

■ Original Research Article

A Randomized Controlled Trial of Aerobic Exercise Versus Standard Care in the Prevention of Pre-Eclampsia Among Primigravida in Aminu Kano Teaching Hospital (AKTH)

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Abstract

Background: Pre-eclampsia is associated with increased maternal and perinatal morbidity and mortality. Lifestyle modification is a recommended strategy for its prevention. **Aim:** To determine the role of supervised exercise in pregnancy in preventing pre-eclampsia among primigravida; and pregnancy outcome in AKTH. **Methodology:** A randomized control trial carried out on 96 primigravida randomized into either the intervention/exercise (n=47) or control group (n=49). Intervention consisted of a circuit of supervised pilates and aerobic exercise training of 60 minutes duration performed twice-weekly for 12 weeks, at moderate intensity. The control had routine antenatal care only. **Result:** Eighty-nine (92.7%) were included in the final analysis [intervention: n=45(50.6%); control n=44(49.4%)]. Supervised moderate exercise in pregnancy was beneficial to primigravida in preventing pre-eclampsia; 27(61.4%) in the control arm developed pre-eclampsia compared to 10(22.2%) in the intervention arm and this was statistically significant (p=0.0001). Mean systolic (sBP) and diastolic blood pressures (dBP) as well as mean gestational weight gain (GWG) in the intervention group at delivery were significantly lower compared to the control [sBP vs dBP: p<0.001; Cohen(d)=0.69 vs p=0.001; d=0.61; GWG (p=0.001)]. Intervention group had a significantly higher incidence of vaginal delivery 39(86.7%) compared to the control 23(52.3%) (p=0.001). Mean gestational age (GA) (p=0.085), macrosomia (p=0.544) and Special Care Baby Unit (SCBU) admission (p=0.585) did not differ significantly between the two groups. **Conclusion:** Supervised physical exercise in pregnancy was a safe preventive measure for pre-eclampsia in primigravida and was associated with increased incidence of vaginal delivery and reduced incidence of excessive gestational weight gain (GWG).

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INTRODUCTION

Pre-eclampsia is a multi-systemic disease of unknown aetiology occurring in the second half of pregnancy that is associated with increased incidence of maternal and perinatal morbidities and mortalities.¹⁻³ It occurs 2-10% of the time globally, causing about 76,000 maternal and 500,000 newborn deaths annually, majority of which occurring in developing countries.^{2,4,5} Primigravida is a moderate risk factor for pre-eclampsia.⁴ Incidence varies widely, occurring

more in developing as compared to developed countries. A pooled incidence of 13% has been reported in sub-Saharan Africa.⁶ In Nigeria, 37,000 women are affected annually,^{7,8} with a reported prevalence ranging between 2% and 16.7%.^{5,9,10} In a recent survey involving 76,563 women in labour in 54 tertiary hospitals in the six geopolitical zones of Nigeria, eclampsia, was the commonest cause of maternal death; accounting for about 20.6% of deaths.¹¹

The relationship between physical exercise during pregnancy and prevention of pregnancy

induced hypertension and pre-eclampsia is not fully established.¹² Previous studies have demonstrated that women who develop pre-eclampsia probably have vascular maladaptation;¹² and are therefore, 9.5 times more at risk of developing cardiovascular disease later in life [hazard ratio (HR)=9.5, 95% CI=4.5–20.3]^{12,13} and nearly five times more at risk for developing end-stage kidney disease (HR=4.96, 95% CI=3.9–6.3).^{12,14} Therefore, preventive therapy, early diagnosis and treatment are advocated. Aerobic exercise training during pregnancy has been recommended as one of the modalities of reducing the incidence of hypertensive disorders in pregnancy (HDP) including pre-eclampsia.

Physical activity prior to and during early pregnancy has been associated with reduced risk of developing pre-eclampsia.¹⁵ There has been conflicting reports on whether physical exercise during pregnancy can reduce HDP including pre-eclampsia or not.¹² While some studies have demonstrated that exercise during pregnancy was associated with significant reduction in the risk of developing pre-eclampsia,¹⁵⁻¹⁸ others reported conflicting results depending on study designs, exercise exposure studied such as (type of exercise, duration and frequencies of the exercise training, the exercise domain), differences in evaluation of the physical activity, inadequate correction for confounding variables and low training adherence.¹⁹⁻²³ The slightly stronger association between pre-pregnancy exercise and pre-eclampsia compared with early pregnancy physical activity, may also be due to higher achievable intensity levels before pregnancy compared with the pregnant state.¹⁴

Globally, several guidelines have recommended aerobic training exercise during pregnancy from 60 to 150 minutes per week with a maximum of 30 minutes per day.²⁴ Pregnant women who exercise according to the guideline have been found to have 30% reduced risk of developing HDP including pre-eclampsia.¹⁶ Exercise in pregnancy is also associated with reduced odds of developing foetal macrosomia and improved cardiovascular health profile of the child at a later age.²⁵ There has not been any evidence of harm associated with exercise during pregnancy especially where not contraindicated.

There has not been any randomized controlled trial in Northern Nigeria on the impact of supervised exercise training on prevention of pre-eclampsia, therefore, this study was carried out to determine the role of supervised physiotherapy exercise on the prevention of pre-eclampsia among primigravida in AKTH.

Aim:

The aim was to determine the role of supervised aerobic exercise in pregnancy in the prevention of pre-eclampsia among women who are pregnant for the first time and pregnancy outcome in AKTH

Specific Objectives

To compare the effect of exercise training in pregnancy on the prevention of pre-eclampsia between the intervention and control groups

To determine the maternal and neonatal outcome between the intervention and control groups

Inclusion Criteria

The study included healthy women who were pregnant for the first time and carried a singleton pregnancy and attended antenatal clinic at Aminu Kano Teaching Hospital at a gestational age of 12 weeks.

Exclusion Criteria

The following category of women were excluded from the study:

- Multigravida
- Multiple gestation
- Pregnant women with known comorbid medical conditions such hypertension, diabetes mellitus, heart disease, sickle cell disease, chronic kidney disease, etc
- Women in second or higher order of marriage but pregnant for the first time

METHODOLOGY

Instruments Used for Data Collection

The following instruments were used for data collection: Informed Consent Form, proforma, used to collect socio-demographic and other relevant data of the participants; Stadiometer (SECA, Germany), used to measure height and weight of participants, Sphygmomanometer (Accusons) and stethoscope (Lithman, USA), used to measure the blood pressure of the participants, Pulse Oximeter, used to assess participants' heart rate and oxygen saturation, Gym balls, used for pilates exercise, each per participant, Resistant Bands of moderate intensity, used for pilates exercises, each per participant, Dumb bells, used for pilates exercises, a pair of 1kg each was given to each participant, Wooden Box of 20 inches by 12 inches by 3 inches, used for aerobic exercises.

Participants' Recruitment

This study started on 12th November 2018 and ended on 25th July 2019. The research took place at the Obstetrics and Gynaecology department and the Physiotherapy department of Aminu Kano Teaching Hospital (AKTH), Kano. Recruitment of the participants took place at the antenatal clinic at a gestational age of 12 weeks. The research personnel included: a Consultant Obstetrician, a Senior Registrar in Obstetrics and Gynaecology and two Women Health Physiotherapy Specialists as well as a Senior Registrar from each team, as research assistants.

Prior to their recruitment, the objectives and methodology of the study were explained to the participants. Those who met the inclusion criteria and who were willing to participate had a written consent obtained from them. A structured Proforma was administered to each participant to obtain their socio-demographic characteristics and other relevant information.

All those recruited continued their routine antenatal follow up and were followed up via phone calls until they came into labour or were admitted into the antenatal ward for ELCS. Each of the participants was given a unique code number which was written clearly on their case notes and questionnaires and those numbers remained their permanent numbers until the end of the study.

Sample Size Determination

The sample size was calculated using the formula below for one-tail randomized controlled trial with categorical outcome variable.²⁶

$$n = \frac{(Z_{\alpha} + Z_{\beta})^2 P (1 - P)^{26}}{(P_T - P_S)^2}$$

Where:

$$Z_{\alpha} = 1.96$$

$$Z_{\beta} = 0.84$$

P_T = prevalence of pre-eclampsia on the intervention/exercise group which is 2.6%²⁷ from another study.

P_S = Prevalence of the comparator group which is 14.6%²⁷ from the same study.

$$P = \text{pooled prevalence} = \frac{P_T + P_S}{2}$$

$$\text{Therefore, } P = \frac{P_T + P_S}{2}$$

$$P_T = 2.6\% = 0.026$$

$$P_S = 14.6\% = 0.146$$

$$P = \frac{0.026 + 0.146}{2} = \frac{0.172}{2} = 0.086$$

$$P = 0.086$$

$$n = \frac{(1.96 + 0.84)^2 \times 0.086 (1 - 0.086)}{(0.026 - 0.146)^2}$$

$$n = \frac{2.82 \times 0.086 \times 0.914}{(-0.12)^2}$$

$$n = \frac{7.84 \times 0.078604}{0.0144}$$

$$n = \frac{0.61625536}{0.0144}$$

$$n = 42.79 \approx 43$$

Considering 10% attrition therefore,

$$n = 10 \times 43 = 4.3$$

$$100$$

$$\text{Hence, } n = 43 + 4.3 = 47.3 \approx 47$$

Therefore, the minimum sample size (n) was 47

Forty-seven women were recruited in each group to achieve a power of 80% and type 1 error of 0.05. The data was collected over 8 months.

Sampling Technique

The recruited participants were randomly assigned into two groups A and B to compare the role of exercise in the prevention of pre-eclampsia. Group A was the intervention/exercise group who received Physiotherapy Educational Classes and physiotherapy aerobic exercise in addition to the standard antenatal care while Group B (Control group) received standard antenatal care alone without any intervention.

The participants were assigned to either of the two groups by balloting. Two sets of 50 opaque envelopes containing pieces of paper designated as A or B were prepared by a research assistant who did not participate in data collection. All 100 envelopes were mixed thoroughly and placed in a box in the antenatal clinic. An envelope was given to each consecutive participant who consented and satisfied the inclusion criteria. The envelopes were handed over to those recruited by the Clinical Assistant at the antenatal clinic. The researcher monitored the impact of the intervention between the two groups till the end of the study.

Intervention

All the participants recruited in the study group were then directed to the Physiotherapy department for physiotherapy educational classes and aerobic physiotherapy exercise. The Physiotherapy Educational Classes were in accordance with the Pelvic Obstetric and Gynecological Physiotherapy Group (POGP)²⁸ and were demonstrated as follows: explaining the Benefits of Exercise in pregnancy including helping them cope with the stress of pregnancy, labour and delivery as well as aiding in faster postpartum recovery, improving the body metabolism thereby helping in prevention of disease conditions such as Gestational hypertension, gestational diabetes, pre-eclampsia, urinary incontinence, back pain and pelvic pain. Some of the exercises that are safe in pregnancy were also explained to them such as walking and cycling.

The participants were also educated on Posture and Ergonomics in pregnancy such as arranging the head in neutral position, when lifting objects participants should try to squat to lift objects from the ground and should not bend their spine, also avoid carrying heavy objects. In sitting position, they were instructed to always maintain an erect posture and sit to the end of chair to rest their back-on-back rest and should not slant their back. A wooden mini stand can be kept on the floor for them to place their feet on top. They were also advised to lie by their sides and slightly flex the hips and knees and when getting up from lying position to drop their feet to the ground, push their body on ipsilateral elbow and then push their body to sitting position with the contralateral hand. They were also advised to not use seat belts across their abdomen rather place above and below the abdomen whenever they are driving or being carried as passengers, and that pregnancy corsets and mattress can also be used.

Procedure For Physiotherapy Exercise

The intervention consisted of a circuit program of supervised pilates and aerobic exercise training of 60 minutes duration performed twice a week for 12 weeks, at moderate intensity consistent with POGP²⁸ and the American College of Obstetricians and Gynaecologists (ACOG) recommendations.²⁹ Each session involved warm-up, aerobic activities (treadmill or stationary bike), strength training (dumbbells, machines or elastic bands), and stretching exercises. The exercise intensity was measured according to each woman's perceived effort. A mean of 24 training sessions were planned for each participant.

Each training session was arranged in stages. The first stage consisted of warm-up period, which lasted for 5 minutes, 15 minutes of aerobic exercise, 35 minutes of strength training/pelvic floor exercises and lastly 5 minutes stretching. The warm up exercises included: the participants lining up to form a wide circle and walking through the highest circumference of the gymnasium for five minutes, including 10 repetitions of lateral neck flexion, flexion and rotation of the shoulders, trunk rotation, flexion of the knees and ankle exercises that involved dorsiflexion and plantar-flexion of ankles for 30 seconds, circling both feet 10 times in each direction.

Following the warm up session, participants received 20 aerobic exercises for 15 minutes in the form of Step aerobics using a wooden step box with length 20 inches, width 12 inches and height 3 inches. They also performed forward stepping on the step box with simultaneous flexion and extension of the shoulders, 1 set of 10 repetitions of each leg. They also performed side stepping on the

same step box with simultaneous shoulder abduction and adduction 1 set of 10 repetitions on each side. This stage was followed by 35 minutes of strength training and pelvic floor exercise which comprised of core stability (including quadruped exercise), pelvic floor muscle exercise, arm and leg strengthening and finally 5 minutes of stretching exercise.

The sessions were supervised by a team of two trained Physiotherapists. Each period of the session comprised of a maximum of five pregnant women in order to offer personalized supervision.

Primary Outcome

The primary outcome was development of pre-eclampsia.

Secondary Outcomes

The secondary outcomes were maternal gestational weight gain (GWG), preterm birth, birth weight, and admission of the baby into special care baby units (SCBU). Gestational age was calculated from their last menstrual period (LMP) and for those who were not sure of their LMP an obstetrics ultrasound scan done before 20 weeks of gestation was used to calculate their gestational ages. Maternal GWG was calculated using weight measured at recruitment subtracted from the weight measured at the last visit to the clinic in consonance with the Institute of Medicine (IOM) recommendations.³⁰ The recommended maternal gestational weight gain during pregnancy for under-weight, normal weight, overweight, and obese women are 12.5-18kg, 11.5-16kg, 7-11.5kg and 5-9kg, respectively.

Ethical Considerations

Approval for the study was obtained from the research ethics committee of AKTH, Kano. The research upheld the fundamental principles of respect of persons, beneficence, non-maleficence and justice. All participants were fully counseled about the study and informed that their participation was voluntary and that there would be no negative consequences for withdrawing at any time during the study. Informed written consent was sought from them and their confidentiality was respected. Names of participants did not appear on the questionnaires; code numbers were used and information obtained was not used against the participants in any way. The participants were informed about the outcome of their result.

Statistical Analysis

The data collected was entered into the personal computer of the researcher and analyzed with the

statistical package for social sciences (SPSS) version 25 (IBM Corp., NY, USA). Data distribution was assessed using the Kolmogorov-Shapiro test of normality. Student's t-test was used to compare means of the continuous data between the study group and control, while chi-square was used for categorical data for statistically significant associations, setting the level of significance (p-value) at $p < 0.05$. The results were presented in tables, texts and figures.

RESULTS

A total of 1024 participants were assessed for recruitment. There were 928 that were ineligible for randomization as shown in the figure below. Forty-seven (49.0%) were randomized to the intervention group and 49 (51.0%) to the control group. Among the participants randomized, 89 were included in the final analysis (intervention group $n=45$; control group $n=44$) as shown in figure 1 below. The predictor variable that was significantly associated with pre-eclampsia was subjected to binary logistics regression analysis.

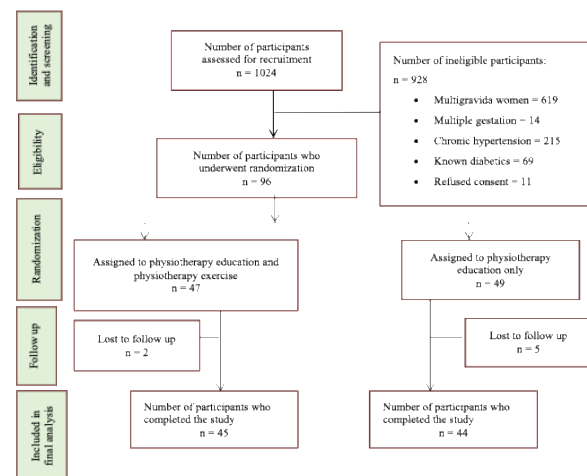


Figure 1: Figure showing flow chart of screening and randomization of the participants (CONSORT flow diagram)

From the above table, the mean age of the participants in the intervention group is 26.2 ± 3.4 years while that of the control is 25.4 ± 2.9 years and this was not statistically significant between the two groups ($p=0.253$). Similarly, there were no statistically significant differences in other baseline sociodemographic characteristics between the intervention and control groups such as the educational status ($p=0.458$) of the women, gestational age at delivery ($p=0.085$) and gender of the neonates ($p=0.381$). On the contrary, the mode of delivery differed significantly between the two groups ($p=0.003$).

From the above table, 22% of the women in the intervention group developed pre-eclampsia while 61.4% in the control arm also developed pre-eclampsia and this was statistically significant

($p < 0.001$). This was similar to maternal gestational weight gain ($p=0.001$) and the mean neonatal birth weight ($p=0.008$). Foetal macrosomia (i.e., foetal birth weight of $\geq 4000g$) was 2.2% and 4.5% in the intervention group and the control respectively and this difference was not statistically significant ($p=0.544$).

Table 1: Sociodemographic characteristics of the participants

Variables	Overall n (%) (n = 96)	Intervention group n (%) (n = 47)	Control group n (%) (n = 49)
Age (years)			
< 20	7 (7.3)	2 (28.6)	5 (71.4)
20-25	49 (51.0)	22 (44.9)	27 (55.1)
26-30	35 (36.5)	19 (54.3)	16 (45.7)
31-35	5 (5.2)	4 (80.0)	1 (20.0)
Mean $\pm$ SD	25.8 $\pm$ 3.2	26.2 $\pm$ 3.4	25.4 $\pm$ 2.9
Educational status			
None	32 (33.3)	12 (25.5)	20 (40.8)
Primary	21 (21.9)	11 (23.4)	10 (20.4)
Secondary	32 (33.3)	18 (38.3)	14 (28.6)
Tertiary	11 (14.5)	6 (12.8)	5 (10.2)
Gestational age at delivery (weeks)			
<38+0	9 (10.1)	2 (4.4)	8 (18.2)
38+0 – 40+0	76 (85.4)	40 (88.9)	35 (79.5)
$\geq 40+1$	4 (4.5)	3 (6.7)	1 (2.3)
Total n(%)	89 (92.7)	45 (95.7)	44 (89.8)
Mean $\pm$ SD	38.8 $\pm$ 1.1	38.9 $\pm$ 1.0	38.7 $\pm$ 1.2
Sex of baby			
Female	30 (33.7)	17 (37.8)	13 (29.5)
Male	59 (66.3)	28 (62.2)	31 (70.5)
Total n(%)	89 (92.7)	45	44
Mode of delivery			
SVD	62 (69.7)	39 (86.7)	23 (52.3)
EM CS	25 (28.1)	6 (13.3)	19 (43.2)
ELCS	2 (2.2)	-	2 (66.7)
Total	89 (92.7)	45	44

X²: Chi square, *: Fishers exact test, †: t-test, SD: Standard deviation, SVD: Spontaneous vaginal delivery, ELCS: Elective caesarean section, EMCS: Emergency caesarean section, n: number, %: percentage

Table 2: Comparison of Development of Pre-eclampsia, Mode of Delivery, Maternal Mean Gestational Weight Gain and Mean Neonatal Weight Between the Intervention and Control Groups

Variables	Intervention group n (%) n = 45	Control group n (%) n = 44	x ²	t	p-value
Pre-eclampsia			15.292		0.0001
Yes	10 (22.2)	27 (61.4)			
No	35 (77.8)	17 (38.6)			
Mode of delivery			13.7.2		0.001
SVD	39 (86.7)	23 (52.3)			
CS	6 (13.3)	21 (47.7)			
Mean gestational weight gain	10.9 $\pm$ 1.7	12.2 $\pm$ 1.9		3.362	0.001
Mean Neonatal birth weight	3.4 $\pm$ 0.4	3.6 $\pm$ 0.3		2.694	0.008
Foetal macrosomia			0.369		0.544
Yes	1 (2.2)	2 (4.5)			
No	44 (97.8)	41 (93.2)			
Missing	--	1(2.3)			

X²: Chi square, t: student t-test, n: number, %: percentage

Table 3: Table comparing the association of some maternal variables with pre-eclampsia

Variables	PE n (%) n = 37	No PE n (%) n = 59	T	p-value
Obesity	14 (37.8)	11(18.6)		0.05*
Mean age of participants	25.6±3.2	25.9±3.2	0.994	0.620
Mean sBP at recruitment	109.2±8.9	111.0±8.1	1.040	0.301
Mean dBP at recruitment	70.8±6.4	69.3±7.2	1.031	0.305

PE: pre-eclampsia, * Fishers Exact Test, sBP: systolic blood pressure, dBP: diastolic blood pressure, n: number, %: percent

Among all the obstetrics variables such as maternal obesity, mean age of participants, mean systolic and diastolic blood pressures at recruitment, only maternal obesity had significant association with pre-eclampsia ($p < 0.05$) and when subjected to binary logistics regression analysis for association between obesity and pre-eclampsia, the result was still statistically significant [$\chi^2 = 4.269$, aOR (95% CI): 2.656(1.0—6.8), $p = 0.040$]

DISCUSSION

Pre-eclampsia is a progressive multi-systemic disease with devastating complications, whose aetiology is not fully understood; and this has made it difficult over the past years, to determine the best way to prevent it. Lifestyle modification in the form of exercise is one of the strategies for its prevention albeit with conflicting results.¹²

The mean age of the intervention group did not differ significantly from the control group (26.2±3.4 years, ranged from 20 to 32 years vs 25.4±2.9 years, ranged from 19 to 33 years), ($p = 0.253$). There were no statistically significant differences in educational status ($p = 0.458$), gestational age at delivery ($p = 0.085$) and gender of the neonates ($p = 0.381$) between the intervention and control groups.

The findings from this study indicate that supervised regular moderate exercise training in pregnancy done twice a week for at least 12 weeks was beneficial to primigravida in preventing pre-eclampsia. About 61.4% of the participants in the control arm developed pre-eclampsia compared to 22.2% in the intervention arm and this was statistically significant ($p = 0.0001$) as shown in table 2. This was similar to the findings of other studies where supervised aerobic exercise training in pregnancy was associated with reduced risk of developing hypertensive disorders of pregnancy including pre-eclampsia^{15-17,19,31,32} but different from the findings of Da Silva and colleagues²² and Zheng and colleagues²³ who found no beneficial effect of exercise training and the risk of developing pre-eclampsia.

While our methodology was similar to Da Silva's, their control group was encouraged to continue their daily activities at home while ours visited the physiotherapy department on each appointment date to receive physiotherapy education thus, believing that such visits to the physiotherapy

department may suffice for the day, whereas their control group may have deliberately engaged in further unsupervised exercise at home leading to the finding of no difference in the risk of developing pre-eclampsia in their study. This implies that supervision of the exercise may ensure compliance thus making the intervention more effective. Kasawara and colleagues¹⁹ in a systematic review in Brazil, reported a protective effect of physical activity in the prevention of pre-eclampsia, which is similar to our finding in AKTH.

The study also found a statistically significant association between maternal obesity and pre-eclampsia ($p < 0.05$) whereas other predictor variables such as mean age of participants ($p = 0.620$), mean systolic blood pressure at recruitment ($p = 0.301$) and mean diastolic blood pressure at recruitment ($p = 0.305$) were not statistically significant. Direct binary logistic regression was performed for the predictor variable that was significantly associated with pre-eclampsia in the univariate analysis (obesity) which made statistically significant association with pre-eclampsia [$\chi^2 = 4.269$, aOR (95% CI): 2.656(1.0—6.8), $p = 0.040$]. The model explained between 4.3% (Cox & Snell R square) and 5.9% (Nagelkerke R square) of the variance in pre-eclampsia. This further implies that maternal obesity was an independent predictor of pre-eclampsia in this study and is associated with more than twice the risk of developing pre-eclampsia among primigravida.

Physical exercise exerts some beneficial effects on the vasculature by exerting some shear forces on the vascular wall,³³ on one hand and by the release of anti-inflammatory and anabolic mediators³⁴ on the other hand leading to functional adaptation of the local and systemic vasculature to meet increased perfusion demands; and structural arterial remodeling by engagement of neuro-humoral and metabolic mechanisms.³⁴ This increased shear force activates endothelial nitrous oxide synthetase (eNOS) and reduces NAD(P)H oxidase activity, resulting in decreased reactive oxygen species (ROS), increased nitrous oxide (NO) bioavailability as well as prevents inflammation-related alterations in eNOS levels and prostacyclin/thromboxane ratio in an atherogenic environment.^{33,35} Physical exercises also reduce the levels of endothelin-1 and noradrenalin³⁶ and at the same time modulates the balance between vasodilating and vasoconstricting factors, by reducing the sympathetic tone and ultimately leading to more vasodilation.^{33,35,37}

Patients with pre-eclampsia have defective remodeling of the spiral arteries which causes placental ischaemia-perfusion damage leading to the production and release of free radicals into the circulation with consequent activation of peripheral leucocytes and platelets resulting in an anti-inflammatory state and finally endothelial dysfunction. This relative placental ischaemia and oxidative stress results in an anti-angiogenic state with

a three-fold increase in antiangiogenic factors such as soluble fms-like tyrosine kinase-1 (sFlt-1) and a 90% reduction in angiogenic factors such as placental growth factors (PGF) and vascular endothelial growth factor (VEGF).^{4,12,38}

sFlt-1 is variant of vascular endothelial growth factor receptor (VEGFR)-1 which competitively binds to VEGF and PGF reducing their bioavailability leading to defective angiogenesis and placentation.^{4,12,38} Soluble endoglin (sEng), which is a modified form of the transforming growth factor (TGF)- β coreceptor^{4,39} is also increased in pre-eclampsia and has been shown to augment the effect of sFlt-1. sFlt-1, PGF and sEng are elevated in the serum of women destined to develop pre-eclampsia several weeks before the clinical manifestation of the disease.^{4,12,39,40}

The mean maternal gestational weight gain (GWG) of 12.2 $\pm$ 1.9kg among the control group was significantly higher than 10.9 $\pm$ 1.7kg recorded among the intervention group ($p=0.001$). This therefore, shows that supervised exercise training in pregnancy among primigravida women is associated with reduced risk of excessive GWG and by implication, they are protected from the untoward effects of excessive weight gain in pregnancy. This finding is in accordance with the Institute of Medicine³⁰ recommendations and similar to the findings of Hamann and colleagues⁴¹ in a systematic review of observational studies supporting the main international findings which suggest that active pregnant women gain less weight compared to inactive women. Our finding is also similar to those of Sanabria-Martínez and colleagues,⁴² Streuling and colleagues⁴³ as well as Xing and colleagues⁴⁴ in a meta-analysis on the effectiveness of physical activity on gestational weight gain.

These findings contrasted the report of Roland and colleagues⁴⁵ where they found no beneficial effect of exercise and GWG. This Roland study took place during the Covid19 pandemic with most of the data being collected by the participants themselves and this was prone to bias and under-reporting or over-reporting by the participants themselves. Self-reported physical activity and weight gain may not reflect the true situation even though the authors used zoom in conducting the exercise as well as motivational training and physical activity and this may therefore, have impact on such studies seeking to explore the risk of GWG outcome.

This study showed a significant positive association of exercise with systolic and diastolic blood pressure changes between recruitment and delivery. This is because the mean systolic and mean diastolic blood pressures of the participants at delivery differed significantly compared to those at recruitment (systolic: $p<0.001$ vs 0.274 and diastolic: $p=0.001$ vs $p=0.660$). The magnitudes of these differences in the means were moderately large, as indicated by the respective effect size values at delivery and recruitment (systolic: delivery $d=0.69$ vs recruitment

$d=0.19$; diastolic: delivery $d=0.61$ vs recruitment $d=0.08$). This implies that 69% and 61% of the variance in systolic and diastolic blood pressure changes may be explained by physical exercise. On the other hand, non-participation in the physical exercise training had very little impact in the control of the blood pressure as indicated by low effect size. This was also similar to other studies.^{44,46}

The mode of delivery differed significantly between the intervention and control groups ($p=0.001$). This study will not conclusively state that this finding was solely due to the intervention given to the participants as there may be other factors that may have had significant impact in such outcome. From this study also, the mean gestational age at delivery and preterm birth did not differ significantly between the two groups ($p=0.085$) similar to the findings of Xing and colleagues⁴⁴ among overweight and obese pregnant women where the meta-analysis results of variables such as preeclampsia, gestational age at delivery, preterm birth and foetal macrosomia in the intervention group were similar to those of the control.

Beyond the impact of supervised physiotherapy exercise on GWG and blood pressure, it also has some beneficial effects on the general health of the pregnant woman including reduction in feelings of fatigue, better postural support, reduced incidence of prolonged labour and delivery complications as well as lowered risk of depression and improved mood.^{41,47,48}

This study, to the best of our knowledge, is the first randomized controlled trial (RCT) in North Western Nigeria evaluating the impact of supervised aerobic exercise in pregnancy among women who are pregnant for the first time for the prevention of pre-eclampsia.

Although the babies born to the women in the control group gained more weight compared to those in the intervention group and which was statistically significant ($p=0.008$), foetal macrosomia between the two groups did not differ significantly ($p=0.544$). This is in contrast to previously documented finding in a meta-analysis of randomized controlled trials which found a 39% reduction in the chances of having a macrosomic baby (OR: 0.61, 95% CI: 0.41 - 0.92) in women who exercised compared to those who did not.¹⁶

CONCLUSION

Lifestyle intervention such as supervised physical exercise in pregnancy was a safe preventive measure for pre-eclampsia in primigravida' in addition to other notable interventions such as drugs and diets; and was also associated with increased incidence of vaginal delivery and reduced incidence of excessive GWG. Supervised moderate physical exercise training during pregnancy is safe and has beneficial effects with resultant good maternal and perinatal outcome.

Recommendation

Exercise in pregnancy should be introduced as part of the routine antenatal procedures for every pregnant woman attending antenatal clinic. Physical exercise in pregnancy should be according to guideline recommendations under the supervision of professionals.

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