and lactation was reviewed by Prentice (2000). In addition to the well-known physiological functions, other possible health effects, including weight and body fat regulation and prevention of some chronic diseases have been suggested for calcium. The negative effects of inadequate calcium consumption on maternal and foetal bone health and development and the positive effects of maternal supplementation with calcium on the blood pressure of the offspring have also been proposed. Most of the calcium is transferred to the fetus during the third trimester of pregnancy. The importance of adequate calcium intake has led to recommendations to include calcium-rich foods/supplements into dietary guidelines. In addition, calcium supplementation was recommended for pregnant women who take =1 serving of calcium-rich food products daily. While available evidence has suggested that a high proportion of Iranian population does not consume enough calcium, data on dietary calcium intake among pregnant women in different parts of the country is lacking. Hence, the aim of this study was to determine the adequacy of calcium intake among urban pregnant women in Ahwaz, south west Iran (Majid, 2005).

Calcium deficiency has been associated with PIH (Hojo, 1995). In numerous controlled trials, oral calcium supplementation has been studied as a possible preventive measure (Hojo, 1997). While most trials have found a significant reduction in the incidence of preeclampsia with calcium supplementation, some have reported no change (Levine, 1997).

An analysis of double-blind trials (Bucher, 1996) found calcium supplementation to be highly effective in preventing PIH. However, a large and well-designed double-blind trial (Levine, 1997) and a critical analysis (Sibai, 1998) of six double-blind trials (Levine, 1997) concluded that calcium supplementation did not reduce the risk of PIH in healthy women at low risk for PIH. For healthy, high-risk (ie, calcium deficient) women, however, the data show a clear and statistically significant beneficial effect of calcium supplementation in reducing the risk of PIH (DerSimonian, 1999).

The National Institutes of Health recommends an intake of 1,200 to 1,500 mg of elemental calcium daily during normal pregnancy. In women at risk of PIH, most trials showing reduced incidence have used 2,000 mg of supplemental calcium per day. Nonetheless, many doctors continue to suggest amounts no higher than 1,500 mg per day (Moutquin, 1994).

Results from epidemiologic studies and clinical trials of non pregnant adults suggest that dietary calcium may play a role in the etiology, prevention, and treatment of primary hypertension (Hamet, 1995). For example, in the Dietary Approaches to Stop Hypertension (DASH) trial, feeding a combination diet consisting of 8–10 servings/d of fruit and vegetables and nearly 3 servings/d of low-fat dairy products resulted in reductions in systolic and diastolic blood pressure of 5.5 and 3.0 mm Hg, respectively, compared with the control diet (low in fruit, vegetables, and dairy products), and reductions of 2.7 and 1.9 mm Hg,

respectively, compared with a diet high in fruit and vegetables only (Appel, 1997). Although the nutrient or nutrients in dairy products responsible for the observed blood pressure–lowering effect could not be identified in the DASH study, calcium is a likely contributor. A recent meta-analysis of 33 randomized, controlled clinical trials involving a total of 2412 patients showed that daily supplementation with 1000–2000 mg Ca+ reduced systolic blood pressure by 1.27 mm Hg (95% CI: -2.25, -0.29) (Bucher, 1996). The more modest reduction in diastolic blood pressure of 0.24 mm Hg (95% CI: -0.92, 0.44) was not significant. Although the effect of calcium on blood pressure in the general population appears modest, calcium supplementation may be more relevant for certain subgroups, such as sodium-sensitive individuals, populations with inadequate calcium intake, and women with PIH (Hamet, 1995; Bucher, 1996).

Magnesium deficiency has been implicated as a possible cause of PIH (Wynn, 1988). Magnesium supplementation has been shown to reduce the incidence of PIH in high-risk women in one trial (Conradt, 1985), but not in another double-blind trial (Spatling, 1988).

Magnesium is an essential element in biological systems. Magnesium occurs typically as the Mg^{2+} ion. It is an essential mineral nutrient for life(Leroy, 1926; Lusk, 1968; Marschner, 1995) and is present in every cell type in every organism. For example, ATP (adenosine triphosphate), the main source of energy in cells, must be bound to a magnesium ion in order to be biologically active. What is called ATP is often actually Mg-ATP. Similarly, magnesium plays a role in the stability of all polyphosphate compounds in the cells, including those associated with DNA- and RNA synthesis.

Mg2+ plays an important role in glucose homeostasis (Paolisso, 1990; yajjket et al, 1984) and it is involved on multiple levels of insulin secretion and action

(Ivandic et al, 1988). The ion has been demonstrated as a second messenger for insulin action (Lastrah, 1974). Thus it has been thought to be an important factor in the pathogenesis of PE. Conflicting evidence, however, exists regarding serum Mg^{2+} level in PIH. Some studies suggest that elevated ionized Mg2+ in the serum may play a role in the prediction of the disease (Sanders et al, 1999). Other studies however showed that a reduction in ionized as well as total serum Mg^{2+} with increasing gestational age is a normal phenomenon in pregnancy and it is also found in cases with PIH (Standley et al, 1997).

Several studies have demonstrated a higher than expected frequency of magnesium deficiency in patients with PIH. Hypomagnesemia may play a role in the development of PIH The mean dietary magnesium intake of pregnant women is 35-58% of the recommended dietary allowance of 450 mg. Low-income women consumed 97-100 mg magnesium/1,000 kcal while women with higher incomes averaged 120 mg/1,000 kcal. Diets high in fat and sugar and low in whole grains, vegetables and fruits have a lower magnesium density. Magnesium content of water can also make a significant contribution to magnesium intake. Magnesium from prenatal supplements, if present, is seldom more than 100 mg. Additional supplementation is needed for adequate magnesium nutriture during pregnancy.

Magnesium intake was determined by Lillien et al(Lillien,1982).as part of a study evaluating diet and ethanol intake during pregnancy. Diet records were determined by a 24-hour recall type interview 1-4 days postpartum. Subjects were asked to recall food intake of an 'average day'. The mean magnesium intake from diet alone for the 578 women was 259 ± 4 mg. When supplements were included, magnesium intake was 316 ± 5 mg.

In the above perspective the present study has been undertaken to investigate the role of dietary Ca and Mg intake in PIH subjects.

HYPOTHESIS

Low dietary intake of Ca and Mg is associated with Pregnancy Induced Hypertension in Bangiadeshi pregnant women.

Chapter 2

OBJECTIVES

2. OBJECTIVES

General objective

- To investigate the dietary intake of caicium and magnesium in subjects with pregnancy induced hypertension.

Specific Objectives

- To measure the dietary intake of Ca and Mg among Non-PIH women.
- To measure the dietary intake of Ca and Mg among PIH women.
- To explore the association of dietary Ca and Mg with PIH on adjusting the confounding risk factor like age, BMI, geographic, socioeconomic status, famiiy history of hypertension etc.

Chapter 3

REVIEW OF LITERATURE

3. LITERATURE REVIEW

Hypertension is one of the major risk factors for cardiovascular disease. It is the most common medical problem encountered during pregnancy, complicating 2-3% of pregnancies (Michael, 2012).

Hypertension

Hypertension (HTN) or high blood pressure, sometimes called arterial hypertension, is a chronicmedical condition in which the blood pressure in the arteries is elevated. This requires the heart to work harder than normal to circulate blood through the blood vessels. Blood pressure involves two measurements, systolic and diastolic, which depend on whether the heart muscle is contracting (systole) or relaxed between beats (diastole). Normal blood pressure at rest is within the range of 100-140mmHg systolic (top reading) and 60-90mmHg diastolic (bottom reading). High blood pressure is said to be present if it is persistently at or above 140/90 mmHg (Carretero, 2000).

Blood pressure

Blood pressure is the pressure in the blood vessels in our body. It is the force with which the blood moves through the blood vessels. Doctors and nurses measure blood pressure by putting a cuff around our upper arm. Then they listen to our blood flow with a stethoscope. High blood pressure (also called hypertension) occurs when our blood moves through our blood vessels at a higher pressure than normal.

High blood pressure/hypertension during pregnancy

There are three types of high blood pressure in pregnant women:

- **Chronic hypertension:** High blood pressure that develops before the 20th week of pregnancy or is present before the woman becomes pregnant. Sometimes a woman has high blood pressure for a long time before she gets pregnant, but she doesn't know it until her first prenatal check-up.
- **Gestational hypertension:** Some women just get high blood pressure near the end of pregnancy. They don't have any other associated symptoms.

Pregnancy-induced hypertension (PIH), also called toxemia or preeclampsia: This condition can cause serious problems for both the mother and the baby if left untreated. PIH develops after the 20th weeks of pregnancy. Along with high blood pressure, it causes protein in the urine, blood changes and other problems (Zamorski, 2001).

Pregnancy-induced hypertension (PIH)

Pregnancy-induced hypertension (PIH) is a form of high blood pressure in pregnancy. It occurs in about 7 to 10 percent of all pregnancies. Another type of high blood pressure is chronic hypertension - high blood pressure that is present before pregnancy begins.

Pregnancy-induced hypertension is also called toxemia or preeclampsia. It occurs most often in young women with a first pregnancy. It is more common in twin pregnancies, and in women who had PIH in a previous pregnancy. Usually, there are three primary characteristics of this condition, including the following:

- High blood pressure (a blood pressure reading higher than 140/90 mm Hg or a significant increase in one or both pressures).
- Protein in the urine.
- Edema (swelling).

Causes of pregnancy-induced hypertension (PIH)

The cause of PIH is unknown. Some conditions may increase the risk of developing PIH, including the following:

- Pre-existing hypertension (high blood pressure).
- Kidney disease.
- Diabetes.
- PIH with a previous pregnancy.
- Mother's age younger than 20 or older than 40.
- Multiple fetuses (twins, triplets).

Symptoms of pregnancy-induced hypertension

The following are the most common symptoms of high blood pressure in pregnancy. However, each woman may experience symptoms differently. Symptoms may include:

Increased blood pressure.

- Protein in the urine.
- Edema (swelling).
- Sudden weight gain.
- Visual changes such as blurred or double vision.
- Nausea, vomiting.
- Right-sided upper abdominal pain or pain around the stomach.
- Urinating small amounts.

- Changes in liver or kidney function tests.

Classification of PIH

It occurs mostly young primis/>35, in 3rd trimester (not before 20 weeks)

A) Hypertension of Pregnancy-

BP >140 / 90 mm of Hg alone or with mild oedema

B) Preeciampsia-

B.I) Mild Preeclampsia-

BP <160/100, mild oedema, proteinuria Trace / 1+, minimal, liver enzymes.

B.II) Severe Preeclampsia-

BP >160/110, marked qedema, proteinuria 2+,headache, visual disturbances, abdominal pain,oliguria,thrombocytopenia,bilirubin,liver enzymes,creatinine,foetal growth retardation, pulmonary

C) Eclampsia -

With convulsion

- Eclampsia is a severe form of pregnancy-induced hypertension. Women with eclampsia have seizures resulting from the condition. Eclampsia occurs in about one in 1,600 pregnancies and develops near the end of pregnancy, in most cases. (Children's Hospital and Health system, 2012).

Pathophysiology of PIH

- Vasospasm haemorrhage & necrosis end organ changes
- Reduced placental perfusion IUGH & foetal death
- Increased cardiac output
- Increased extra cellular fluid volume
- Haemoconcentration

- Hypercoagulability-dic-reduced clotting factors-bleeding
- Reduced GFR-oliguria-anuria
- No electrolytic imbalance (Shitole,2011)

Pregnancy-induced hypertension (PIH) is estimated to affect 7% to 10% of all pregnancies in the United States. Despite being the leading cause of maternal death and a major contributor of maternal and perinatal morbidity, the mechanisms responsible for the pathogenesis of PIH have not yet been fully elucidated. Studies during the past decade, however, have provided a better understanding of the potential mechanisms responsible for the pathogenesis of PIH. The initiating event in PIH appears to be reduced uteroplacental perfusion as a result of abnormal cytotrophoblast invasion of spiral arterioles. Placental ischemia is thought to lead to widespread activation/dysfunction of the maternal vascular endothelium that results in enhanced formation of endothelin and thromboxane, increased vascular sensitivity to angiotensin II, and decreased formation of vasodilators such as nitric oxide and prostacyclin. The quantitative importance of the various endothelial and humoral factors in mediating the reduction in renal hemodynamic and excretory function and elevation in arterial pressure during PIH is still unclear. Investigators are also attempting to elucidate the placental factors that are responsible for mediating activation/dysfunction of the maternal vascular endothelium. Microarray analysis of genes within the ischemic placenta should provide new insights into the link between placental ischemia and hypertension. More effective strategies for the prevention of preeclampsia should be forthcoming once the underlying pathophysiologic mechanisms that are involved in PIH are completely understood (Granger,2001).

Pregnancy-induced hypertension a concern

With high blood pressure, there is an increase in the resistance of blood vessels. This may hinder blood flow in many different organ systems in the expectant mother including the liver, kidneys, brain, uterus, and placenta.
There are other problems that may develop as a result of PIH. Placental abruption (premature detachment of the placenta from the uterus) may occur in some pregnancies. PIH can also lead to fetal problems including intrauterine growth restriction (poor fetal growth) and stillbirth.

If untreated, severe PIH may cause dangerous seizures and even death in the mother and fetus. Because of these risks, it may be necessary for the baby to be delivered early, before 37 weeks gestation.

HELLP syndrome is a complication of severe preeclampsia or eclampsia. HELLP syndrome is a group of physical changes including the breakdown of red blood cells, changes in the liver, and low platelets (cells found in the blood that are needed to help the blood to clot in order to control bleeding).

Diagnosis of pregnancy-induced hypertension

Diagnosis is often based on the increase in blood pressure levels, but other symptoms may help establish PIH as the diagnosis. Tests for pregnancy-induced hypertension may include the following:

- Blood pressure measurement.
- Urine testing.
- Assessment of edema.
- Frequent weight measurements.
- Eye examination to check for retinal changes.

- Liver and kidney function tests.
- Blood clotting tests (Children's Hospital and Health system, 2012).

Treatment for pregnancy-induced hypertension:

Treatment of preeclampsia begins with getting regular prenatal care, ideally before a pregnancy begins, or as soon as possible during pregnancy. Prenatal visits include the checking of blood pressure and testing of urine for the presence of protein.

Mild preeclampsia is treated with rest, limiting salt intake and antihypertensive medication for some women. Regular prenatal visits that include ultrasound imaging of the fetus' growth and amount of amniotic fluid are crucial to monitoring the condition. Regular prenatal care ensures that preeclampsia can be quickly treated more aggressively if it becomes more serious.

Hospitalization is necessary for more severe preeclampsia. Treatment in the hospital includes regular monitoring of the fetus and the mother's blood pressure, antihypertensive medication and medication that helps rid the body of excess fluid. In some cases, the baby may need to be delivered quickly in order to protect the health of the mother and child. This is done by induction or labor or cesarean section (Coll, 1996).

Specific treatment for pregnancy-induced hypertension will be determined by physician based on:

- Pregnancy, overall health and medical history.
- Extent of the disease.
- Tolerance for specific medications, procedures, or therapies.

- Expectations for the course of the disease.
- Opinion or preference.

The goal of treatment is to prevent the condition from becoming worse and to prevent it from causing other complications. Treatment for pregnancy-induced hypertension (PIH) may include:

- Bed rest (either at home or in the hospital may be recommended).
- Hospitalization (as specialized personnel and equipment may be necessary).
- Magnesium sulfate (or other antihypertensive medications for PIH).
- fetal monitoring (to check the health of the fetus when the mother has PIH) may include:
    - Fetal movement counting - keeping track of fetal kicks and movements. A change in the number or frequency may mean the fetus is under stress.
    - Nonstress testing - a test that measures the fetal heart rate in response to the fetus' movements.
    - Biophysical profile - a test that combines nonstress test with ultrasound to observe the fetus.
    - Doppler flow studies - type of ultrasound that uses sound waves to measure the flow of blood through a blood vessel.
- Continued laboratory testing of urine and blood (for changes that may signal worsening of PIH).
- Medications, called corticosteroids, that may help mature the lungs of the fetus (lung immaturity is a major problem of premature babies).
- Delivery of the baby (if treatments do not control PIH or if the fetus or mother is in danger). Cesarean delivery may be recommended, in some cases.

Prevention of pregnancy-induced hypertension:

There is no proven way to prevent preeclampsia. Most women who develop signs of preeclampsia, however, are closely monitored to lessen or avoid related problems. The only way to "cure" preeclampsia is to deliver the baby (Coll , 1996).

Early identification of women at risk for pregnancy-induced hypertension may help prevent some complications of the disease. Education about the warning symptoms is also important because early recognition may help women receive treatment and prevent worsening of the disease (2012 Children's Hospital and Health system). Some of the measures that have been mentioned as possibly preventative for pregnancy induced hypertension may include those below.

Calcium: Calcium is a mineral that is vital for a normal function of the heart, muscles, and nervous system, healthy blood pressure, and strong bones and teeth. Calcium is available in supplements and in dairy products, milk and leafy green vegetables (Coll, 1996).

Magnesium: Magnesium is classified a 'major' mineral. Over 50% of the body's magnesium is contained in the bones with the remainder being in the muscles and tissues and only a minimal amount in the blood stream. Like calcium, our bones constantly absorb and release magnesium, releasing stored magnesium as the body needs it (Ascherio,1996).

Green vegetables such as spinach provide magnesium because of the abundance of chlorophyll molecules which contain the ion. Nuts (especially

cashews and almonds), seeds, dark chocolate, roasted soybeans, bran, and some whole grains are also good sources of magnesium (Lorrene, 1998). Although many foods contain magnesium, it is usually found in low levels. As with most nutrients, daily needs for magnesium are unlikely to be met by one serving of any single food. Eating a wide variety of fruits, vegetables, and grains will help ensure adequate intake of magnesium.

Recommended Daily Intake (RDI) of magnesium is about 250 - 300mg. This can be easily provided with a normal or vegetarian diet. Magnesium works with calcium to help with muscle contraction and blood clotting, as well as regulating blood pressure and the functioning of the lungs. Magnesium is also necessary for energy metabolism, the body's use of glucose for energy and the synthesis of protein and fat. It helps to keep calcium in tooth enamel to prevent decay and supports the normal functioning of the immune system.

Magnesium and calcium are thought to be protective against heart disease and high blood pressure. Magnesium deficiency is rare, but may occur with alcohol abuse, prolonged vomiting and diarrhoea, a diet lacking in protein, people with kidney disorders or those who take medications or natural preparations as a 'diuretic' (a substance that makes you pass more urine). A severe magnesium deficiency can lead to weakness, confusion, convulsions, twitching, hallucinations, and difficulty swallowing (Lorrene, 2000).

The Role of Calcium Plays in Pregnancy Nutrition and in Pregnancy Induced hypertension

One of the main jobs of calcium is to aid in the growth, development and maintenance of bones and teeth. As an expectant mom, must meet both

own requirements for bone and tooth health, and also provide for bone formation and development in baby.

For pregnant women who get low amounts of calcium in their diet, calcium supplementation averaging 1,300 milligrams (mg) a day during the second and third trimesters of pregnancy can increase the bone mineral content of the baby by about 15 percent, says a study in the October 1999 issue of Obstetrics & Gynecology. However, in women with adequate dietary calcium intake, calcium supplements are unlikely to result in major improvement in how your baby mineralizes it into his or her bones.

Most pregnant women need to add calcium-rich foods to the diet. Milk, yogurt, frozen yogurt, ice cream, ice milk and cheeses are calcium-rich foods. Non-fat and low-fat dairy products supply equal amounts of calcium with fewer calories than higher-fat counterparts. Green leafy vegetables, tofu and canned salmon (bones included) are other good sources of calcium. Calcium-fortified foods, such as some orange juices and breakfast cereals, also provide significant amounts of calcium, especially for women who do not eat dairy products. During pregnancy, women should consume at least four servings of calcium-rich foods a day, or the equivalent of one quart of milk.

Nutritionist Martha Belury notes, "In addition to being sure to incorporating calcium-rich foods into our daily eating plan, calcium-rich non-fat dried milk may be added to baked goods, smoothies, and soups to meet calcium needs." Further, many products now on the market contain fortification with calcium, including juices, soy milk and bread products.

To provide the calcium necessary for fetal bone mineralization, the maternal demand for calcium during pregnancy is elevated by as much as 300 mg/d. The normal expansion of maternal blood volume and the pregnancy-induced increase in urinary calcium excretion that occur in well-nourished women add further to the physiologic calcium requirement. This additional calcium is normally provided by an increase in maternal intestinal calcium absorption (Jose, 1991). An increase in dietary calcium intake may not be necessary. Recently, the Food and Nutrition Board of the Institute of Medicine set the dietary reference intake for calcium at 1000 mg/d for women aged 19–50 y, and at 1300 mg/d for women ≤ 18 y, irrespective of pregnancy.

The precise factors involved in the pathogenesis of PIH are unclear, but several associated alterations in calcium metabolism have been identified. Possible metabolic abnormalities include a decrease in serum 1,25-dihydroxyvitamin D concentration , a decrease in serum ionized calcium concentration, and a decrease in urinary calcium excretion. Whether these biochemical abnormalities are a consequence of PIH or result from impaired calcium absorption, inadequate dietary calcium intake, or both is unclear. Calcium absorption has not been measured in hypertensive pregnant women. Epidemiologic data suggest, however, an inverse correlation between dietary calcium intake and incidence of PIH in diverse populations.

For example, in rural Guatemala, despite the low socioeconomic status and low intake of protein and energy of women, the incidence of eclampsia is low (≈0.4 per 1000 births). Dietary calcium in this population is relatively high (≈1100 mg/d), in large part because of the incorporation of lime-processed tortillas as a staple component of the diet. Alternatively, in Colombia and India, where calcium intakes range from 250 to 350 mg/d, the incidence of eclampsia is higher (1.6 and 12.0 per 1000 births, respectively). In a study by

Marcoux et al of women with a relatively high intake of dietary calcium, an association between the incidence of gestational hypertension and dietary calcium intake was observed. For gestational hypertension there was a continuous decrease in the adjusted odds ratio from 1 to 0.60 for the lowest (median: 764 mg/d for control subjects) to the highest (median: 2330 mg/d for control subjects) tertiles of calcium intake. Interestingly, no such association was observed for women with preeclampsia. The researchers hypothesized that women with gestational hypertension are a heterogeneous group; some women may experience a less severe form of preeclampsia whereas other women may have primary hypertension first revealed during pregnancy. Women with primary hypertension that is exposed during pregnancy may be most responsive to dietary calcium.

Another biochemical abnormality observed in some hypertensive pregnant women is an elevated concentration of intracellular free calcium. For example, compared with normotensive control subjects, women with preeclampsia have elevated intracellular calcium concentrations in erythrocytes and platelets. Not all studies, however, found significant differences in the intracellular calcium concentration between hypertensive and normotensive women. In the prospective study by Zemel et al , although no significant difference in basal platelet intracellular calcium concentration was found, preeclamptic patients had significantly greater intracellular calcium concentrations in platelets in response to stimulation by arginine vasopressin than did normotensive women. Differences in timing of blood measurements, biochemical methods used, experimental design, and dietary intakes of subjects may have contributed to contrasting study results. If established, however, an increase in intracellular calcium in vascular smooth muscle cells during pregnancy is consistent with development of

vasoconstriction and resultant hypertension. Analogously, an increase in intracellular calcium in uterine smooth muscle cells is consistent with induction of preterm labor. Alternatively, it has been hypothesized that calcium affects smooth muscle cell contractility indirectly by influencing the production of other vasoactive agents such as nitric oxide, prostacyclins, or angiotensin (via the renin-angiotensin-aldosterone metabolic pathway) (Lorrene, 2000).

Ascherio et al (1996) examined a prospective study (in the department of Nutrition, Harvard School of Public Health, Boston, Mass 02115, USA.) of the relation of nutritional factors with hypertension and blood pressure levels among 41,541 predominantly white US female nurses, aged 38 to 63 years, who completed a detailed semi quantitative food frequency questionnaire in 1984 and were without diagnosed hypertension, cancer, or cardiovascular disease. During 4 years of follow-up, from 1984 to 1988, 2,526 women reported a diagnosis of hypertension. Age, relative weight, and alcohol consumption were the strongest predictors for the development of hypertension. Dietary calcium, magnesium, potassium, and fiber were not significantly associated with risk of hypertension, after adjusting for age, body mass index, alcohol, and energy intake. Among women who did not report hypertension during the follow-up period, calcium, magnesium, potassium, and fiber were each significantly inversely associated with self-reported systolic and diastolic pressures, after adjusting for age, body mass index, alcohol consumption, and energy intake. When the four nutrients were added simultaneously to the regression model, only fiber and magnesium intakes retained significant inverse associations with systolic and diastolic pressures. In analyses of food groups, intakes of fruit and vegetables were inversely associated with systolic and diastolic pressures, and intakes of

cereals and meat were directly associated with systolic pressure. These results support hypotheses that age, body weight, and alcohol consumption are strong determinants of risk of hypertension in middle-aged women. They are compatible with the possibilities that magnesium and fiber as well as a diet richer in fruits and vegetables may reduce blood pressure levels (Ascherio,1996).

Majid Karandish et al, (2005) conducted a case control study to determine the pattern of dietary calcium intake among urban pregnant women in Ahwaz City in south west Iran. Participants comprised 339 pregnant women (26±5.5 yrs) in the 28th-32nd week of gestation, who had attended selected urban health centers in Ahwaz City in 2004. Dietary calcium intake was estimated using a 43-item food frequency questionnaire (FFQ). Calcium intakes equivalent to, or more than, 1000 mg/d were considered as "adequate". Mean (±SD) daily intakes of dietary calcium and dairy products were 644±255 mg and 1.3±0.7 servings per day, respectively. On average, dairy products provided 49% of dietary calcium. About 43% of participants were consuming =1 serving of dairy products per day; and 89% of them did not meet adequate intake of calcium. A high proportion of pregnant women in Ahwaz City did not take enough calcium and dairy products. It is suggested that the consumption of enough calcium and dairy products should be emphasized in the nutrition education component of maternal health program. Further research at the country level should be undertaken in order to assess the need for fortification of food with calcium and/or to provide calcium supplements to vulnerable groups (majid, 2005).

Belizán et al, (1991) conducted an epidemiologic study, they described an inverse relation between calcium intake and gestational hypertension and

eclampsia. they also found that calcium supplementation lowered blood pressure in pregnant and nonpregnant women. These results have been supported by recent studies of hypertensive subjects and pregnant women. Although the mechanism of this effect is not yet understood, the largest reduction of blood pressure occurred among pregnant women with low pretreatment serum calcium concentrations and plasma renin activity, and women given calcium supplements had both lower blood pressure and higher levels of urinary calcium excretion. Conversely, low levels of urinary calcium excretion have been described in women with preeclampsia. Thus, lowering blood pressure through changes in calcium metabolism may prevent hypertensive disorders in pregnancy. On the basis of this evidence, they proposed that a large randomized, controlled trial be conducted to assess the preventive effect of 2 g of supplemental calcium per day on the incidence of hypertensive disorders of pregnancy. The results of such a trial are reported here (Belizán, 1991).

Hofmeyr et al, (2007) conducted a comparative study and the data were extracted and analyzed using Review Manager Software, eligibility and trial quality were assessed. Here twelve studies (15528 women) were included, all of good quality. Most women were at low risk and had low dietary calcium. High blood pressure was reduced with calcium supplementation rather than placebo (11 trials, 14 946 women: relative risk [RR] random effects model 0.70; 95% CI 0.57–0.86), as was pre-eclampsia (12 trials, 15 206 women: RR 0.48; 95% CI 0.33–0.69). The effect was greatest for women at high risk (five trials, 587 women: RR 0.22; 95% CI 0.12–0.42) and for those with low baseline calcium intake (seven trials, 10 154 women: RR 0.36; 95% CI 0.18–0.70). There was heterogeneity, with less effect in the larger trials. The composite outcome maternal death or serious morbidity was reduced (four

trials, 9732 women: RR 0.80; 95% CI 0.65–0.97). The syndrome of hemolysis, elevated liver enzymes and low platelets was increased (two trials, 12 901 women: RR 2.67; 95% CI 1.05–6.82). There was no overall effect on the risk of preterm birth or stillbirth or death before discharge from hospital. so, the study suggest that, calcium supplementation appears to reduce the risk of pre-eclampsia and to reduce the rare occurrence of the composite outcome 'maternal death or serious morbidity'. There were no other clear benefits or harms (Hofmeyr, 2007).

Hofmeyr et al, (2003) conducted a study to assess the effects of calcium supplementation during pregnancy on hypertensive disorders of pregnancy and related maternal and child adverse outcomes. It was a systematic review of randomized trials that compared supplementation with at least 1 g calcium daily during pregnancy with placebo. The Cochrane Pregnancy and Childbirth Group trials register (October 2001) and the Cochrane Controlled Trials Register (Issue 3, 2001) were searched and study authors were contacted. Eligibility and trial quality were assessed. The result showed, there was a modest reduction in the risk of preeclampsia with calcium supplementation (relative risk (RR) 0.68, 95% confidence interval (CI): 0.570.81). The effect was greatest for women at high risk of hypertension (RR 0.21, 95% CI: 0.110.39) and those with low baseline calcium intake (RR 0.32, 95% CI: 0.210.49). There was no overall effect on the risk of preterm delivery, although there was a reduction in risk among women at high risk of hypertension (RR 0.42, 95% CI: 0.230.78). There was no evidence of any effect of calcium supplementation on stillbirth or death before discharge from hospital. There were fewer babies with birth weight < 2,500 g (RR 0.83, 95% CI: 0.710.98). In one study, childhood systolic blood pressure > 95th percentile was reduced (RR 0.59, 95% CI: 0.390.91). They concluded that,

Calcium supplementation appears to be beneficial for women at high risk of gestational hypertension and in communities with low dietary calcium intake (Hofmeyr, 2003).

Cong et al, (1995) conducted a study that Pregnancy induced hypertension (PIH) is a common complication in pregnancy and prenatal stage. Because the direct and indirect relationship between low calcium intake and many diseases, such as rachitis, young age myopia and hypertension, calcium supplementation has been a hot topic among nutritionists. Randomized trials of calcium supplementation during pregnancy were conducted in 212 healthy primipara. They were divided into 4 groups and gave 120mg, 240mg, 1g or 2g of calcium daily from 20 to 28 wks of gestation up to delivery respectively. As a result, the incidence of PIH was 8.9%, 7.5%, 8% and 4% respectively in these groups. The control group (106 pregnant women) who did not receive calcium gave an incidence of 18%. Supplementation of 2g of calcium daily showed significant results in lowering the incidence of PIH ($P < 0.05$) without any adverse effects. In 1992 calcium supplementation was widely used in antenatal clinic. 200 cases with intake of 2g calcium were compared with corresponding noncalcium supplementation cases, and the incidence of PIH was 7.5% and 16.5% ($P < 0.005$) respectively. Mediating parathyroid hormone and renin activity are thought to be the effect of calcium on decreasing the incidence of PIH (Cong, 1995).

SanchezRamos et al, (1994) conducted a study to evaluate the efficacy of oral supplemental calcium in reducing the incidence of pregnancy induced hypertension (gestational hypertension or preeclampsia) in angiotensinsensitive nulliparas. Sensitivity to intravenously infused angiotensin was determined at 2428 weeks' gestation in 281 nulliparous women who had positive rollover tests. Angiotensin sensitive women were

given 2 g/day of oral elemental calcium or placebo in a randomized, double blind clinical trial. The tablets were dispensed by the hospital pharmacy in serially numbered computerized pill bottles so as to assess compliance. Repeat angiotensin sensitivity test was performed at 34-36 weeks' gestation. Result showed that Sixty three of 67 angiotensin sensitive nulliparas were valuable; 29 received calcium and 34 received placebo tablets. Four of 29 calcium treated subjects (13.8%, 95% confidence interval [CI] 432%) developed preeclampsia, compared to 15 of 34 (44.1%, 95% CI 2762%) in the placebo group (relative risk [RR] 0.37, 95% CI 0.150.92; P = .01). The incidence of any type of hypertension was nine of 29 (31%, 95% CI 1551%) with calcium treatment, compared to 22 of 34 (64.7%, 95% CI 4680%) with placebo (RR 0.46, 95% CI 0.250.86; P = .01). Their conclusion was Calcium supplementation given in pregnancy to high risk nulliparas reduces the incidence of pregnancy induced hypertension (SanchezRamos, 1994).

Zhonghua and Zhi (1993), find out the relationship between calcium and pregnancy induced hypertension (PIH), it was a prospectively studied. 150 normal pregnant women were divided into 3 groups: group A with supplement of calcium element 1g/day, group B 2g/day and group C with no calcium supplement. 8%, 4% and 18% of each group had developed PIH respectively. It seems that supplement of 2 gram calcium per day gave the best result. Furthermore the study was expanded: 200 cases with supplement of calcium element 2 g/day from 2028th week of pregnancy, another 200 pregnant women without calcium supplement. The occurrence of PIH was 7.5% and 16.5% respectively. There was no adverse effect with 2 g calcium supplement. The metabolism of calcium in normal pregnancy and PIH was discussed. Supplement of calcium during pregnancy may benefit by reduction of PIH incidence (Zhonghua, 1993).

Belizan et al, (1991) undertook this prospective study to determine the effect of calcium supplementation on the incidence of hypertensive disorders of pregnancy (gestational hypertension and preeclampsia) and to determine the value of urinary calcium levels as a predictor of the response. They studied 1194 nulliparous women who were in the 20th week of gestation at the beginning of the study. The women were randomly assigned to receive 2 g per day of elemental calcium in the form of calcium carbonate (593 women) or placebo (601 women). Urinary excretion of calcium and creatinine was measured before calcium supplementation was begun. The women were followed to the end of their pregnancies, and the incidence of hypertensive disorders of pregnancy was determined. The result showed that, the rates of hypertensive disorders of pregnancy were lower in the calcium group than in the placebo group (9.8 percent vs. 14.8 percent; odds ratio, 0.63; 95 percent confidence interval, 0.44 to 0.90). The risk of these disorders was lower at all times during gestation, particularly after the 28th week of gestation ($P = 0.01$ by life table analysis), in the calcium group than in the placebo group, and the risk of both gestational hypertension and preeclampsia was also lower in the calcium group. Among the women who had low ratios of urinary calcium to urinary creatinine (less than or equal to 0.62 mmol per millimole) during the 20th week of gestation, those in the calcium group had a lower risk of hypertensive disorders of pregnancy (odds ratio, 0.56; 95 percent confidence interval, 0.29 to 1.09) and less of an increase in diastolic and systolic blood pressure than the placebo group. The pattern of response was similar among the women who had a high ratio of urinary calcium to urinary creatinine during the 20th week of gestation, but the differences were smaller. Authors finally conclude that pregnant women who receive calcium supplementation

after the 20th week of pregnancy have a reduced risk of hypertensive disorders of pregnancy (Belizan, 1991).

Panam (1991), recently suggested causalrelationship between dietary calcium deficiency and PIH, with the proposal that calcium supplements be given throughout pregnancy in order to prevent the disease. This article reviews a series of clinical tests carried out over a six year period which have demonstrated that calcium supplementation is an effective low-cost measure for reducing the frequency of PIH in women whose intake of the mineral is low. It is not yet known how calcium reduces the risk of PIH. It is suggested that adequate intake of the mineral keeps serum levels of calcium within its narrow physiological limits; these are crucial for the synthesis of nitric oxide in the vascular endothelium, a substance that appears to be responsible for maintaining the vasodilatation that characterizes normal pregnancy. However, before the general use of calcium supplements can be recommended, it will be necessary to conduct epidemiological studies on larger numbers of women (Panam, 1991).

Villar et al, (1990) conducted a study that Calcium supplementation during pregnancy may reduce preterm delivery in high risk populations. Here, results are presented of a randomized, double blinded controlled clinical trial of calcium supplementation (2.0 gm of elemental calcium as calcium carbonate) and a placebo. All participants were 17 years of age or less and clinically healthy. Patients were enrolled by the twenty third week of gestation. The mean duration of calcium supplementation or placebo was approximately 14 weeks. Treatment consisted of 2.8 (+/ 1.5) tablets per day in the placebo group (N = 95) and 3.0 (+/ 1.4) tablets per day in the calcium group (N = 94). Dietary calcium intake was similar in both groups at about 1200 mg/day.

The calcium group had a lower incidence of preterm delivery (less than 37 weeks; 7.4% vs 21.1%; p = 0.007); spontaneous labor and preterm delivery (6.4% vs 17.9%; p = 0.01); and low birth weight (9.6% vs 21.1%; p = 0.03). This effect was also present after stratified analysis by level of treatment compliance, urinary tract infection, and chlamydial infection. Life table analysis demonstrated an overall shift to a higher gestational age in the calcium group compared with the placebo group (log rank test, p = 0.02). As suggested previously, the observed effect could be mediated by a reduction in uterine smooth muscle contractibility. If confirmed by future research, these results could represent an important preventive intervention for prematurity in high risk populations (Villar, 1990).

Reusser et al, (1994) conducted a study in the department of Medicine, Oregon Health Sciences University, Portland. In this study, five micronutrients have been shown to directly influence blood pressure: sodium, calcium, potassium, magnesium, and chloride. The data presented here are based on accumulated findings from epidemiologic, laboratory, and clinical investigations, many of which focused primarily on a single nutrient. However, as also discussed here, nutrients are not consumed in isolation, and their physiologic interactions and combined effects on blood pressure are the subjects of much of the current research in the area of diet and hypertension (Reusser, 994).

The Role Magnesium Plays In Pregnancy Nutrition and in Pregnancy Induced hypertension

Similarly, magnesium plays a role in the stability of all polyphosphate compounds in the cells, including those associated with DNA- and RNA synthesis. Magnesium-containing Epsom salts are especially used in treating

the hypertension of eclampsia. Even if the case is not eclampsia, there may be antihypertensive effects of having a substantial portion of the intake of sodium chloride (NaCl) exchanged for e.g. magnesium chloride; NaCl is an osmolite and increases arginine vasopressin (AVP) release, which increases extracellular volume and thus results in increased blood pressure. However, not all osmolites have this effect on AVP release, so with magnesium chloride, the increase in osmolarity may not cause such a hypertensive response (Top 10 Foods Highest in Magnesium).

Magnesium is also an important element for health and disease. It is an essential element in biological systems. Magnesium occurs typically as the Mg^{2+} ion. It is an essential mineral nutrient for life and is present in every cell type in every organism. For example, ATP (adenosine triphosphate), the main source of energy in cells, must be bound to a magnesium ion in order to be biologically active (Top 10 Foods Highest in Magnesium). Magnesium, the second most abundant intracellular cation, has been identified as a cofactor in over 300 enzymatic reactions involving energy metabolism and protein and nucleic acid synthesis. Approximately half of the total magnesium in the body is present in soft tissue, and the other half in bone. Less than 1% of the total body magnesium is present in blood. Nonetheless, the majority of our experimental information comes from determination of magnesium in serum and red blood cells. At present, we have little information about equilibrium among and state of magnesium within body pools. Magnesium is absorbed uniformly from the small intestine and the serum concentration controlled by excretion from the kidney. The causes of hypo magnesemia are reduced intake (poor nutrition or IV fluids without magnesium), reduced absorption (chronic diarrhea, mal absorption, or bypass/resection of bowel), redistribution (exchange transfusion or acute pancreatitis), and increased

excretion (medication, alcoholism, diabetes mellitus, renal tubular disorders, hypercalcemia, hyperthyroidism, aldosteronism, stress, or excessive lactation)

Mizushima et al, (1998) conducted a observational study by the published reports of 30 separate sets of analyses from 29 observational studies relating dietary intake of magnesium to blood pressure (BP) were identified through a comprehensive search using MEDLINE and BIDSEMBASE. Three studies were prospective, 24 cross-sectional (25 reports), of which four also contained a longitudinal component, and two were obtained from baseline data in a trial. Various dietary methodologies were used: 24-h dietary recall , food-frequency questionnaire, food record , and duplicate diet (2). Twelve reports compared magnesium intake or BP level between subgroups. Seven showed a negative association between magnesium intake and BP level, and five reported no association. From 18 of the 30 sets of analyses either a regression estimate or a Pearson correlation coefficient was reported. Many reports also allowed identification of subgroups by sex, age and race. Ninety population samples and subgroups could thus be identified from the 30 reports. All 11 Pearson-r correlation coefficients reported for systolic BP (SBP) (three significant, P , 0.05) and 10 (out of 12) Pearson correlation coefficients reported for diastolic BP (DBP) (four significant) were negative. Seven reports (13 subgroups for SBP, 11 subgroups for DBP) gave partial regression coefficients after adjustment; 10 (seven significant) and eight (six significant) were negative for SBP and DBP, respectively. For 13 subgroups in five papers, Pearson-r correlation coefficients were reported after adjustment for confounding factors. Eight (out of 13) showed a negative relationship for SBP and DBP. This review points to a negative association between dietary magnesium intake and BP. A systematic quantitative overview is needed to reconcile the

inconsistencies of the results of individual studies and to quantify the size of such relationship (Mizushima, 1998).

Joffres MR, 1987, published a study that, Relationship of magnesium intake and other dietary factors to blood pressure: the Honolulu heart study. Associations between blood pressure and intakes of 61 dietary variables assessed by 24-h recall method were investigated in 615 men of Japanese ancestry living in Hawaii who had no history of cardiovascular disease or treated hypertension. Magnesium, calcium, phosphorus, potassium, fiber, vegetable protein, starch, vitamin C, and vitamin D intakes were significant variables that showed inverse associations with blood pressure in univariate and a multivariate analyses. Magnesium had the strongest association with blood pressure, which supports recent interest in its relation to blood pressure. Nevertheless, it was not possible to separate the effect of magnesium from that of other variables because of the problem of high inter correlation among many nutrients. While recommendations based upon cross-sectional studies must be viewed cautiously, these results suggest that foods such as vegetables, fruits, whole grains, and low-fat dairy items Blaine Journal, January 1998 (Joffres MR, 1987).

Kay (1987) conducted a study, entitle 'Magnesium Intake during Pregnancy' which was presented at the 4th International Symposium on Magnesium, USA. The result of this study showed that, the mean dietary magnesium intake of pregnant women is 35-58% of the recommended dietary allowance of 450 mg. Low-income women consumed 97-100 mg magnesium/1,000 kcal while women with higher incomes averaged 120 mg/1,000 kcal. Diets high in fat and sugar and low in whole grains, vegetables and fruits have a lower magnesium density. Magnesium content of water can also make a significant

contribution to magnesium intake. Magnesium from prenatal supplements, if present, is seldom more than 100 mg. Additional supplementation is needed for adequate magnesium nutriture during pregnancy (Kay, 1987).

Chapter 4

SUBJECTS AND METHODS

4. SUBJECTS AND METHODS

Study design

It was an observational analytic study with a group comparison design.

Place and duration of the Study

It was a collaborative study conducted in the Institute of Nutrition and Food Science (INFS), University of Dhaka and Bangladesh Institute of Heaith Sciences (BIHS), Mirpur Darussalam. The study subjects were collected from the Out-Patient Departments of some tertiary level hospitals of Dhaka city i.e. Dhaka Medical College Hospital, Bangabandhu Sheikh Mujib Medical University Hospital, Bangladesh Institute of Health Sciences Hospital, Monowara Hospital etc after approval of institutional heads and Ethical Review Committee as appropriate. The study subjects were referred to the Bangladesh Institute of Health Sciences (BIHS). The study was carried out during the period of January 2010 to December 2011.

Subjects

Study Population

A total of 300 Subjects were included, on the basis of availability, pregnant mothers from, within last 12 weeks (3^{rd} trimester) of gestation, attending the out patient departments of the selected hospitals, were the study population. All the potential subjects were included at their last prenatal visit on the basis of availability. a. Subjects were categorized in the 2 following groups:

- Healthy pregnant Women(Non-PIH): (n = 150)

- Pregnant women with Pregnancy Induced Hypertension: (n = 150)

Sample Size Determination:

Sample size calculation by following formula:

$n \geq 50+8m$

Here,

n=Required sample size.

m=Number of independent variable to be considerable model.

DV=Pregnancy induced hypertension.

Inclusion criteria

All the patients were aged between 17 to 40 years and were in the 3rd trimester of pregnancy.

- All subjects were primegravida.
- PIH was diagnosed by hypertension, edema and proteinuria.

Diagnostic criteria for detection of PIH:

PIH was diagnosed by hypertension, with or without proteinuria and/or edema (William, 1994).

Hypertension was defined following the criteria of the American College of Obstetrics and Gynecology (ACOG).

- BP equal to or greater than 140/90 mm of Hg,
- Rise of systolic BP 30 mm/Hg or more

- Rise of diastolic BP (point of muffiing i e point IV) 15 mm of Hg or more.

Edema was defined as per William (1994): Dependent edema greater than 1+ pitting after 12 hours of rest in bed/or weight gain in excess of 2 pounds per week, or particularly sudden weight gain over 1or2 days.

Proteinurea was defined as per William (1994):

Excretion of 0.3 g/l in 24 hour urine collection or greater than 1 g/l in a random sample or two random clean catch urine specimen with 2+ or more on reagent strip.

Exclusion criteria

- Pregnancy with diabetes mellitus
- Multiple pregnancies
- Pregnancy with chronic renal disease.
- Pregnancy with chronic hypertension.
- Patient with previous neurological disorders.
- Thyroid dysfunction
- Pregnancy with other medical diseases

Methods

The study was explained to each individual subject and informed consents were taken. Detailed sociodemographic data, family history and medical history and Dietary history were taken on predesigned an interviewer-administered questionnaire. Pre-test was conducted. Dietary history of normal pregnant and PIH subjects was taken by Food Frequency Questionnaire. Energy expenditure of the subjects was calculated by factorial method

(WHO/FAO/UNU1985). Anthropometry was recorded and Biochemical reports of the patients were collected from patient's Guidebook.

Development of Questionnaire

A questionnaire was developed to obtain relevant information of demographic and socio-economic data such as age, area, educational status, occupation, family parson, family monthly income, family history of hypertension, anthropometric data, drug history, medical history and clinical information were recorded on a pre-designed data sheet appropriately (Appendix-I). The questionnaire were coded and pre-tested before finalization and both closed and open ended. All interviews were conducted in the hospital. Dietary history was taken by Food Frequency Questionnaire and anthropometric measurements (height, weight) of each subject were taken and recorded in a pre-designed checklist form. Obstetric examination was performed and recorded for every patient. The data were collected from DMCH, BIHS, BSMMU and Monowara hospital.

Anthropometric Data

- ***Weight***

  Body weight was measured on a lever balance (Detecto-Medic, Detecto Scales, Inc, USA). The balance was calibrated every day before use. The body weight was measured bare footed to the nearest 0.1 kg with clothes on. The average weight (0.5 kg) of the clothes was later substracted from the measured weight. The measurement of weight done after the bladder has been emptied and before a meal.

- ***Height***

Heights of the subjects were measured barefooted in the standing position with a stander scale to the nearest 0.1 cm (Detecto-Medic, Detecto Scale Inc., USA).

During measuring height some precautions were taken. When measuring height, the subjects stands straight with the head positioned such that the Frankfurt plane is horizontal, feet together, knees straight, and heeis, buttocks and shouider biades in contact with the vertical surface of the stadiometer.

- ***Body Mass Index (BMI)***

Body mass index was calculated from the body weight and height of the subjects using the following formula weight in kg divided by height in meter Square.

$$BMI = \frac{\text{Weight in kg}}{(\text{Height in meter})^2}$$

Measurement of Blood Pressure as per ACOG *(Fernando, 1993):*

BP was measured with the patient in lying position keeping sphygmomanometer at the level of the heart. Hypertension was defined following the criteria of the American College of Obstetrics and Gynecology (ACOG-Fernando, 1993).

Dietary Assessment Technique:

- ***Assessment of Ca and Mg rich dietary intake:***

- Ca and Mg rich dietary practices of the respondents were assessed through food frequency method.
- There was about 100 questions in the questionnaire regarding intake of Ca and Mg rich vegetables, green ieafy vegetables, fruits, cereals, legume and animal foods etc.
- By using food frequency method, dietary history (daily/weekly/monthly/1st 6 months of pregnancy/never) and frequency of Ca and Mg rich foods intake among the pregnant women were assessed.
- In order to estimate the amount of usual Ca and Mg intake during pregnancy, the fractional portion size of each food consumed per day was multiplied by its Ca and Mg content, obtained from the national food composition table (Gopalon, Helen Keller; Swaminathan).
- The value were then summed up to obtain an estimate of an individual's total daily Ca and Mg intake

Statistical analysis:

- Data were expressed as M±SD for parametric values and median (range) for non-parametric values. Comparison between groups was done using Independent t-test to compare means and Mann-Whitney U test for skewed data. To test the association between two variables was examined using Spearman's coefficient correlation (r) analysis. Logistic regression was calculated for association with other confounding variable. Multiple regression analysis was done to better assess the relationships within the variables and the influencing other

variables. P value of <0.05 was considered sufficient for rejecting the nuli hypothesis of no difference among groups. All statistical analysis was performed with the software SPSS 16 for Windows (SPSS, Inc. Chicago. IL. USA).

Chapter 5

RESULTS

5. RESULTS

Out of 300 subjects enrolled in this study, a total number of PIH subjects were 150 (who had pregnancy induced hypertension) and 150 subjects were normotensive as Non-PIH.

Sociodemographic characteristics of the study subjects (Table: 1)

Location of the respondents:

There are significantly higher group of PIH 75(50%) subjects come from rural area compare to Non-PIH 49(32.7%). 92 (61.3%) Non-PIH women lives in urban area compare to PIH 56(37.3%). And 9(6%) Non-PIH group from semi-urban where as 19(12.7%) PIH subjects from semi-urban ($p<0.001$).

Education of the respondents:

7(5%) of Non-PIH and 10(6.7%) of PIH women are illiterate and up to primary is 31(21%) Non-PIH and 28(18.7%) subjects are PIH. Education level of class 6-10 is 38(25.3%) Non-PIH and 34(22.7%) in PIH. 42(28%) in Non-PIH and 37(24.7%) in PIH are SSC pass, HSC are 18(12%) and 20(13.3%) and lastly 14(9.4%) in Non-PIH and 21(14%) PIH subjects are graduate. There are no significant difference between the two groups ($p=0.288$).

Occupation of the respondents:

Majority of the respondents of both groups were housewives, 130(86.7%) Non-PIH and 136(90.7%) PIH. Others included service holder [6(4%) in Non-PIH and 5(3.3) in PIH], Business [6(4%) in Non-PIH and 3(2%) in PIH], Student [5(3.3%)

in Non-PIH and 2(1.3%) in PIH] and Maidservant [3(2%) in Non-PIH and 3(2%) in PIH]. There are no significant difference between the two groups (p=0.622).

Monthly income of the respondents:

According to income level of the respondents, 36(24%) PIH subjects are lower class groups than the Non-PIH 18(12%).

Family history of HTN of the respondents:

Positive family history of HTN are significantly higher in the PIH 66(44%) compare to the Non-PIH 33(22%) group (p<0.001).

Table: 1 Sociodemographic characteristics of the study subjects (n=300)

Characteristics	Non-PIH	PIH	P value
Location			
Urban	92(61.3)	56(37.3)	<0.001
Rural	49(32.7)	75(50)	
Semi Urban	9(6)	19(12.7)	
Educational status			
Illiterate	7(5)	10(6.7)	0.288
Primary	31(21)	28(18.7)	
6-10 class	38(25.3)	34(22.7)	
Secondary	42(28)	37(24.7)	
Higher secondary	18(12)	20(13.3)	
Graduate	14(9.4)	21(14)	
Occupation			
House wife	130(86.7)	136(90.7)	0.622
Service Holder	6(4)	5(3.3)	
Business	6(4)	3(2)	
Student	5(3.3)	2(1.3)	
Maidservant	3(2)	4(2.7)	
Monthly income			
Low income	18(12)	36(24)	0.022
Middle	92(61.3)	89(59.3)	
Upper middle	34(22.7)	22(14.7)	
Upper	6(4)	3(2)	
Family history of HTN			
Yes	33(22)	66(44)	<0.001
No	104(69.3)	48(32)	
Don't know	13(8.7)	36(24)	

Results are expressed as number (%), the results calculated by cross tab analysis, n= number of subjects, PIH=Pregnancy Induced Hypertension, HTN=Hypertension

The Clinical characteristics of the total study subjects (Table:2)

The age (in years; M±SD) of the different study groups are as follows: Non-PIH 25±5 vs PIH 26±5. There are no significant differences in age (p=0.299). The BMI (Mean±SD) significantly higher in PIH groups (34±3.7) as compared to Non-PIH subjects (26± 3.5) (p<0.001). There are also significant difference of Gestational weeks between the two groups (p<0.001). Gestational weeks [in weeks; median (range)] of the study subjects are as follows: Non-PIH 36(26-40) vs PIH 35(20-40).

The median (range) of systolic blood pressure (mmHg) is significantly higher in 150(130-230) PIH groups as compared to 120(58-130) Non-PIH groups (p<0.001). Similarly the median (range) of diastolic blood pressure (mmHg) is significantly higher in 100(80-140) PIH groups as compared to 70(62-90) Non-PIH groups (p<0.001). The median (range) of mean blood pressure (mmHg) is also significantly higher in 120(105-170) PIH groups to compared to 86(70-100) Non-PIH groups (p<0.001).

Table:2 The Clinical characteristics of the total study subjects (n=300)

Characteristics	Non-PIH	PIH	P value
Age (yrs)	25±5	26±5	0.299
BMI (kg/m^2)	26±3.5	34±3.7	<0.001
Gestational wks	36(26-40)	35(20-40)	<0.001
SBP (mm of Hg)	120(58-130)	150(130-230)	<0.001
DBP (mm of Hg)	70(62-90)	100(80-140)	<0.001
MBP	86(70-100)	120(105-170)	<0.001

Results are expressed as Mean±SD and median (range) as appropriate; n= number of subjects; Independent t-test, Mann-Whitney 'U' test were done as tests of significance, according to the nature and distribution of variables. BMI=Body Mass Index, SBP=Systolic Blood pressure, DBP=Diastolic Blood Pressure, MBP=Mean blood pressure.

The daily dietary Ca and Mg intake of the study subjects (Table:3)

The dietary Ca intake (gm/day), (Mean±SD) and [median (range)] are significantly lower in PIH [(272.9±69), 265(111-487)] as compared to Non-PIH, [(390.8±160), 350(201-984)]. In case of dietary Mg intake also significantly lower in PIH [(237.1±52), 235(122-391)] when compared to Non-PIH [(313.6±72), 309(306-497)], ($p<0.001$).

Table: 3 The daily dietary Ca and Mg intake of the study subjects (n=300)

Variables	**Non-PIH** (n=150)	**PIH** (n=150)	**P value**
Dietary intake Calorie (kcal)	1584±355	1658±394	0.073
	1587(1000-3048)	1622(1027-2895)	0.054
Dietary intake of Ca (mg/day)	390.8±160	272.9±69	0.001
	350(201-984)	265(111-487)	0.001
Dietary intake of Mg (mg/day)	313.6±72	237.1±52	<0.001
	309(306-497)	235(122-391)	0.001

Results are expressed as Mean±SD and median (range) as appropriate; n= number of subjects; Independent t-test, Mann-Whitney 'U' test were done as tests of significance, according to the nature and distribution of variables

The main sources of Ca intake of the study subjects (Table:4)

This table shows the main dietary sources of Ca among the Non-PIH and PIH groups. Intake of Ca from GLV [mg/day, median (range)] 5.7(.08-38.3) and 5.7(0.21-33.7); from Veg, [mg/day, median (range)] 17.1(6.38-75.4) and 17.8(3.02-63.9); from fruits [mg/day, median (range)] 9.5(2.62-143.9) and 9.1(2.96-43.4); and from some other foods (like betel leaves, Kathaler Bichi, lemon, orange, Fast food, Bakery products) [mg/day, median (range)] 1.3(0.00-66.9) and 1.8(0.00-20.3), there are no significant differences of Ca intake from those foods between the groups.

Significant differences of Ca intake from cereals, fish, legume sources. From cereals [mg/day, median (range)] 47.7(19.45-95.9) in Non-PIH and 45.5(19.47-79.7) in PIH, (p=0.008); fish [mg/day, median (range)], 138.1(41.49-345.9) and 128.9(24.35-376.2), (p=0.008) and from legume [mg/day, median (range)] 33.4(1.64-194.2) in Non-PIH and 27.5(0.57-85.5) in PIH, (p=0.011).

But, intake of Ca from meat and poultry [mg/day, median (range)] 43.8(2.45-603) in Non-PIH and 15.6(1.06-345.7) in PIH there are highly significant differences between Non-PIH and PIH groups ($p<0.001$).

Table:4 The main sources of Ca intake of the study subjects (n=300)

Variables	**Non-PIH** (n=150)	**PIH** (n=150)	**P value**
Cereal	47.7(19.45-95.9)	45.5(19.47-79.7)	0.008
Legume	33.4(1.64-194.2)	27.5(0.57-85.5)	0.011
GLV	5.7(.08-38.3)	5.7(0.21-33.7)	0.839
Veg	17.1(6.38-75.4)	17.8(3.02-63.9)	0.890
Fruits	9.5(2.62-143.9)	9.1(2.96-43.4)	0.672
Fish	138.1(41.49-345.9)	128.9(24.35-376.2)	0.008
Meat & Dairy	43.8(2.45-603)	15.6(1.06-345.7)	<0.001
Others	1.3(0.00-66.9)	1.8(0.00-20.3)	0.017

Results are expressed as median (range); n= number of subjects; Mann-Whitney U test were done as tests of significance, GLV-Green leafy vegetables; Veg-vegetables

The main sources of Mg intake of the study subjects (Table:5)

Table:4 shows the main dietary sources of Mg among the Non-PIH and PIH group. Dietary Mg come from cereals [mg/day, median (range)] 139.8(67.57-293.6) in Non-PIH and 135.2(63.97-287.6) in PIH.

From Legume sources [mg/day, median (range)] in Non-PIH 32.7(1.08-174.5) and in PIH 26.6(.73-86.2); from GLV [mg/day, median (range)] 4.6(.62-15.4) and 4.6(1.06-15.4); from Vegetable [mg/day, median (range)] 9.7(4.83-37.08) and 9.8(1.45-27.6); from fruits [mg/day, median (range)] 42.7(2.5-208.9) and 43.2(0.75-476.2); and from fish [mg/day, median (range)] 0.5(.00-2.03) and 0.3(0.00-3.0); there are no significant differences of Mg intake from those food groups between the groups.

But, intake of Mg from meat and poultry [mg/day, median (range)] 8.7(1.13-88.9) in Non-PIH and 5.3(.70-47.2) in PIH and from some other foods (like betel leaves, Kathaler Bichi, lemon, orange, Fast food, Bakery products) 1.3(0.00-129.4) and 1.2(0.00-27.3), there are highly significant differences between Non-PIH and PIH groups ($p<0.001$).

Table:5 The main sources of Mg intake of the study subjects (n=300)

Variables	**Non-PIH** (n=150)	**PIH** (n=150)	**P value**
Cereal	139.8(67.57-293.6)	135.2(63.97-287.6)	0.211
Legume	32.7(1.08-174.5)	26.6(0.73-86.2)	0.060
GLV	4.6(0.62-15.4)	4.6(1.06-15.4)	0.911
Veg	9.7(4.83-37.08)	9.8(1.45-27.6)	0.675
Fruits	42.7(2.5-208.9)	43.2(0.75-476.2)	0.351
Fish	0.5(0.00-2.03)	0.3(0.00-3.0)	0.096
Meat &Dairy	8.7(1.13-88.9)	5.3(0.70-47.2)	<0.001
Others	1.3(0.00-129.4)	1.2(0.00-27.3)	<0.001

Results are expressed as median (range); n= number of subjects; Mann-Whitney U test were done as tests of significance, GLV-Green leafy vegetables; Veg-vegetables

The correlation coefficient of Ca intake with other variables in the Non-PIH and PIH groups (Table:6)

The (Table:6) shows that correlation coefficient of Dietary Ca intake with other variables in the Non-PIH and PIH group. There is significantly positive correlation find out between dietary intake of Ca with family income (r-0.246, p<0.001) and MBP(r=0.276, p=0.001) in PIH group.

Also find out significantly positive correlation of dietary intake of Ca with family income (r-0.430, p=0.002)

Table:6 The correlation coefficient of Ca intake with other variables in the Non-PIH and PIH groups (n=300)

Parameter	**Non-PIH** (n=150)		**PIH** (n=150)	
	r	**P**	**r**	**p**
Age (yrs)	0.046	0.580	0.025	0.763
BMI (kg/m^2)	-0.112	0.476	-0.030	0.733
Gestational week	-0.154	0.060	0.036	0.666
FHHTN	0.061	0.459	0.081	0.323
Family Income	0.430	0.002	0.246	<0.001
SBP	-0.056	0.498	0.075	0.361
DBP	-0.056	0.496	-0.051	0.536
MBP	0.045	0.638	0.276	0.001

Spearman's correlation coefficient's test was done as a test of significance. FHHTN=Family history of hypertension, SBP=Systolic Blood pressure, DBP=Diastolic Blood Pressure, MBP=Mean Blood Pressure

The correlation coefficient of Mg intake with other variables in the Non-PIH and PIH groups (Table:7)

On correlation analysis shows, dietary Mg intake is significantly positive correlation with family income (r-0.312, p<0.001); MBP (r-0.940, p=0.021) in PIH group respectively.

Table:7 The correlation coefficient of Mg intake with other variables in the Non-PIH and PIH groups (n=300)

Parameter	**Non-PIH** (n=150)		**PIH** (n=150)	
	r	**P**	**r**	**p**
Age (yrs)	0.083	0.319	0.049	0.551
BMI (kg/m^2)	0.045	0.636	0.158	0.070
Gestational week	-0.090	0.273	-0.065	0.430
FHHTN	0.044	0.595	0.119	0.147
Family Income	0.128	0.120	0.312	<0.001
SBP	0.003	0.969	0.040	0.624
DBP	0.001	0.990	0.096	0.244
MBP	0.957	0.056	0.940	0.021

Spearman's correlation coefficient's test was done as a test of significance. FHHTN=Family history of hypertension, SBP=Systolic Blood pressure, DBP=Diastolic Blood Pressure. MBP=Mean Blood Pressure

Association of PIH with various parameters as explored by binary logistic regression (Table:8)

The (Table:8) shows that logistic regression analysis, when the PIH group is dependable variable and other risk factors are adjusted then the significant association shows with Family history of HTN ($p<0.001$), and lower Ca and Mg intake are strongly associated with PIH subjects ($p<0.001$).

Table:8 Association of PIH with various parameters as explored by binary logistic regression (n=300)

Variable	β Value	P value	Exp(B)	95% CI	
				Lower	Upper
Age	0.026	0.384	1.026	0.968	1.088
Family history of HTN	0.187	0.000	1.206	1.095	1.328
Family Income	0.178	0.460	1.195	0.745	1.918
Dietary intake of Ca	-0.009	<0.001	0.991	0.988	0.995
Dietary intake of Mg	-0.016	<0.001	0.984	0.979	0.989

β for standardized regression coefficient. PIH was taken as dependent variable whereas other variables were taken as independent variable; n = number of subjects

Association of MBP with various parameters as explored by multiple linear regressions (Table:9)

On multiple regression analysis, MBP as DV and others factor is adjusted their effect to find out significantly positive association of MBP with FHHTN (β=0.179, p=0.000) and negatively associated with dietary Ca (β=-0.266, p<0.001) and Mg (β=-0.335, p<0.001) intake.

Table:9 Association of MBP with various parameters as explored by multiple linear regression (n=300)

Variable	β Value	P value	95% CI	
			Lower	Upper
Age	0.019	0.707	-0.294	0.433
Family history of HTN	0.179	0.000	0.416	1.443
Family Income	0.062	0.249	-1.194	4.591
Dietary intake of Ca	-0.266	<0.001	-0.052	-0.021
Dietary intake of Mg	-0.335	<0.001	-0.114	-0.059

β for standardized regression coefficient. MBP was taken as dependent variable whereas other variables were taken as independent variable; n = number of subjects, DV= Dependable variable

Chapter 6

DISCUSSION

6. DISCISSION

Deficiency of calcium and magnesium has been implicated in the etiopathogenesis of PIH. Few interventional studies have also provided evidence that supplementation with Ca and Mg may help in preventing and managing the disorder. There is, however, paucity of data on the dietary origin of Ca and Mg deficiency and also on the association between PIH and dietary deficiency of these minerals.

Dietary imbalance and inadequacy is fairly common among Bangladeshi pregnant women. On the other hand around 10-20% of the pregnant women in our country suffer from PIH. It is thus rational to hypothesize that dietary deficiency of Ca and Mg are associated with PIH in our population.

The daily Ca intake in the Non-PIH women in the present study ranged from 201 to 984 mg/day (with a median of 350mg). The recommended dietary allowance (RDA) during pregnancy is 1000 mg/day (Source: Institute of Medicine, 2010). Thus the dietary calcium intake is 20%-98% with maximum subjects taking much lower than even 50% of RDA. In the PIH Group the ranges were even lower without supplementation (ranged from 111 to 487 mg a day and this intakes are 11%-48.7% of the recommended dietary allowance (RDA) of 1000 mg) and the median value was 265 mg/day. It is thus evident that Ca intake is in general grossly inadequate in our pregnant women and it is further inadequate in the group who develop PIH. The data corresponds with the study (Zamzam et al, 2007) done on an Iranian population where PIH women had significantly lower Ca intake compare to Non-PIH group.

In a study of Iranian population Karandish et ai (2005) showed that a high proportion of pregnant women do not consume enough calcium, as well as calcium.

In contrast to Ca intake, the dietary intake of Mg was much better in the Non-PIH group. The range of daily dietary Mg intake was 306-497 mg and the median value was 309 mg.

Against a RDA of 350 mg/day for pregnant women (Institute of medicine, 1997) the intake thus range from 87.4% to 142% of RDA (median 88%), here only some women had even more intake than RDA. However, it can also be seen that a substantial percentage of women also had inadequate intake of Mg. The deficiency of intake became more evident in the PIH Group, where the range was 122 to 391 mg/day (34.8% to 111% of RDA) and the median was 236 mg (67.4% of RDA). A study in USA (ref) showed that mean intake of dietary Mg (without supplementation) was 158 to 259 mg [35-58% of the RDA (450 mg) in us population].

In the study of Johson and Philips (Johnson, 1980) estimated the Magnesium intake and it's ranged from 103 to 333 mg/day (Mean 204 mg/day) and none of the subjects reached the RDA of 450 mg/day.

The main focus of the present study was to explore the association of dietary Ca and Mg deficiency with PIH. The data shows that calorie intake of PIH women, compared to their Non-PIH counterparts, are not significantly different (and even has a higher tendency). The dietary intake of Ca and Mg are grossly low (table-3). This may depicts that lack of consciousness regarding food diversity (to ensure adequate intake of macro and micro-nutrients) rather than shortage of food in general is related to deficient intake of ca and mg which seems to have an association with PIH.

The association is further evident in table 6 and 7, where both Ca and Mg intake are significantly associated with MBP in the PIH group. A more conclusive evidence arisen from the strong negative association ($p<0.001$) of data PIH and MBP with dietary Ca and Mg intake on logistic and multiple regression analysis respectively.

The present data conforms to the findings that, dietary Ca and Mg is associated with PIH, and there are some previous studies, ex- the study conducted by Zamzam et at (2008), that 'Dietary determinants of pregnancy induced hypertension in Isfahan', it's result was that, calcium intake in women with PIH was lower than that in those without PIH. In case of Mg, Johnson and Philips estmated the inadequate intake of Mg in PIH women, this also found significant association of PIH with Ca and Mg deficiency.

An attempt was made in the present study to indentify the particular food types which may be related to the dietary deficiency in the present population, Legume, fish , meat and dairy products were consumed at a much lesser amount by the PIH Group and particularly deficient intake of fish, meat and dairy products and seem to have a link with much lower intake of Ca and Mg in PIH subjects(Table 4-6).Since both Ca and Mg intake were found to have strong association with family incomes(Table 6 and 7) it may be indirectly inferred that due to the relatively high price of the fish, meat and dairy products, financial constraints may be a determinant of the dietary deficiency of the two minerals in pregnancy. These factors, particularly in relation to the PIH, needs to be investigated further.

In conclusion the present data indicate that,a) Dietary consumption of Ca and Mg during pregnancy is much lower than those recommended in our population;b) PIH seems to have an association with dietary deficiency of ca

and Mg in our pregnant women;c) Inadequate dietary intake of ca and mg are related to low intake of fish, meat and dairy products, which, in turn, may have a linkage with family income of a woman.

Chapter 7

CONCLUSIONS AND RECOMMENDATIONS

7. CONCLUSIONS AND RECOMMENDATION

CONCLUSIONS

The data lead to the following conclusions:

- Dietary consumption of Ca and Mg during pregnancy are much lower than those recommended in our population,
- PIH seems to have an association with dietary deficiency of Ca and Mg in our pregnant women, and
- Inadequate of Ca and Mg are related to low intake of fish, meat and dairy products which, in turn, may have a linkage with family income of a woman.

LIMITATIONS OF THE STUDY

The study had the following limitations:

1. We used FFQ for dietary assessment, which may have underreporting and over reporting biases as the information are dependent on memory.
2. We did not determine the validity and reproducibility of the FFQ, which was one of our limitations.
3. Because of cost involvement, the serum levels of calcium and magnesium levels could not be

RECOMMENDATIONS

- The issue of dietary diversity should be promoted and popuralized to ensure more balanced diet particularly during pregnancy;
- Special program should be taken to ensure adequate Ca and Mg intake (if necessary by supplementation) during pregnancy,
- Further studies should be undertakes to explore the determinants of dietary Ca and Mg deficiency during pregnancy.

Chapter 8

REFERENCES

8. REFERENCES

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Chapter 9

APPENDICES

Appendix- I

CASE RECORD FORM

ID: ☐ **Date:**

Institution:

Patient Name t .....

Present Address:-

Ph no:-

Serial no	Subjects	Code
1.	**ID** ☐☐ **Date** ☐☐ **Day** ☐	
2.	**Age** ☐☐	
3.	**Area:** 1)Town 2)Village 3)Mid Town	☐☐☐
4.	**Rellgious:**1) Muslim 2)Hindhu 3)Christian 4)Bodho	☐☐☐☐
5.	**Educational Backgrownd** :	
	Illiterate -0 Primary-1 6-class 10 -2 SSc -2	
	HSc-3 Graduate-4 Post graduate-5	
6.	**Profession**	
7.	**Family persons**	
8.	**Monthly income**	

9.	**Famiiy history:-Hypertension: yes/ no/don't know**					
	Relation					
10.	**Pregnancy Period**					
	LMP ☐☐☐		**EDD** ☐☐☐		☐☐☐	

11.	**Delivery Date:**

12. Physical/Clinical Examination	
Height	
BP	
Weight	

13. Treatment History					
Diet	Drug			Exercise	How Many Times
	Name	Dose	Mg		

b)FOOD FREQUENCY QUESTIONNAIRE (FFQ):

Food items eaten	Never eaten or less per month	Frequency of eaten/month	Frequency of eaten/week	Frequency of eaten /day	Cooking procedure	Portion size (g/day)
Cereals						
Rice (Shidha Chal)						
Bread (Loaf)						
Atta (Ruti)						
Moori						
Chira						
Legumes, Nuts & seeds						
Chola						
Cholar dal						
Mug dal						
Moshur dal						
Sharisha						
Pasta,macaroni						
Fried Peanut (China badam bhaza)						
Green leafy vegetables(sources of Mg)						
Data shak						
Sharisha pata						
Sabuj kochu shak						
Pui shak						
Paalong shak						

Other vegetables					
Spring onion					
Green mango					
Carrot					
Kochu					
Borbati					
Sajna data					
Potol					
Shim (Bean)					
Uchche / Korola					
Cauliflower					
Cucumber					
Dherosh					
Kolar mocha					
Motorshuti					
Data					
Cabbage					
Chal Kumra					
Misti Kumra					
Lau					
Green Papaya					
Kacha kola					
Fruits					
Water melon					
Dates (Dry)					
Black berry (Kalo jaam)					
Amra (Hog Plum)					
Olive (Jalpai)					
Guava					
Bangee (Melon)					
Mango (Ripe)					
Pine apple					

Apple					
Amloki					
Atafol					
Kamranga					
Banana					
Citrus fruits (lemon)					
Citrus fruits (orange)					
Fish (Sources of Ca)					
Shrimp					
Chital					
Shole (Cat fish)					
Hilsha					
Shingi					
Gura Chanda mach (small)					
Tengra					
Photi					
Bele/Poa					
Gura Chingree Shukna					
Koi,					
Telapia					
Pabda					
Rul					
Puti					
Mrigel					
Meat, Poultry					
Beef					
Chicken					
Duck					
Mutton					
Goat liver					
Cow liver					

Egg (Duck)					
Egg (Chicken)					
Dairy (Milk & Milk product) product					
Cow milk					
Cheese					
Full cream milk powder					
Shemai					
Shuji					
Firni/paesh					
Shondesh					
Chomchom					
Yogurt					
Borhani					
Other food items					
Betel Leaves					
Kathaler Bichi					
Biscuit					
Shinggara,					
Shamucha					
Patties					
Burger					
Pizza					
Soya					
Role					
Bakery products (cake, pastry)					
Cola drink					
Chocolate					
Tea					

Interviewer Signature

.....

Appendix- II

Consent Form

I Mrs ..... hereby give my well informed and coercion free consent to participate in the study conducted by Ummy Salma Munni, fully understand that my participation in the study will bring fruitful medical and dietary information to be useful for many others in future.

I am convinced that during participation in the study, I shall not be exposed to any physical, psychological, social or legal risks. My privacy and confidentiality will be safeguarded and any anonymity will be protected. I would like/ would not like to be monetarily compensated because of my loss of work. I also consent to use my blood and urine for the study.

Signature of the Principal Investigator	Signature of the Subjects/ Thumb Impression
Date:	Date: