

## The Rate of Pre-Eclampsia at Al-Wahda Hospital Derna, Libya: A Prospective Clinical Trial Study

Soad Ajroud<sup>1</sup>, Raga A. Elzahaf<sup>2,3\*</sup>, Manal Younis<sup>4</sup>

<sup>1</sup>Departement Gynae & Obst, Omar Elmukhtar University, Faculty of Medicine, and Al-Wahda hospital / Derna, Al Bayda, Libya

<sup>2</sup>College of Medical Technology, Derna, Libya

<sup>3</sup>MENA Research Group, Libya

<sup>4</sup>Consultant Obstetrics and Gynecology, Cork University Hospital, Wilton, Cork, Ireland

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\*Corresponding author

Raga A. Elzahaf

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**Abstract:** Pre-eclampsia, is an obstetric disorder characterized by hypertension and proteinuria that prevails all over the world. It presents as a pressing peril for fetal and maternal lives. Though inflammation, increased levels of TXA2, ischemic placenta, dysfunction of endothelium are discerned, the exact pathophysiology yet remains a mystery. The absolute treatment is still to be discovered, however its prevention by low dose aspirin and calcium supplementation present as promising preventative measures for pre-eclampsia. To observe the effect of aspirin and calcium in prevention of preeclampsia. This was a prospective clinical trial study for evaluation of role of aspirin and calcium in prevention of pre-eclampsia in primigravidas. It was carried out at department of Obstetrics and Gynecology at AL-Wahda hospital Derna from Jan 2016 to Dec 2016. Three hundred and forty four primigravidae were included in the study. Their age ranged from 16 to 45 years with a mean  $26.32 \pm 4.88$  years. Out of the 344 healthy primigravidae, 63 (18.3 %) developed preeclampsia. Both (aspirin and calcium) supplementations were associated with a reduction preeclampsia. There was significant difference between the group taken both (aspirin & calcium) group and prevent pre-eclampsia ( $X^2= 6.07, P= 0.014$ ). In Conclusion, It was noted in the present study that low dose aspirin and calcium might have beneficial effect in the prevention of preeclampsia.

**Keywords:** Calcium, clinical trial, low-dose aspirin, pre-eclampsia.

### INTRODUCTION

Pre-eclampsia is a disorder that is unique to human pregnancy, and the only known cure for this complication is delivery [1]. It is a major cause of maternal and perinatal morbidity and mortality worldwide, particularly in developing countries [2]. Pre-eclampsia, is an obstetric disorder characterized by hypertension and proteinuria. Though inflammation, increased levels of TXA2, ischemic placenta, dysfunction of endothelium are discerned, the exact pathophysiology yet remains a mystery. The absolute treatment is still to be discovered, however its prevention by low dose aspirin presents as a relieving factor for pre-eclampsia [3]. Moreover the incidence of hypertension is higher in primigravidas in developing countries, compared to multigravidas. When the hypertension is accompanied by proteinuria or convulsions it is called as pre-eclampsia /eclampsia respectively [4].

During the past two decades, numerous

clinical trials were conducted to evaluate the effectiveness of various methods to prevent or reduce the incidence of pre-eclampsia [2]. The results of several clinical trials and meta-analyses have suggested that calcium supplementation [5] or low-dose aspirin reduces the incidence of pre-eclampsia [6]. Further trials also have shown the beneficial effects of these compounds in reducing the occurrence of pre-eclampsia [7].

Low calcium intake may cause high blood pressure by stimulating either parathyroid hormone or renin release, thereby increasing intracellular calcium in vascular smooth muscle, leading to vasoconstriction. A possible mode of action for calcium supplementation is that it reduces parathyroid release and intracellular calcium, and so reduces vascular smooth-muscle contractility. By a similar mechanism, calcium supplementation could also reduce uterine smooth-muscle contractility and prevent preterm labour and delivery. Calcium might also have an indirect effect on

smooth-muscle function by increasing magnesium levels. Calcium supplementation is attractive as a potential intervention to reduce the risk of women developing pre-eclampsia [8]. It is relatively cheap and readily available. Also, it is likely to be safe for the woman and her child, although this safety would need to be clearly demonstrated in pregnant women before any attempt at widespread introduction into clinical practice. Prevention of pre-eclampsia would be a great step forward in prenatal care. One such primary prevention is oral supplementation of calcium and aspirin.

### Aim

The effects of use of Aspirin and calcium supplement during pregnancy in reduction the rate of pre-eclampsia in primigravidae.

### METHODS

This is a prospective clinical trial study. This study was conducted at department of obstetrics and gynecology at Al-Wahda hospital / Derna from Jan 2016 to Dec 2016 on 344 healthy primigravidae women who were agree to participate. They were randomly allocated into four groups by computer generation randomization table. 32 primigravidae women were given aspirin 100 mg (one tablet) per day from 16 weeks of gestation until 34 weeks, 158 primigravidae women were given calcium 1000 mg (one tablet) per day from 14 weeks gestation until delivery. 113 took both (aspirin & calcium) in same protocol. The last group did not receive medication. Each woman was informed regarding the details of the study and written consent was obtained from each of them before engaging in the trial.

All women were examined every 4 weeks till delivery initially. Details recorded were maternal age history regarding hypertension during this pregnancy and family history of hypertensive disorders. Blood Pressure of all primigravidae women were measured, edema and proteinuria. When the primigravidae women arrived in labour ward for the delivery, all their details of current pregnancy were taken into consideration including mode of delivery, baby sex, baby weight and gestational age.

### Statistical analysis

Data analysis was performed using SPSS software version 20. Descriptive statistics, including percentage, mean, range, and standard deviations, were calculated for all variables. Proportions were compared using Chi-square tests and *P*-value less than 0.05 was considered statistically significant. Logistic regression analysis was performed to estimate the association between the potential risk factors and pre-eclampsia among primigravidae.

### RESULTS

Three hundred and forty four (344) primigravidae women were included in the study. There were no losses of follow-up, all women continued antenatal care, and were delivered at the same maternity unit. The ages of the primigravidae ranged from 16 to 45 years with a mean age of  $26.32 \pm 4.88$  years. Out of the 344 healthy primigravidae women observed, 63 (18.3%) developed pre-eclampsia. The difference in age was not statistically significant between primigravidae who developed pre-eclampsia and who do not develop pre-eclampsia ( $X^2=1.44$ ,  $P=0.485$ ). However, pre-eclampsia occurred 1.84 times in age 36-45 years than other age group (Table-1).

Pre-eclampsia occurred (18, 28.6%) among women in the calcium group, (11,17.5%) among women in the aspirin group and (29,46%) among women in the group taken both (Aspirin and calcium).

39.7% of primigravidae who developed pre-eclampsia had family history of preeclampsia. There was a statistically significant difference between pre-eclampsia occurrence in primigravidae who had family history compared with those who did not have a positive family history ( $X^2 = 32.23$ ,  $P = 0.001$ ) (Table-1). Preeclampsia was 5.50 times more in those with positive family history than primigravidas with no family history.

There was a statistically significant difference between gestational age and development of pre-eclampsia. The rate of preterm delivery, defined as birth before 37 weeks of gestation, in the aspirin, calcium and both group was 10.7% ,9.7% and 11.1% (statistical significant ( $X^2 = 7.86$   $P = 0.020$ ) (Table 1).

Also, there was a statistically significant difference between mode of delivery and development of pre-eclampsia ( $X^2 = 22.15$ ,  $P=0.001$ ). While, the majority of the primigravidae delivered with induction 237(68.9%). However, primigravid women who developed pre-eclampsia, 33(52.4%) of them delivery with cesarean.

The rate of low birth weight LBW (<2500) was 14.8% among primigravidae who developed pre-eclampsia and 8.5% who did not develop pre-eclampsia. However, the mean baby weight at birth  $\pm$  SD was  $3230 \pm 555.05$ g,  $3207 \pm 564.31$ g in cases treated with aspirin,  $3216.94 \pm 537.6$  g in those under calcium supplementation, and  $3190.23 \pm 503.24$ g in the both medication group. However, there is no relationship between baby weight and pre-eclampsia (Table-1).

Calcium supplementation was associated with significant reduction pre-eclampsia ( $X^2= 9.358$ ,  $P= 0.002$ ). While 50.2% have not developed pre-eclampsia

and have not taken calcium and 71.4 have not taken calcium and developed pre-eclampsia

Also, there was significant difference in aspirin group to prevent pre-eclampsia while 92.5% have not developed pre-eclampsia and have not taken aspirin and 82.5% have not taken aspirin and developed preeclampsia. Aspirin supplementation was associated

significant with reduction in pre-eclampsia ( $X^2= 6.084$ ,  $P= 0.014$ ).

Aspirin and calcium supplementation were both associated with a reduction in pre-eclampsia. There was significant difference between the group taking both (aspirin & calcium) in prevention pre-eclampsia ( $X^2= 6.07$ ,  $P= 0.014$ ). The pre-eclampsia prevented between primigravidae women who taken both (aspirin & calcium) twice than other (Table-2).

**Table-1: Demographic and clinical data of primigravidae women (n = 344)**

Primigravidae Characteristics	No (%)	Pre-eclampsia No (%)	None-pre-eclampsia No (%)	$X^2$	$P$	OR (95%CI)
<b>Age (Years)</b>						
16-25	170(49.4)	28(16.5)	142(83.5)	1.44	0.485	-
26-35	158(45.9)	33(20.9)	125(79.1)			1.38(0.29-6.41)
36-45	16(4.7)	2(12.5)	14(87.5)			1.84(0.40-8.50)
<b>Family History</b>						
No	189(84)	38(60.3)	251(89.3)	32.23	0.001	-
Yes	55(16)	25(39.7)	30(10.7)			5.50(2.92-10.34)
<b>gestational ageG</b>						
Preterm	37(10.9)	13(35.1)	24(64.9)	7.86	0.020	-
Term	237(68.9)	39(16.5)	198(83.5)			
Postterm	70(20.3)	11(15.7)	59(84.3)			
<b>Mode of Delivery</b>						
Spontaneous	194(56.4)	19(30.2)	175(62.3)	22.15	0.001	-
Induction	43(12.5)	11(17.5)	32(11.4)			0.24(0.13-0.45)
Caesarean Section	107(31.1)	33(52.4)	74(26.3)			0.77(0.34-1.77)
<b>Baby weight (g)</b>						
<2500	(9.5)32	9(14.8)	23(8.4)	2.36	0.101	-
≥2500	(90.5)304	52(85.2)	252(91.6)			1.89(0.83-4.33)

**Table-2: Drugs supplementation for the prevention of preeclampsia**

Drug use		Pre-eclampsia No (%)	None-pre-eclampsia No (%)	$X^2$	$P$	OR (95%CI)
Calcium	Yes	18(28.6)	140(49.8)	9.358	0.002	-
	No	45(71.4)	141(50.2)			0.40(0.22-0.73)
Calcium	Yes	11(17.5)	21(7.5)	6.084	0.014	-
	No	52(82.5)	260(92.5)			2.61(1.19-5.75)
Both	Yes	29(46)	84(29.9)	6.07	0.014	-
	No	34(54)	197(70.1)			2.0(1.14-3.49)

**DISCUSSION**

The results of this study, which was performed on 344 healthy primigravidae women in Derna, Libya, showed that 63 (18.3 %) developed pre-eclampsia. This might increase the morbidity and mortality of the mother and fetus. The prevalence of pre-eclampsia in this study was slightly higher than other study conducted among women attending delivery service in southwest Ethiopia which was 15.2% [9]. Also, the prevalence of pre-eclampsia among pregnant women in turkey was 4.34% [10] and in India was 3.7% [11]. Difference in rates of pre-eclampsia could be methods used, sample size, genetic and lifestyle and culture like diet.

Our study revealed that calcium supplementation in primigravidae women was associated with a statistically significant reduction in preeclampsia incidence similar to other clinical studies and randomized controlled trials [5, 12, 13].

Other studies using 2 g of calcium daily did not achieve a reduced incidence or severity of pre-eclampsia nor did it delay its onset. However, the dose used in these studies was different from the dose used in our study [14].

Aspirin supplementation was associated with significant reduction in pre-eclampsia. Our results are supported by several randomized and clinical trials and

meta-analyses that have suggested the effectiveness of aspirin supplementation in reducing the incidence of pre-eclampsia [6, 15].

The use of aspirin and calcium supplementation daily reduced the occurrence of pre-eclampsia. These were statistically significant. The same results were found in study by Karamali and Asemi they used a combination of calcium and aspirin supplementation that resulted in lower rise in pre-eclampsia among pregnant women [16].

Aspirin and calcium should be seriously considered in the management of pre-eclampsia and it is likely to be safe. The dose, timing and the population to be targeted are still being thoroughly investigated.

## CONCLUSION

Our results suggest that prescription of aspirin and calcium during pregnancy in healthy primigravidae women is effective in reducing the occurrence of pre-eclampsia. We suggest that aspirin and calcium can be used as an effective and inexpensive preventive measure to reduce the risk of pre-eclampsia in healthy women.

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