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The effect of maternal exercise program on fetal growth in pre-eclampsia: a prospective, randomized controlled clinical trial

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Background
Pre-eclampsia affects 2–8% of all pregnancies globally and the condition is estimated to account for 10–15% of maternal deaths worldwide. Preterm birth accounts for 15% of pre-eclampsia disorders. Pre-eclampsia-associated morbidities and mortality can also lead to intrauterine growth restriction and death. So a maternal exercise program has been recommended to prevent and/or decrease pre-eclampsia complications for both the mother and the fetus.

Objective
The aim of this study was to assess the effect of maternal exercise program on fetal growth in pre-eclampsia.

Patients and methods
Thirty pregnant women who suffered from pre-eclampsia were selected from the inpatient Clinic of Mansoura University Hospitals; they were at 27th week of gestation. The participants were randomly assigned into two groups (control and study). The participants in the study group received a designed maternal exercise program. The outcome measure was fetal growth.

Results
Fetal growth measures were significantly higher in the study group compared with the control group ($P < 0.013$).?

Conclusion
It was concluded that the maternal exercise program improved fetal growth in pre-eclampsia.

Keywords:
fetal growth, maternal exercises, pre-eclampsia

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Introduction

Pre-eclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm that occurs after 20 weeks of gestation. Pre-eclampsia is defined as the presence of a systolic blood pressure greater than or equal to 140 mmHg or a diastolic blood pressure greater than or equal to 90 mmHg or higher, on two occasions at least 4 h apart in a previously normotensive patient. In addition to the blood pressure criteria, proteinuria of greater than or equal to 0.3 g in a 24-h urine specimen is a sign for the development of pre-eclampsia [1].

Pre-eclampsia is believed to be one of the leading causes of maternal and fetal mortality and morbidity worldwide [2–4]. Severe pre-eclampsia is associated with different degrees of fetal injury. The main impact on the fetus is undernutrition as a result of uteroplacental vascular insufficiency, which leads to growth retardation [5,6]. So the most common consequences associated with pre-eclampsia is restriction of intrauterine growth, low birth weight, and prematurity [7,8].

Intrauterine growth restriction (IUGR) refers to the poor growth of a fetus while in the mother's womb during pregnancy. The causes involve poor maternal nutrition or lack of adequate oxygen supply to the fetus (uteroplacental effect resulting from pre-eclampsia) [9,10]. IUGR is a fetal weight that is below the 10th percentile for gestational age as determined through an ultrasound [11].

Small for gestational age newborns are those who are smaller in size than normal for the gestational age (a birth weight below the 10th percentile for gestational age) [12]. Low birth weight (LBW) is defined by the WHO as the weight of an infant at birth of less than 2500 g, regardless of the gestational age [13]. small for gestational age and LBW are associated with fetal and perinatal mortality and morbidity, cognitive development, and inhibited growth. LBW is an important predictor of newborn survival and health [14].

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Fetal growth is a useful marker for fetal well-being [15,16]. The changes in fetal growth are assessed by means of anthropometric measurements, fetal weight, and fetal morphometric (head circumference, abdominal circumference, and femur length) [17]. Fetal growth was assessed by two-dimensional ultrasound fetal weight was estimated in grams and fetal morphometric were measured in millimeters.

As a result, perinatal exercise has been recommended as strategies to prevent and/or decrease pre-eclampsia complication for both mother and the fetus especially when performed under professional guidance and supervision [18,19]. Exercise promotes placental growth and maternal angiogenic balance [20]. Several reports also showed that exercise positively influence fetal growth and later developmental milestones in addition to the fetoplacental effect of exercise [21].

Intermittent reduction in fetal and placental oxygen supplies as a result of pre-eclampsia is believed to be the stimulus for exercise-induced increases in placental growth and vascularity. The placental size will increase only to the extent that is necessary to meet fetal and placental demands [21]. The adoption of a supervised, low-to-moderate intensity strength training program during pregnancy can be safe and efficacious for pregnant women [22]. The aim of this study was to assess the effect of a designed maternal exercise program on fetal growth in pre-eclampsia.

Patients and methods

A prospective, randomized controlled trial was conducted between September 2017 and January 2018 at the Inpatient Clinic of Mansoura University Hospitals. The mothers participated in the study after signing an informed consent form before data collection. Recruitment began after approval was obtained from the Ethics Committee of the Faculty of Physical Therapy, Cairo University. This trial is registered with Clinical Trials PACTR 201804003312421.

Inclusion criteria

Pregnant women from 27th week of gestation to up to 34th week of gestation, suffered from pre-eclampsia, their age ranged from 20 to 35 years, were primigravida, had a BMI of less than 35, and delivered by elective cesarean section at week 34 of gestation based on the recommended reference (NICE guidelines) [23] were included if they were clinically and medically stable.

Exclusion criteria

Pregnant women who suffered from any problem that could affect the results at the end of the study, which include cervical insufficiency, vaginal bleeding, heart disease, and systemic lupus erythematous. In addition, pregnant women suffered from eclampsia (the onset of seizures in a mother with pre-eclampsia) and uncontrolled hypertension would be early terminated during the study. Stillbirth fetus and fetus who suffered from any congenital anomalies were excluded from the study.

Participants were referred from the obstetrician. The study program started at 27th week of gestation. At first contact, the participants were asked to complete the evaluation form. Blood pressure, proteinuria, and BMI were evaluated for all participants. They were selected from the inpatient clinic of Mansoura University Hospitals after an initial evaluation. The participants were randomly divided into two groups of equal numbers (n=15): the study group and the control group.

The participants were randomly assigned to the study group (n=15) or to the control group (n=15) by an independent person who took a sealed opaque envelope from a box following a numerical sequence; the envelope contained a letter indicating whether the participants would be allocated to the study or the control group.

Treatment procedures

Both groups received antihypertensive medication under supervision of the obstetrician and participated in activities of daily living freely.

The participants in the control group did not participate in any organized regular physical exercise during pregnancy.

All participants in the study group received the same treatment protocol on a weekly basis, three times per week (60 min/session) from the 27th week of gestation until birth [24].

The treatment protocol involved aerobic exercises, muscular strengthening, and flexibility exercises which met the standard of the American Congress of Obstetricians and Gynecologists [25]. The participants' heart rate was monitored during the training session (heart rate was consistently$<$70% of the age predicated maximum and the rating of perceived exertion scale ranged from 12 to 14 somewhat hard) [26]. Each exercise session was preceded and followed by a gradual warm-up and cool-down periods, respectively (10–12 min duration each). This period involved walking and light static stretching of different muscle groups. The cool-down period included relaxation exercises [24]. Aerobic exercises were applied on treadmill for 10 min: firstly programmed workouts were used until the participant was comfortable with the manual setting. The participant would be able to customize her workout to feel somewhat hard [26]. It offered feedback on distance, calories, heart rate, incline, pace, speed, target heart rate, and time.

The main exercise session included moderate resistance exercises for 25–30 min, performed through the full range of motion and engaged major muscle groups (pectoral, shoulder, and, upper and lower limb muscles); one set (10–12 repetition) was conducted using low to medium resistance with Therabands.

Resistance band (Theraband, Mega Fox, China): a thin, flexible loop that is made of rubber and used to hold things together; it is capable of recovering the size and shape after deformation, relating to or being a collision between particles in which the total kinetic energy of the particles remain unchanged, capable of recovering quickly especially from depression or disappointment.

Outcome measures

The fetal growth was assessed before starting the treatment procedures at the 27th week of gestation and every 2 weeks until the 34th week of gestation (or giving birth) using two-dimensional ultrasound. It was used for the assessment of fetal weight and body morphometrics (circumference and bone length). Fetal weight was estimated in grams. Fetal morphometric measures of femur length, head circumference, and abdominal circumference were measured in millimeters [27]. The participants who develop eclampsia or delivered before the 34th week of gestation were excluded from the study.

Ultrasound examination provides fetal survey, an evaluation of fetal biometry, and an anatomic screening examination. The survey includes a confirmation of fetal number, viability, position, assessment of amniotic fluid volume, and location of the placenta. In the current study, it was used to assess fetal growth including head circumference, abdominal circumference, and femur length. The estimation of fetal weight is a clinically useful parameter which is computed from the fetal growth measurements [27].

The outcome variables were recorded at each assessment in the beginning of the 2 weeks to monitor the growing process of fetuses, while the reading of the 34th week were taken immediately before labor; the time of delivery is decided by obstetricians.

Data analysis was performed using a Statistical Software Program (SPSS Inc., Chicago, Illinois, USA). Normal distribution of variables was tested with the Shapiro–Wilks test. Data were normally distributed; therefore, mean and SD were statistically analyzed and presented. Repeated measures analysis of variance was used to assess the statistically significant effect for the five time points for each group, using the mean differences that were calculated from the equation

$$\text{Post} - \text{treatment (34th week)} \\ - \text{pretreatment (27th week)}.$$

Independent t-test was performed to assess the statistical differences between the two groups. The Bonferroni method was used to adjust the inflation of type I error. For statistical analysis, the results of repeated measures were considered significant at P less than 0.05 and the results of independent t-test were considered significant at P of up to 0.013.

Results

In all, 38 participants were eligible to participate in the study. All participants completed the first assessment at the 27th week of gestation and 30 participants completed the entire study [study group (n=15) and control group (n=15)] (eight participants were excluded because of eclampsia and delivered before the 34th week of gestation; Fig. 1).

Demographic and clinical characteristics of the participants

The baseline assessment showed that there were no significant differences between the two groups as regards the basic demographic and initial clinical characteristics (age, blood pressure, BMI, and proteinuria) (Table 1).

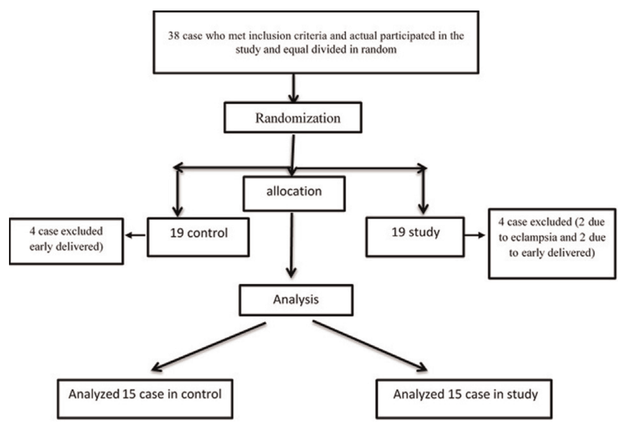
Fetal weight mean±SD at 27th, 29th, 31st, 33rd, and 34th week in the control group was 960±31,1132±49, 1459±59, 1858±72, and 2263±77, respectively, and that of the study group was 973±29, 1299±40, 1692±38, 2018±67, and 2486±69, respectively. Gestation time at which the variables were measured affects the fetal weight in both control and study groups (Table 2).

Moreover, there was a significant increase in the fetal weight of the study group compared with the control group ($P<0.013$), while there was no significant increase in this parameter in the 27th week (Table 3).

Head circumference mean±SD at 27th, 29th, 31st, 33rd, and 34th week of gestation in the control group was 242±4.8±4, 271±1.8, 284±2.4, and 302 ±1.6, respectively, and that of the study group was 242±3±2.1, 278±3, 292±3, and 307±1.8, respectively. In control and study groups, time was found to have a significant effect on head circumference (Table 2).

Moreover, there was a significant increase in the head circumference of the study group compared with the control group ($P<0.013$), while there was no significant increase in this parameter in the 27th week (Table 3).

Figure 1



Flowchart of study participants.

Femur length mean±SD at 27th, 29th, 31st, 33rd, and 34th week in the control group was 48.3±1.1, 49.9±1.4, 53.9±0.9 60.4±1.2, and 61.3±1.4, respectively, and that of the study group was 48.7±1.1, 54±0.8, 57.3±1.2, 63.2±1.2, and 65.9±0.9, respectively. Time was found also to have a significant effect on the femur length in both control and study groups (Table 2).

Moreover, there was a significant increase in the femur length of the study group compared with the control group ($P<0.013$), while there was no significant increase in this parameter in the 27th week (Table 3).

Abdominal circumference mean±SD at 27th, 29th, 31st, 33rd, and 34th week in the control group was 225±3.2, 235±2.90, 260±1.2, 277±3.3, and 299±2.70, respectively, and that of the study group was 226±2.99, 250±5.3, 266±3.3, 288±3.95, and 307±1.90, respectively. In the control and study groups, time was found to have a significant effect on abdominal circumference (Table 2).

Moreover, there was a significant increase in abdominal circumference of the study group compared with the control group ($P<0.013$), while there was no significant increase in this parameter in the 27th week (Table 3).

Discussion

Pre-eclampsia is characterized by a decrease in uteroplacental blood flow and ischemia, which is a significant risk factor in the development of IUGR [28]. Abnormal placentation (defect in the placental

Table 1 Descriptive statistics and *t*-test for the mean age, blood pressure, proteinuria, and BMI of both groups (control and study)

	Control group (mean±SD)	Study group (mean±SD)	*t*-Value	*P* value	Significance
Age (years)	29.47±4.31	28.00±5.54	−0.744	0.464	NS
Blood pressure (mmHg)	157/109±8/3.5	157/107±8/5	0.1	0.921	NS
Proteinuria (g)	0.51±0.10	0.47±0.07	−1.044	0.307	NS
BMI (kg/cm^2)	32.67±1.43	32.43±1.28	−0.436	0.667	NS

P value, probability value; *t*-value, unpaired *t*-value.

Table 2 Comparison of the outcomes at 27th, 29th, 31st, 33rd, and 34th weeks of gestation between the control and study groups (*N*=15)

Weeks	Fetal weight (g)		Head circumference (mm)		Abdominal circumference (mm)		Femur length (mm)	
	Control group	Study group	Control group	Study group	Control group	Study group	Control group	Study group
27th	960±31	973±29	242±4.8	242±3	225±3.2	226±2.99	48.3±1.1	48.7±1.1
29th	1132±49	1299±40	256±4	265±2.1	235±2.90	250±5.3	49.9±1.4	54±0.8
31st	1459±59	1692±38	271±1.8	278±3	260±1.2	266±3.3	53.9±0.9	57.3±1.2
33rd	1858±72	2018±67	284±2.4	292±3	277±3.3	288±3.95	60.4±1.2	63.2±1.2
34th	2263±77	2468±69	302±1.6	307±1.8	299±2.70	307±1.90	61.3±1.4	65.9±0.9
Wilks' λ value	0.003	0.001	0.005	0.002	0.001	0.001	0.012	0.004
P value	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Table 3 Comparison between mean values of fetal outcome variables t between groups (*N*=15)

	Control	Study	*t*-Value	*P* value
Fetal weight (g)				
27th week	960±31	973±29	−1.211	0.236
34h week	2263±77	2468±69	–	–
Mean difference	1303.67±92.01	1488.67±69.47	−6.215	0.001
Head circumference (mm)				
27th week	242±4.8	242±3	0.318	0.753
34th week	302±1.6	307±1.8	–	–
Mean difference	59.47±5.69	64.40±3.25	−2.915	0.007
Femur length (mm)				
27th week	48.3±1.1	48.7±1.1	−0.673	0.506
34th week	61.3±1.4	65.9±0.9	–	–
Mean difference	13.00±1.77	17.20±1.26	−7.469	0.001
Abdominal circumference (mm)				
27th week	225±3.2	226±2.99	0.058	0.954
34th week	299±2.70	307±1.90	–	–
Mean difference	73.53±3.66	82.27±3.58	−6.609	0.001

$P \leq 0.013$, significant after the Bonferroni adjustment.

cytotrophoblast differentiation pathway that leads to hypoperfusion of the placenta) that is associated with pre-eclampsia is important in the pathogenesis of small gestational age [29].

This study was designed to investigate the effect of a designed maternal exercise program on fetal growth (fetal weight, head circumference, abdominal circumference, and femur length) in pre-eclampsia.

Results of the study showed that there were significant increases in fetal weight, head circumference, abdominal circumference, and femur length in the study group compared with the control group at 29th, 31st, 33rd, and 34th week ($P<0.05$).

Improvement in fetal growth was expressed as an improvement in fetal weight, head circumference, abdominal circumference, and femur length. The biparietal diameter is less reliable in predicting fetal growth that is a result of the brain sparing effect, which is a fetal adaptive reaction to placental insufficiency and preferential shunting of blood to the brain that occurs in pre-eclampsia [30,31].

There was no significant difference in fetal weight, head circumference, abdominal circumference, and femur length between the study and the control group at the 27th week. This was attributed to the effect of exercises at the 27th week and still has no significant influence on the measured parameters.

Maternal exercises are considered to be beneficial for placental and fetal growth, as they divert blood toward the muscle and the skin and thus create a short-lived hypoxic environment [32]. Placentas from trained mothers have a reduced nonfunctional tissue volume and an increased functional volume [33].

Therefore, the placenta has an improved surface area available for gas and nutrient exchange [34]. As a result, trained women have been reported to have a greater total placental and fetal mass during normal pregnancy [35] along with a greater placental growth rate [33]. In addition to increased availability of maternal fuels in particular glucose and amino acids, it leads to the stimulation of fetal insulin and insulin-like growth factor-I, which assumes a primary role in the stimulation of fetal growth [35]. So these factors may contribute to the reduction of fetal complications associated with pre-eclampsia, such as intrauterine growth restriction and improved fetal growth.

The findings of this study are in agreement with those of Barakat *et al.* [24], who proved that maternal exercise may be a preventive tool for hypertension and excessive gestational weight gain, and may also control offspring size at birth in addition to reducing the comorbidities related to chronic disease risk.

Also, these findings agree with Moyer *et al.* [36], who reported that various types of exercises thought during pregnancy have been proved to be safe and efficacious for the mother and her fetus. Moderate intensity aerobic exercise is safe and recommended for improved maternal, fetal growth and fetal health outcomes such as cardiovascular health, management of GWG, prevention of chronic diseases, neonatal morphometric, and childhood health measures.

The results of the present study are also consistent with those of Hopkins *et al.* [37], who proved that regular aerobic exercises during pregnancy elicit maternal and fetal adaptations that seem to be specific to the period of gestation in which training is initiated and maintained. This review considers the evidence for both positive and negative long-term health outcomes for the offspring. Exercises training during pregnancy enhance pregnancy adaptation in a manner beneficial for fetoplacental growth.

Their observations indicated that the physiological changes in maternal insulin sensitivity in pregnancy are regulated strongly to achieve optimal fetal growth and are not sensitive to modest increase in energy expenditure through exercise which supports the safety of maternal exercise for fetal well-being [37]. The findings of this study can be explained with the downstream effects of maternal physical activity that may trigger beneficial adaptations to environmental stressors, which may lead to health benefits in later life. The intrauterine environment plays a critical role in downstream child health; this was supported with the work of Zachary *et al.* [38].

Thus, in the present study, the effectiveness of maternal exercise program may be attributed to many factors such as increased functional capacity of the placenta to appropriately deliver nutrients by an increase in placental surface area, improvements in blood flow, and an enhanced perfusion balance [32,34]. The impact of exercise on fetal growth involves an effect on maternal insulin sensitivity, a major determinant of fetal nutrient supply.

There is no evidence to support the use of bed rest in hypertensive disorders of pregnancy, and there is a probable harm from reduced mobility increasing the risk of thrombosis, infection, and psychosocial harm [39].

Although exercise is not routinely offered to women with hypertensive disorders of pregnancy, the accumulating evidence appears to show benefit with no evidence of harm to maternal or fetal health. Exercise seems to modify the possible primary and secondary pathology of pre-eclampsia and could be a preventive measure. Additionally, it could modify long-term cardiovascular health in women who had pregnancies complicated by pre-eclampsia [40].

Limitations of the study

This study was limited by the following factors: physical and psychological condition of the participants during the period of treatment, possible human error in the application of measurement or therapeutic procedures, cooperation of the participant, and variability between participants regarding their reaction to assessment and treatment procedures.

Conclusion

From the results of this study, it was concluded that maternal exercise program improves fetal growth in pre-eclampsia. The effectiveness of the physical exercise programs, the impact of physical activity on pre-eclampsia and birth weight is lacking and findings regarding the impact of physical activity on the risk of pre-eclampsia have been conflicting. High-quality RCTs are still necessary to clarify the optimal frequency, type, duration, and intensity of physical exercise required for beneficial health outcomes during pregnancy. Additional research is needed, in particular, to study the effects of physical exercise on the newborn's outcomes.

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Conflicts of interest

There are no conflicts of interest.

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