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Effect of calcium supplementation in early pregnancy Libyan women with high risk of pre-eclampsia

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Abstract
Pre-eclampsia (PE) and gestational hypertension (GH) are the main forms of Hypertensive Disorder of Pregnancy. Calcium (Ca) is involved in many body functions. Hypertension complicates 5% of all pregnancies and 11% of first pregnancies and half of these cases are associated with preeclampsia (gestational hypertension plus proteinuria). Calcium supplementation seems to be advantageous but currently it is only considered for patients with poor dietary intake and high risk for PE. This study has conducted to find the use of calcium supplementation in the risk reduction among the Preeclampsia women. The results demonstrated a positive association between 1500 mg calcium daily supplementation and reduction in risk of pregnancy loss among Libyan women who were at pre-eclampsia risk. The introduction of calcium supplementation in maternal health program is strongly recommended among Libyan population with low dietary intake of calcium. 1500 mg -2000 mg of calcium supplement are necessary to reduce the complications during the pregnancy among the women.

Keywords: preeclampsia, calcium supplementation, Libyan women, Zliten

Introduction

Hypertension is estimated to complicate 5% of all pregnancies and 11% of first pregnancies, and half of these cases are associated with pre-eclampsia (gestational hypertension plus proteinuria) (Kassebaum, 2014) [8]. Hypertensive disorders of pregnancy (HDP) are the direct cause of death of about 30 000 women annually, or approximately 14% of maternal deaths, most of which occur in low-income countries (Souza, 2013) [16]. Low-dose aspirin as prevention of preeclampsia (PE) has been widely examined but indication for prescription, timing of treatment initiation, and dosage vary widely between the different studies and guidelines (Lowe, 2015) [13].

Several reference values of daily Ca intake for reproductive age, which vary from 550 mg to 1300 mg, have been established (Kyozuka *et al*., 2020) [10]. Low calcium intake may cause high blood pressure by stimulating either parathyroid hormone or renin release, thereby increasing intracellular calcium in vascular smooth muscle and leading to vasoconstriction (Belizan, 1988) [2]. Vitamin D deficiency during pregnancy has been linked with a number of serious short and long-term health problems in offspring, including impaired growth, skeletal problems, type 1 diabetes, asthma, and schizophrenia (Michael, 2006) [14]. Blood pressure is regulated by intracellular calcium in vascular smooth muscle cell via vasoconstriction and variations of the vascular volume (Yim and Yoo, 2008) [17]. Therefore, appropriate Ca intake for women who hope to conceive is essential not only for preventing future osteoporosis, which may be reduced by the combination of Ca with the appropriate 25-hydroxyvitamin D intake, but also for reducing the risk of HDP. Dietary factors have been suggested to play a role in the prevention of HDP, including GH and PE, and pre-pregnancy Ca intake is thought to an important factor to reduce the risk of HDP. Gestational hypertension is one of the most common medical problems occurring during pregnancy. It is particularly important for pregnant women to be trained on this condition and to learn proper self-care for its prevention and control. Butler *et al*. (1999) [5] reported that only 24% of women with gestational hypertension can manage their blood pressure. Kumar *et al*., (2009) [9] clinical studies have reported that a high dose of Ca supplementation (> 1.5 g/day) could prevent PE.

A study conducted in Uganda on women with normal blood pressure who suffered from preeclampsia and severe hypertension during their postpartum period found 64% of the women to have a high level of knowledge about pregnancy-induced hypertension; however, those women had no knowledge about self-care for this condition (Singh, 2015). There is no much study in Libya. Therefore the researchers aim to study the Effect of Calcium supplementation Early pregnancy women with high risk of Pre-eclampsia in Zliten area, Libya.

Materials and Methods

This study was conducted in the department of Obstetrics and Gynecology, Zliten Teaching Hospital, Zliten, Libya for one year between January 2018 and December 2018. Total 180 cases with Pre-eclampsia and eclampsia were included in this study. They were divided into two groups (90 participants were given with 500 mg calcium tablet and another 90 participants were given with 1500 mg of calcium tablets daily from enrolment early pregnancy until 20 weeks' gestation. The incidence of pregnancy loss were noted at the end result of the study. Basic informations like, age, pregnancy details and socioeconomic details were

collected from the cases by giving questionnaire. Cases with insufficient data and Hypertension before pregnancy were excluded from the study. Calcium level was noted based on the labels of mineral supplement in the tablets cover.

Results and Discussion

Preeclampsia is characterized by 3rd trimester supine blood pressure exceeding 140 mmHg systolic and 90 mmHg diastolic, or a rise of 30 mmHg systolic or 15 mmHg diastolic compared with the 1st trimester levels on two occasions at least 6 h apart, and proteinuria of 30 mg/dl measured by dipstick (Aghamohammadi and Zafari, 2015) [1]. World Health Organization (WHO, 2013) [16] states that health and poor nutrition in pregnant women and newborns are still the significant contributors of their morbidity and mortality (Brilian and Virginia, 2017) [4]. Calcium is one of micronutrients that plays an important role in pregnancy. Insufficient consumption of calcium in pregnant women could lead to preterm birth, which is a major cause of neonatal mortality.

There were 180 cases included in the study. Women with the age of 21-22 years old were more involved (37.78%) in this study (Table 1). Lamminpaa *et al*., 2012) suggested that the preeclampsia is more in the advanced maternal age (AMA) groups. They pointed out that the Women of AMA were 1.5 times more likely to have preeclampsia compared to women less than 35 years of age.

In the present study, the highest percentages (47.22%) of women were with no previous child birth (Table 2). It is new to them that inexperience makes them more afraid and increase the mental stress during their first pregnancy. Luo *et al* (2007) [12] explained the Pre-eclampsia as a disease of first pregnancies. The association between primiparity and pre-eclampsia is so widely accepted that it is at the core of several pathophysiological theories. It has been proposed that pre-eclampsia is the consequence of a maternal immune reaction against paternal antigens expressed in the placenta and that this reaction might result in defective trophoblast invasion and subsequent placental dysfunction. The lower risk of pre-eclampsia among multiparous women has been attributed to desensitisation after exposure to paternal antigens in the placenta during previous pregnancies (Hemenedz-Diaz *et al*., 2009) [6].

Table 1: Distribution of Women's age in this study.

S. No.	Age (Years)	Nos	%
1	18-20	38	21.11
2	21-22	68	37.78
3	23-25	36	20.00
4	26-28	16	08.89
5	>29	22	12.22
	Total	180	100.00

(% calculated from the total 180 cases)

Table 2: Distribution of Previous pregnancy in this study group.

S. No.	No. of Pregnancy	Nos	%
1	0	85	47.22
2	1	56	31.11
3	>1	39	21.67
	Total	180	100.00

(% calculated from the total 180 cases)

The present generation girls/women are highly educated in all over the world. In this study also the largest amount of women (51.11%) was highly educated and studied college or equivalent education qualification (Table 3). This helps them to understand the severity of the problem in the pregnancies and having knowledge about the Preeclampsia. Once they understand, it will be easy to reduce the risks by taking necessary medication and follow-up.

Table 3: Level of Education among the women involved in the study

S. No.	Level of Education	Nos	%
1	Pre School	27	15.00
2	School	61	33.89
3	College/Equivalent	92	51.11
	Total	180	100.00

(% calculated from the total 180 cases)

Always problem arise with the middle class or middle income group people. The low income people suffer but their social resistance or herd immunity among them overcomes any problems among them. 57.77% of the women in this study were belong to the middle income group (monthly income 2000Libyan Dinars) with the high risks of Preeclampsia (Table 4). Present result is in the support of Bhandari *et al*., 2014) [3].

Table 4: Level of Income among the women in the study

S. No.	Income Leve l(LD/Month)	Nos	%
1	Low (<500LD)	12	06.67
2	Medium (2000LD)	104	57.77
3	High (>2000LD)	64	35.56
	Total	180	100.00

(% calculated from the total 180 cases)

Despite many research efforts, the pathophysiology of preeclampsia remains uncertain. Such probable mechanisms consist of changes in vascular smooth muscle membrane stabilization and/or calcium-regulating hormones, natriuresis and associated changes in sodium homoeostasis, direct or indirect effects on cell Ca 2+ metabolism, or depletion of phosphate (Aghamohammadi and Zafar, 2015) [1]. It is believed that low calcium intake causes PTH and renin to increase and this causes an increase in intracellular calcium and leads to vasoconstriction and hypertension. Density of extracellular calcium does not increase by increasing calcium intake and this leads to reduction of nitric oxide (NO) secretion from the vascular endothelium. NO leads to vasoconstriction and hypertension. In the preeclampsia, NO was increased and calcium supplement may reduce preeclampsia by reducing NO.

Calcium supplementation was given to all the cases. 90 cases with low calcium level (500mg/day) and the remaining 90 cases were with normal or recommended level of Calcium (1500mg/day) (Table 5). An increased daily calcium dose in the present study reduced the risks and increased the live birth from 15% to 47.78%. The pregnancy loss after 20 week gestation also reduced significantly (From 8% to 0.56%) after the calcium supplementation. The results of Jain *et al*., (2010) [7] in favour of the results of the present study. They reported that the dietary supplementation of calcium, magnesium and zinc reduce the risks of Preeclampsia.

Table 5: Pregnancy outcomes for all participants with the Calcium supplements.

S. No	Pregnancy Outcomes	Daily Calcium supplement			
		500mg	%	1500mg	%
1	Pregnancy loss<20 weeks gestation	47	26.11	03	01.66
2	Pregnancy loss≥20 weeks gestation	16	08.89	01	00.56
3	Live birth	27	15.00	86	47.78
	Total	90	50.00	90	50.00

Recent evidence suggests that calcium could also increase magnesium levels and have an effect on smooth muscle function of the uteroplacental blood flowSufficient calcium requirements during pregnancy have a potency to minimize the risk of developing high blood pressure during pregnancy which is the significant cause of maternal mortality and the risk of preterm birth (Reddy *et al*., 2014).

Conclusion and Recommendation

Preeclampsia is a major cause of maternal and neonatal death and morbidity. Preterm birth (birth before 37 weeks) is often caused by high blood pressure and is the leading cause of newborn deaths, particularly in low-income countries. In Zliten city of Libya, this study has conducted to find the use of calcium supplementation in the risk reduction among the Preeclampsia women. The study demonstrated a positive association between 1500 mg calcium daily supplementation and reduction in risk of pregnancy loss among Libyan women who were at pre-eclampsia risk. This finding of this research is a step towards addressing the issue among the Libyan women with the same complications.

Currently, the introduction of calcium supplementation in maternal health program is strongly recommended among populations with low dietary intake of calcium. 1500 mg -2000 mg of calcium supplement are necessary to reduce the complications during the pregnancy among the women. Libyan Ministry of Health should make awareness among the Libyan women during pregnancy about the importance of Calcium.

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