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Prenatal Dexamethasone Exposure Malfunctions Maternal Outcome of Albino Rats

Ndung'u C. Wangui[1], Kweri J. Kariuki[2], Thuo Reuben[3], Kafaya G. Kibe[4]
[1](*Department of Human Anatomy, Jomo Kenyatta University of Agriculture and Technology Kenya)*
[2]*(School of Medicine (SoMed), Jomo Kenyatta University of Agriculture and Technology, Kenya)*
[3]*(College of Health Sciences (COHES), Jomo Kenyatta University of Agriculture and Technology, Kenya)*

Abstract
Background information*:The normal morphogenesis of maternal body has been shown to be disrupted by the prenatal exposure to dexamethasone when used during pregnancy, however the specific effects of varied doses of dexamethasone on various organs at different gestion period have not been refined. Such perturbation has been shown to interfere with the normal structural and metabolic function such a in secretion of digestive juices as well as control of the glucose metabolism, neurobehavior abnormalities and gross impairments of functional organs such as pancreas, kidneys, skeletal muscles, adrenal gland, thymus gland, spleen and adipose tissue. Corticosteroids also have also been shown to destroy normal flora leading to pneumocystis carinii and also reducing the immunity of the body. Such perturbations can help in explaining some of the adulthood chronic disorders of the like diabetes type I, hypertension, pancreatic carcinomas, diabetic type II, neurobehavior abnormalities such as hyperactivity, among others without a clear known cause.*
Study design*: The study was experimental study.*
Materials and methods*: 40 pregnant albino rats were used in this study. The albino rats were divided as; albino rats for control group and 37 albino rats for the experimental group. Each experimental group was further subdivided to high, medium and low group and received each group 10 rats. Pregnant albino rats were given peritoneal dexamethasone which varied from HDG 0.65 mg/kg/d, MDG.6.5 mg/kg/d, LDG 13 mg/kg/d during their first trimester, second trimester and third trimester. Control rats received food and water at ad libitum. Daily maternal weight and food intake were recorded.30 rats were randomly selected on day 20th day of gestation and sacrificed.*
Results:*high doses of dexamethasone lead to massive loss of weight especially to the first trimester also there was massive resorption of fetus and dead fetuses. Other parameters included severe loss of weight of placenta and reduction of little size.*
Conclusion*:Fetal growth and organ and development are negatively impaired by chronic and high doses of glucorticoids.*
Key words*: glucorticoids, dexamethasone, prenatal*

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I. INTRODUCTION

Synthetic glucorticoids such as a dexamethasone have been used during pregnancy especially in the treatment of diseases like crohns diseases, multiple sclerosis, cerebral edema, inflammatory bowel diseases, allergies, Addison disease, hyperemesis gravidarum, HELLP syndrome, dermatomyosis[1234]. Dexamethasone also when used during pregnancy have also been shown to efficiently go across the placenta barrier and are consequently universally exercised in the management of virilizing congenital adrenal hyperplasia in females, and enhancement of fetal maturation in utero, intraventricular hemorrhage, and necrotizing enterocolitis[44–6],.Conversely, in spite of its copious clinical reputation's at birth, animal and human experimental reports have exhibited various chronic manifestations to the maternal effect of dexamethasone [7,78]. Use of dexamethasone may precedent to manifold metabolic effects like glucose intolerance, hyperglycemia which could have indirect or direct effect to the pancreas of developing embryo or fetus[7,9,10].Studies done on animal and human have proved that prenatal dexamethasone hampers with metabolic rat prominent to low birth weight, intrauterine growth retardation, tinny fetuses which have been the contributing factors to the increasing chronic diseases such as diabetes mellitus,hypertension.permanent wounding, in the pathogenesis of diabetes type 2,dexamethasone alters the beta cells leading to insulin resistance and chronic hyperglycemia hence diabetes[11,12].According dexamethasone impairs spiny mouse folliculogenesis and enhances follicular atresia through induction of autophagy or combined autophagy and apoptosis[13,14]. Glucorticoids also have numerous unfavorable outcomes to the countless main organs in the body involving muscles, liver, brain, lung, spleen and

heart. Jones et al reveled-on research done narrative primates that lasting prenatal glucorticoid damages motor, affective and cognitive behaviors, working memory and attention deficit, anxiety, depressive disorders.[15,16].Dexamethasone also impedes the normal hypothalamic pituitary axis piloting to disruption of gastro-intestinal motility and adrenal Axis [17], this have aided to irritable bowel syndrome. In early pregnancy, steroids may be used in women for the treatment of recurrent miscarriage or fetal abnormalities such as congenital adrenal hyperplasia[4,18,19] . Prenatal dexamethasone is the drug of choice especially during mid and late trimesters of pregnancy for enhancement of lung maturity for pregnancy mothers with risk of premature delivery[5,20–23].For that reason, the aim of this study is to determine the effect of prenatal dexamethasone exposure to the maternal outcome.

II. Material And Methods

2.1 Experimental animals

40 female nulliparous albino rats were resourced from SAFARI animal biomedical department in Jomo Kenyatta University of Agriculture and Technology (JKUAT). The rats were weighing between 200g to 300 grams. They were lodged in universal rat cages and exposed to 12-hour dark cycles under humid tropical conditions 24°C at the same resource. The cages were marked with a cage tag showing experimental name of the animal, initial date of experiment, prescribed amount of the drug, Age, total sum of experimental rats, type of the rat. The rats were allowed unrestricted access to universal feed Rodent pellets obtained from UNGA Mills as established by American institute of nutrition (1977 (Unga feeds Kenya). and water ad libitum throughout the experimental period. The rats were carried out in agreement with the guiding principles of laboratory animals' recommendations. Two females were instituted to one male albino rat ushered into a cage overnight. The next day, the males were taken back to their individual cages.Vaginal smears were taken from the 40 mated females the next morning and pregnancy was determined by the presence of spermatozoa in the smears followed by vaginal wash 24 hours later to determine changes in estrous which will denote the first day of gestation (GD1)[24,25]. The animals were operated solitary by the skilled investigator associate for the determination of procurement each day weights, consumptions and dexamethasone dispensation. All animals were killed on day 20th using carbon dioxide gas asphyxiation[26]. After pregnancy were established, animals were randomly assigned to either the control or the experimental group. The 36 rats in the experimental category were divided into three marked study groups of 12 rats each allotted low dexamethasone group (LDG), medium dexamethasone group (MDG) and high dexamethasone group (HDG). Each of the marked subgroups was further subdivided into first trimesters (TM1), second trimester (TM2) and third trimester (TM3) trimesters comprising of 4 rats each. All animals received rodent pellets and water ad libitum.Dams were given peritoneal dexamethasone via intragastric gavage (Gauge 1.8 2R2 needle) at through the pregnancy period in first trimester, second trimester and third trimester[27] .

2.2 Feeding and Prenatal Dexamethasone dispensation

All experimental group received oral dexamethasone dissolved in normal saline via gastric gavage (Gauge 1.8 2R2 needle) and rodent pellets and water ad libitum between 8:00 am to 9: am.the control group received only the rodent pellets and water ad libitum between 8:00am to 9: am.the dexamethasone groups received(HDG 0.65mg/kg/d, MDG 7mg/kg/d, LDG 13 mg/kg/d) during the gestation period in first trimester, second trimester and third triminster.the dosage used in this study have been found to be comparable with human dose used during pregnancy (0.5-10mg/kg). The 12 albino rats in trimester 1 received dexamethasone treatment from day one of gestation all through to day 20; those in trimester two study category received dexamethasone treatment starting day 7 all throughout to the last day of gestation day 20, while the 12 albino rats in trimester III start receiving the dexamethasone treatment from day 14 all through to- day 20 the last day of gestation.

2.3 Sample Size Determination

Minimum and Maximum Sample Sizes for Three ANOVA Designs Design[28]. $DF = N – k = kn – k = k (n – 1)$, where N = total number of subjects,
k = number of groups,
and n = number of subjects per group.
DF is degrees of freedom for the error term in an analysis of variance (ANOVA) is between 10 to 20 for minimum and maximum respectively
therefore,
n is given as: $n = DF/k + 1$
DF Minimum $n = 10/k + 1$; $10/10+1=2$
DF Maximum $n = 20/k + 1$; $20/10+1=3$
total Minimum N required = Minimum n x k: $N=2\times10=20$

total Maximum N required = Maximum n x k: N=3×10=30
because of reported death rates[29] the number will be raised by 25% to cater for non-response during fertilization ,resorptions and deaths during the experimental period.
Therefore, overall sample size=sample size/1-(%attrition/100)
30/1-25/100=30/0.75=40.

2.4 **Calculation of Animal Equivalent Dose weighing average 250g**. [30].
Dexamethasone dosage in human; Dexamethasone is given in usual doses of 0.5 to 10 mg daily, depending on the disease being treated. In more severe disease conditions doses above 10 mg per day may be required.[31]
Antenatal dexamethasone 12mg for five days [32]
AED (mg/kg) =human dose (mg/kg) ×Km ratio.
AED (mg/kg) in low dose=0.5mg/kg× (37/7) =2.6mg/kg.
2.6mg/kg given to a rat weigh average weight of 250g=
= (2.6×250)/1000
=0.65mg/kg
AED (mg/kg) in low dose =5.5mg/kg× (37/7) =28mg/kg.
5.5 mg/kg given to a rat weigh average weight of 250g=
= (28×250)/1000
=7mg/kg

AED (mg/kg) in low dose=10mg/kg× (37/7) =52mg/kg.
52mg/kg given to a rat weigh average weight of 250g=
= (52×250)/1000
=13mg/kg

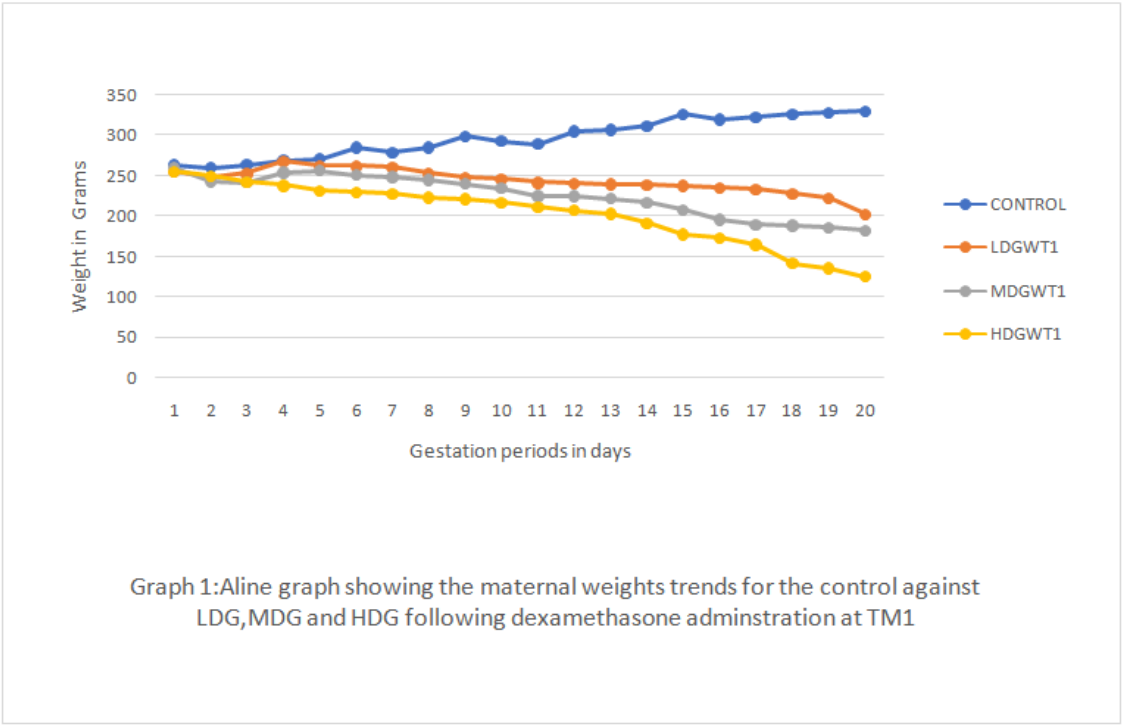
Ethical approval
The ethical approval was obtained from JKUAT Animal Ethical Committee (AEC) before commencement of the study[26].

III. Results

3.1 Statistical analysis

The study sought to analyze the maternal outcomes. The data was analyzed using SPSS and Excel statistical software and was expressed as mean ± standard error (SEM). The study compared how the three dose levels (Low, medium and high) and control in the three trimesters (T1, T2 and T3), affected the different parameters. These parameters were: Initial maternal weight, terminal maternal weight, weight gain, litter size, Resorbed fetuses, Placenta weight, congenital abnormalities and Dead fetuses. To determine the significance, a one-way analysis of variance with Tukey post hoc test was used and 5% significance level (α = 0.05) was assumed. The results were considered to be significant whenever the probability value (sig. value) is less than 0.05 ($p<0.05$). The results were presented below per each trimester.A Pearson correlation value of 0 indicates absence of a linear relationship between the variables. The direction of the relationship is indicated by the sign of the Pearson Correlationvalue.

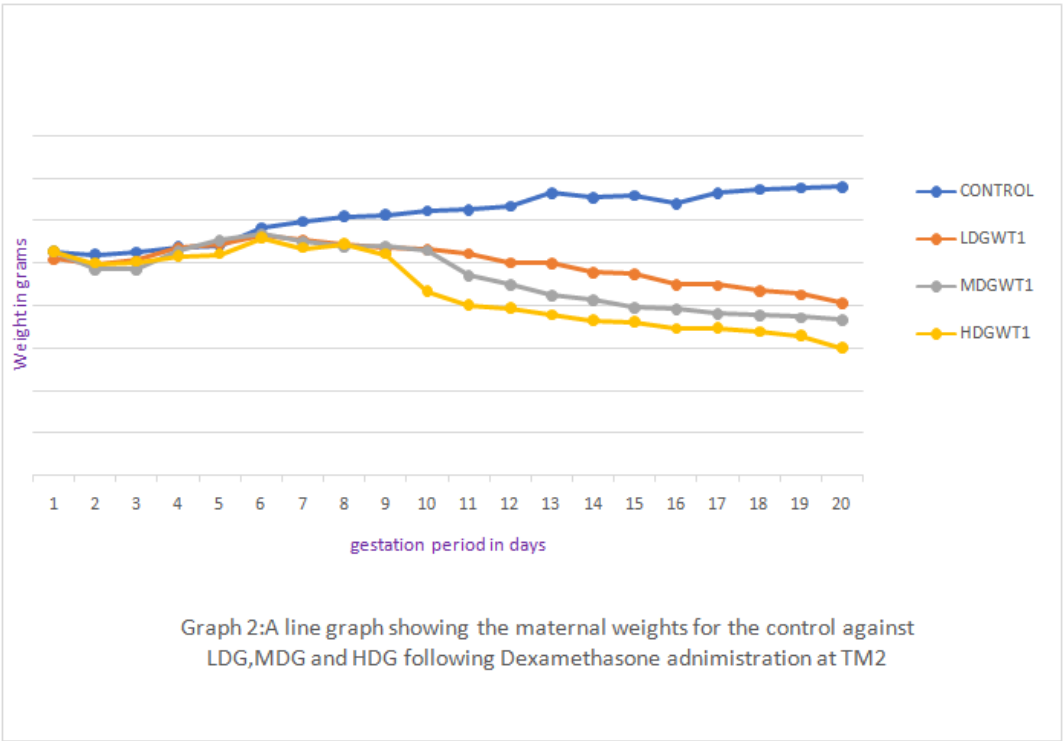
Graph1:graph pointingcomparison amongst maternal weight of control against the low dexamethasone group(LDG), medium dexamethasone group(MDG), and high dexamethasone group (HDG) in trimesters 1(TM1).



Graph 1:Aline graph showing the maternal weights trends for the control against LDG,MDG and HDG following dexamethasone adminstration at TM1

From graph 1 above: It shows that there was a significant decrease in maternal weight gain in all dexamethasone treated groups compared with the control at gestation day 20. These maternal weight losses were found to be statistically significant when compared with the control [LDG p=0.000; MDG p=0.000; HDG p=0.000]. By day 20th, the maternal weight reduced by 47% in the HDG,29.6% in the MDG, and 20.3% in the LDG while the control group gained 25.8% of the initial weight.

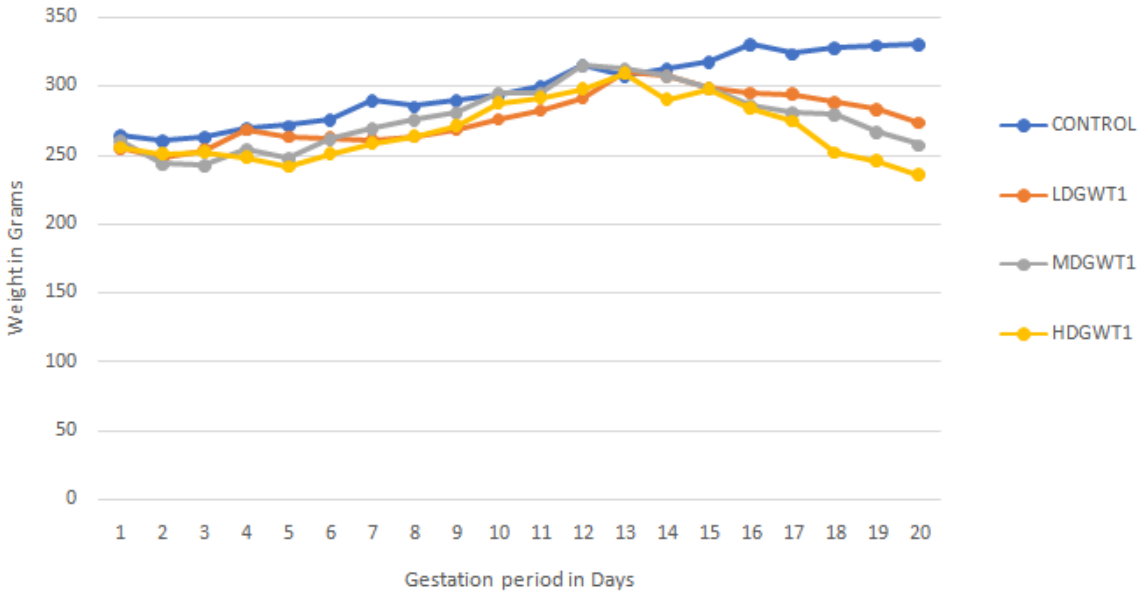
Graph2: Graph showing comparison between maternal weight of control against the low dexamethasone group (LDG), medium dexamethasone group (MDG), and high dexamethasone group (HDG) in trimesters TM2



Graph 2:A line graph showing the maternal weights for the control against LDG,MDG and HDG following Dexamethasone adnimistration at TM2

From graph 2 above: It can be observed that there was a steady weight gain in all groups starting from GD_1through GD_7. This was followed with marked massive weight drop in all dexamethasone groups for a period of 14 days up to GD20. The mean weight loss for the dexamethasone treated groups were found to be statistically significant {LDG p=0.047; MDG p=0.001; HDG p=0.001} when compared with the control.

Graph 3: Graph showing comparison between maternal weight of control against the low dexamethasone group (LDG), medium dexamethasone group (MDG), and high dexamethasone group (HDG) in trimester TM3.



Graph 3:A line graph showing the maternal weights trends for maternal weights for the control against LDG,MDG and HDG following Dexamethasone adminstation at TM3

From the graph 3 above: It can be observed that there was a steady weight gain in all groups starting from GD_1through GD_{14}. This was followed with a marked and sudden weight drop in all alcohol groups on GD_{15} following introduction of dexamethasone treatment. The animals continued with massive loss of weight then rapidly to GD_{20}. The mean weight loss for the dexamethasone treated groups were found to be statistically significant {LDG p=0.016; MDG p=0.021; HDG p=0.001} when compared with the control.

Table1. shows the trends of the effect of control against, low dexamethasone group (LDG),medium dexamethasone group (MDG), and high dexamethasone group (HDG) in trimesters1 of the different parameters.

Parameter	**Control**	**Low dexamethasone group (0.65mg/kg)**	**Medium dexamethasone group (7mg/kg)**	**High dexamethasone group (13mg/kg)**	**F**	**P-value**
Mean initial maternal weight	259.33±4.67a	254±.58a	258±2.52a	264.7±4.91a	1.48	0.29
Mean terminal maternal weight	330.3±15.06a	225.33±11.35b	218.33±23.67b	163.67±2.96b	20.97	0.000*
Mean weight gain	71±12.58a	-28.67±10.81b	-39.67±21.17bc	-101±5.86c	26.79	0.000*
Mean little size	11.77±0.27a	9.07±0.52b	7.6±0.70b	2.23±0.62c	52.78	0.000*
Mean resorbed fetuses	3.67±0.93a	3.87±0.48b	5.4±0.85ab	7.53±0.37b	6.54	0.02*
Mean dead fetuses	1.33±0.33a	3±0.58a	7±2.08a	25.5±4.5b	27.77	0.000*

*The means, followed by the same letter in a row are not statistically different at (P<0.05) using one-way ANOVA with Tukey test on post-hoc t-tests. * indicates significance (p<0.05).*

The Initial maternal weight in the control group (259.33±4.67) was found to be statistically insignificant from that in the low dexamethasone dose group (254±.58), medium dexamethasone dose group (258±2.52) and the high dexamethasone dose group (264.7±4.91); F=1.48, *p*=0.29. This indicated that the dose level in the first trimester did not affect the initial maternal weight.

Terminal maternal weight in the control group (330.3±15.06) was found to be significantly higher than that in the low dexamethasone dose group (225.33±11.35), medium dexamethasone dose group (218.33±23.67) and high dexamethasone dose group (163.67±2.96); *F*=20.97 *P*=0.0001. This indicated that the dose level in the first trimester had an effect on the terminal maternal weight.

Weight gain in the control group (71±12.58) was found to be significantly higher than the low dexamethasone dose group (-28.67±10.81), the mediumdexamethasone dose group (-39.67±21.17) and the high dexamethasone dose group (-101±5.86). This was indicated by a significant p-value, p<0.0001 which was less than 0.05 significance level. However, results in post hoc indicated that the high dose group was again significantly different from the low and the medium dexamethasone groups which were not significantly different from each other.

Litter size in the control group (11.77±0.27) was found to be significantly different (higher) than the low dose group (9.07±0.52), the medium dexamethasonedose group (7.6±0.70) and the high dexamethasone dose group (2.23±0.62), F =52.78, p=<0.0001. However, post hoc test results indicated that the high dose group was again significantly different from the low and the medium groups which were not significantly different from each other.

The effect of the dosage on reabsorbed fetus was statistically significant. The reabsorbed fetus for the control group (3.67±0.93a) was found to be significantly lower than the low dexamethasone dose group (3.87±0.48) and the high dexamethasone dose group (7.53±0.37b). This was indicated by a significant p-value, p = 0.02 which was less than 0.05 significance level.

The effect of the dosage on placenta weight was statistically significant. The placenta weight under the control group (499±15.63) was found to be significantly higher than the low dose group (481.67±11.29), the medium dose group (373.33±18.77) and lowest in the high dose group (250.33±10.57). This was indicated by a significant p-value, p<0.0001 which was less than 0.05 significance level. The placenta weight was also found to be different in all the dose levels. Therefore, the dose levels were found to significantly affect (lower) the placenta weight.

Dead fetuses in the high dexamethasone dose group (25.5±4.5) was found to be statistically different from that in the control group (1.33±0.33) the low dexamethasone dose group (3±0.58) and the medium dexamethasone dose group (7±2.08). This was indicated by a significant p-value, p = 0.001 which was less than 0.05 significance level. However, the three dose levels were not significantly different. This informed that only dosage in high levels affect the number of dead fetuses.

Trimester two

Table 2: shows the trends of the effect of control against, low dexamethasone group (LDG), medium dexamethasone group (MDG), and high dexamethasone group (HDG) in trimesters1 of the different parameter second trimester.

Parameter	**Control**	**Low dexamethasone group (0.65mg/kg)**	**Medium dexamethasone group (7mg/kg)**	**High dexamethasone group(13mg/kg)**	**F**	**P-value**
Mean initial maternal weight	210.67±4.06a	211±3a	252.33±24.29ab	275±6.92a	6.13	0.02*
Mean terminal maternal weight	302.67±3.38a	182.33±12.6b	196.3±30.75b	191.67±10.48b	10.45	0.004*
Mean weight gain	92±1.73a	-28.67±15.03b	-56. ±9.87bc	-83±8.35c	60.4	0.000*
Mean little size	11.83±0.88a	6.7±0.25ab	8.43±0.81bc	3.23±1.01d	20.28	0.00*
Mean resorbed fetuses	1.8±0.3a	3.9±0.85ab	4.7±0.61b	5.7±0.23b	9.11	0.006
Mean dead fetuses	500±7.5a	454.67±5.61b	420±12.34b	286.27±8.66c	107.4	0.000*
Mean dead fetuses	2.67±0.33a	5±2a	6.3±0.88a	15±2.89b	8.8	0.001*

*The means, followed by the same letter in a row are not statistically different at (P<0.05) using one-way ANOVA with Tukey test on post-hoc t-tests. * indicates significance (p<0.05).*

The Initial maternal weight in the control group (210.67±4.06) was found to be significantly lower than that in the low dose group (211±3), medium dose group (252.33±24.29) and high dose group (275±6.92), this was indicated by a significant p-value, p=¸0.02 which is less than 0.05 significance level However the effect of the three doses on the initial maternal weight was not statistically different from each other..

Terminal maternal weight in the control group (302.67±3.38) was found to be significantly higher than that in the low dose group (182.33±12.6) medium dose group (196.3±30.75) and high dose group (191.67±10.48) F=10.45 P = 0.004. The terminal maternal weight in low dose the medium dose and high dose was not statistically different from each other.

Weight gain in the control group (92±1.73) was found to be significantly higher than that in the low dose group (-28.67±15.03), then the medium dose group (-56. ±9.87) the high dose group (-83±8.35). This was indicated by a significant p-value, p = <0.0001 which was less than 0.05 significance level. The test showed that the effect of the low dose and medium dose was not statistically different.

Litter size in the control group (11.83±0.88) was found to be significantly different (higher) than the low dose group (6.7±0.25), the medium dose group (8.43±0.81b) and the high dose group (3.23±1.01), F =20.28, as indicated by the p value p=<0.0001 which was less than 0.05.The medium dose group however was not statistically different from the low dose group.

The effect of the dosage on reabsorbed fetus was statistically significant. The reabsorbed fetus under the control group (1.8±0.3) was found to be significantly lower than low dose group (3.9±0.85), medium dose group (4.7±0.61) and in the high dose group (5.7±0.23). This was indicated by a significant p-value, p = 0.006 which was less than 0.05 significance level. The effect of the three doses was not statistically different from each other

According to post hoc test results the placenta under the control group (500±7.5) was found to be significantly higher than that in the low dose group (454.67±5.61), the medium dose group (420±12.34) and the high dose group (286.27±8.66). This was indicated by a significant p-value, p = 0.0001 which was less than 0.05 significance level. The low dose group and the medium dose group were not statistically different from each other.

Dead fetuses in the control group (2.67±0.33) was found to be significantly lower than that in the low dose group (5±2), medium dose group (6.3±0.88) and high dose group (15±2.89). This was indicated by a significant p-value, p = 0.001 which was less than 0.05 significance level. The low dose group and the medium dose group were not statistically different from each other.

Trimester Three

Table 3: below shows the results of the effect of control, low, medium and high dose levels on the different parameters in the third trimester.

Parameter	**Control**	**Lowdexamethasone group (0.65mg/kg)**	**Mediumdexamethasone group (7mg/kg)**	**High dexamethasone group (13mg/kg)**	**F**	**P-value**
Mean initial maternal weight	235.67±9.60a	217.33±13.33a	224.67±10.65a	216.3±9.28a	0.68	0.59
Mean terminal maternal weight	312.67±13.17a	255.67±14.43b	247±9.81b	230±9.30b	9.11	0.006*
Mean weight gain	73.67±5.90a	38.33±4.63b	22.33±2.40bc	13.67±0.88c	44.72	0.000*
Mean little size	10.6±0.79a	9±2.31a	8.13±0.13a	10.83±6.66a	0.13	0.94
Mean resorbed fetuses	1.93±0.66a	2.87±0.79ab	4.47±0.35b	6.17±0.60b	9.0	0.006*
Mean dead fetuses	520±23.01a	460.33±9.84ab	388±39.95b	344.67±20.21b	9.14	0.006
Dead fetuses	2±0.58a	5.33±0.88ab	7.67±0.67b	12.67±0.88c	34.46	0.000*

*The means, followed by the same letter in a row are not statistically different at (P <0.05) using one-way ANOVA with Tukey test on post-hoc t-tests. * indicates significance (p<0.05).*

According to the post hoc test results the Initial maternal weight in the control group (235.67±9.60) was found to be insignificantly higher than the low dose group (217.33±13.33), medium dose group (224.67±10.65) and high dose group (216.3±9.), this was indicated by a significant p-value, p = 0.59 which was greater than p=0.05 The initial maternal weight in the medium dose group however was not statistically different from the low dose group and high dose group

Terminal maternal weight in the control group (312.67±13.17) was found to be significantly higher than the low dose group (255.67±14.43), medium dose group (247±9.81) and high dose group (230±9.30); F=9.11, P=0.006. The terminal maternal weight in low dose, medium dose and high dose were not statistically different from each other.

Weight gain in the control group (73.67±5.90) was found to be significantly higher than that in the low dose group (38.33±4.63), then the medium dose group (22.33±2.40) and the high dose group (13.67±0.88). This

was indicated by a significant p-value, p = <0.0001 which was less than 0.05 significance level. The low dose and medium dose group however was not statistically different from each other.

According to the post hoc test results Litter size in the control group (10.6±0.79) was found to be insignificantly different (higher) than the low dose group (9±2.31) and the medium dose group (8.13±0.13) the high dose group (10.83±6.66). F =0.13, as indicated by the p value p=<0.94) which was greater than 0.05. The medium dose group however was not statistically different from the low and high dose group.

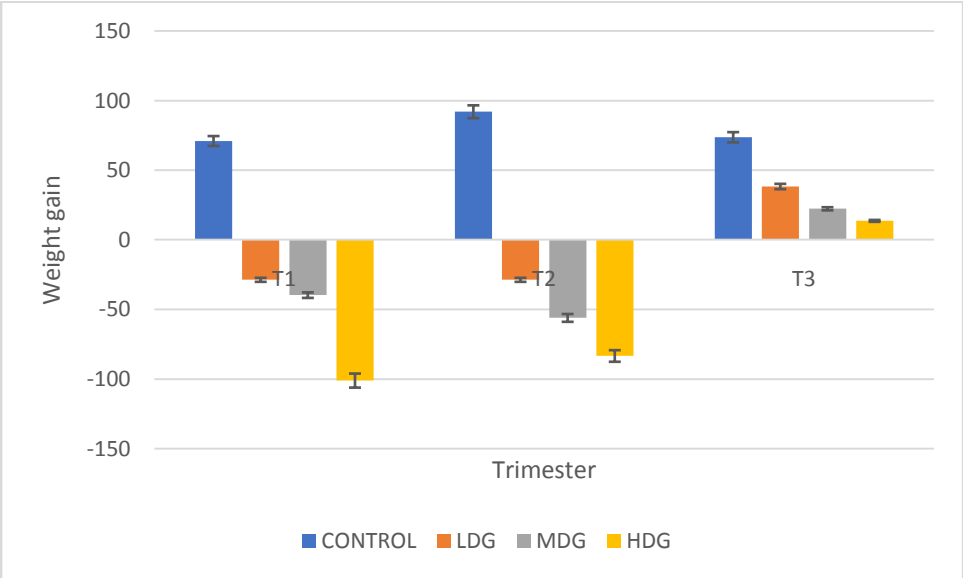
The effect of the dosage on reabsorbed fetus was statistically significant. The reabsorbed fetus under the control group (1.93±0.66) was found to be significantly lower than low dose group (2.87±0.79), medium dose group (4.47±0.35) and the high dose group (6.17±0.60). This was indicated by a significant p-value, p = 0.006 which was less than 0.05 significance level however the effect of the three doses were not statistically different from each other.

The placenta in the control group (520±23.01) was found to be significantly higher than that in the low dose group (460.33±9.84), the medium dose group (388±39.95) and the high dose group (344.67±20.21b). This was indicated by a significant p-value, p = 0.006 which was less than 0.05 significance level. The test also showed that the low dose group, medium dose group and the high dose group were not statistically different from each other.

Dead fetuses under the control group (2±0.58) was found to be significantly lower than that in the low dose group (5.33±0.88), the medium dose group (7.67±0.67) and the high dose group (12.67±0.88). This was indicated by a significant p-value, p<0.001 which was less than 0.05 significance level. However, the medium dose and low dose were not statistically different from each other.

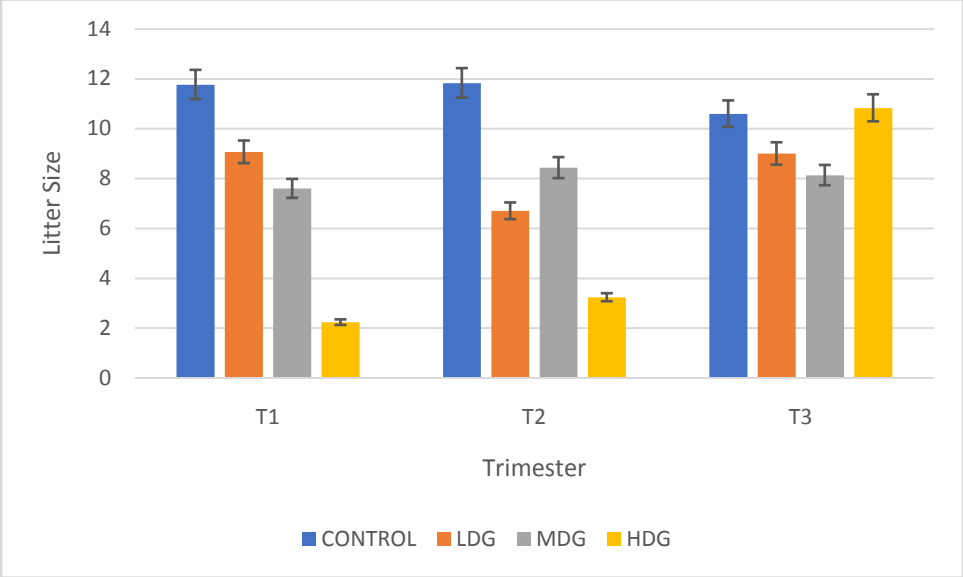
Graph4: Thebelow results were then presented in form of a graph comparing the different doses and control in Trimester 1, 2 and 3

Weight gain



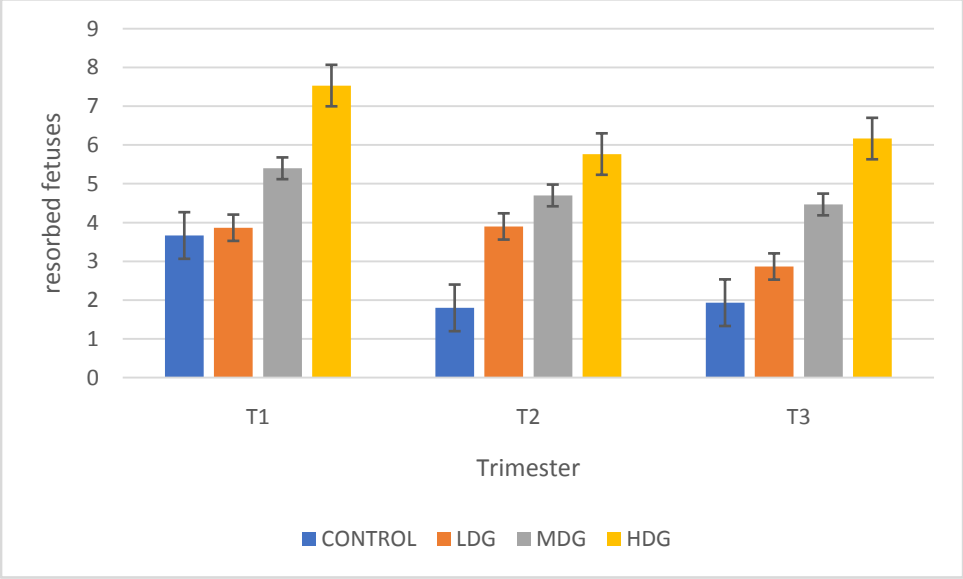
It can be observed that the weight ranges between the minimum and the maximum weight gain for the animal treated at TM1, TM2 and TM3 were {HDG-TM_1-90 to-120 gms; HDG-TM_2 -58 to 86gms; HDGTM_3 -34 to 8 gms} These ranges in weight gains were found to be statistically significant when compared with the control [HDG-TM_1 p=0.000; HDG TM_2 p=0.001; HDG-TM_3 p=0.001].

Little size

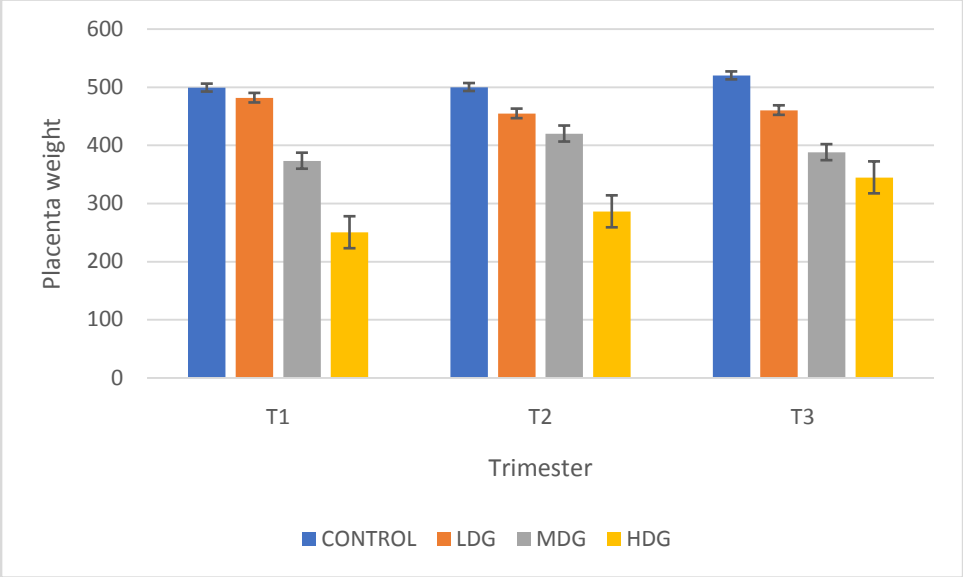


The mean litter size was found to be highest in the control group (11.7+_0.47) and the lowest in the high dexamethasone group (2.33+_0.5). a statistical significant difference in the mean litter size was found to exist between the LDG, MDG and HDG subgroups treated at trimester one(TM_1) and trimester two(TM_2) when compared with the control{LDG-TM_1p=0.000, LDG-TM_2 p=0.047; MDG-TM_1 p=0.000, MDG-TM_2 p=0.001); HDG-TM_1 p=0.000, HDG-TM_2 p=0.047 respectively}. Assessing the statistically significant difference in the mean litter size between the dexamethasone groups and the control at trimester three (TM_3), there was no difference in all the groups(p>0.05).

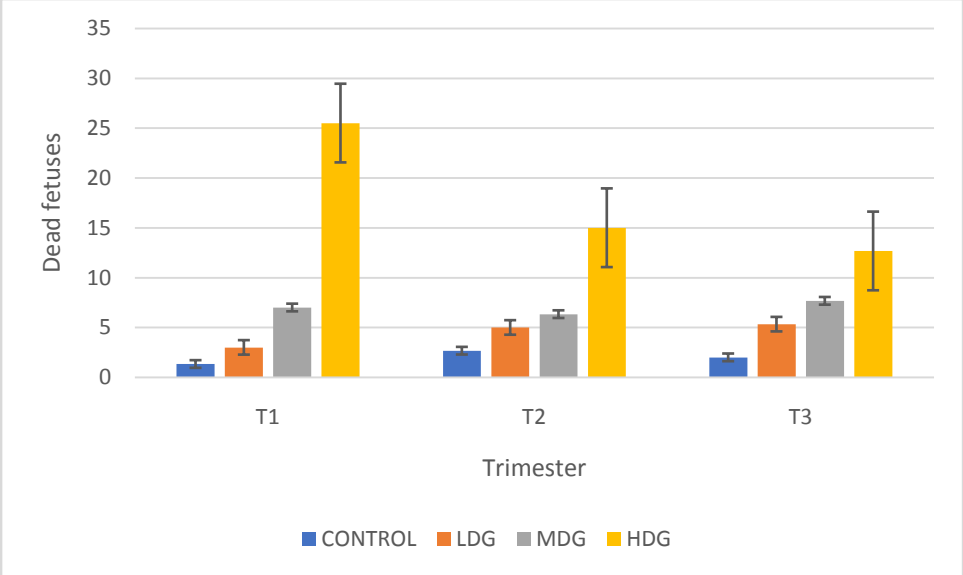
Resorbed fetuses



Placenta



Dead fetuses



3.2 Correlation analysis

This section of the study sought to establish the significance, strength and direction of the linear relationship of our parameters namely: Initial maternal weight, terminal maternal weight, weight gain, litter size, Resorbed fetuses, Placenta weight, and Dead fetuses. Kothari (2014) stated that an absolute correlation value of 0.5 and above indicates a strong linear relationship between variables, a value between 0.3 and 0.5 indicates a moderate linear relationship while a value below 0.3 indicates a weak relationship[33].

		Mean weight gain	Mean initial maternal weight	Mean terminal maternal weight	Mean little size	Mean resorbed fetuses	Mean placental weight	Mean dead fetuses
Mean weight gain	r	1						
	P							
Mean initial maternal weight	r	.125	1					
	P	.467						
Mean terminal maternal weight	r	.177	.243	1				
	P	.303	.153					
Mean little size	r	.603**	.118	-.011	1			
	P	.000	.493	.951				
Mean resorbed	r	-.722**	-.033	-.020	-.403*	1		

fetuses	P	.000	.848	.908	.015			
Mean placental	r	.715**	.139	-.077	.457**	-.773**	1	
weight	P	.000	.418	.655	.005	.000		
Mean dead fetuses	r	-.639**	-.211	.192	-.470**	.731**	-.843**	1
	P	.000	.225	.270	.004	.000	.000	

*NB: r is the Pearson's correlation coefficient, P is the p-value, * and ** indicate significance i.e. p<0.05*

A Pearson correlation value of 0 indicates absence of a linear relationship between the variables. The direction of the relationship is indicated by the sign of the Pearson Correlationvalue. Finally, the significance of the relationship is achieved through p-values. If a p-value of a given relationship is less than 0.05 at 95% confidence level, this indicates that the linear relationship between variables of interest is statistically significant and vice versa.

IV. Discussion

This research paper demonstrates that the injurious effects of prenatal effect to varying doses of dexamethasone have remarkable consequences leading to reduced maternal weight gain during gestation periods, reduced litter size, intrauterine growth retardation(IUGR) ,and a wide range of congenital anomalies to the fetuses, were observed in fetuses whose mothers were exposed to dexamethasone in the first and second trimester and third trimesters. These injurious effects were consequently observed to be contingent on the time and the dose of dexamethasone administered. Dexamethasone being a group of glucorticoids drugs have been shown to have numerous toxic effects especially when given systematically in large doses and chronic use of drug [34,29].

Unlike humans, the rats weight gain reduced massively especially with high doses and chronic doses intake of maternal dexamethasone which lead to death of some of the rats, this was contributed by the lessened food intake which was associated with; reducedappetite for food and water intake, loss of muscles and adipose tissue[293536]. These manifestations were as result of distortion of a genethat is concernedwith the synthesis of adipose tissues called (Ob) gene and leptin hormone which controls body weight by decreasing food consumption. Others contributors to massive weight loss include protein synthesis inhibition leading to loss of muscle bulkiness and decreasedenergy, and fatty acid synthesis impairement[34].Moreover, glucorticoids inhibits hypothalamic corticotropin-releasing-hormone resulting in reduction in body weight set point[12].

Although prenatal dexamethasone consumption during pregnancyespecially to women prone to premature deliveries, dexamethasone enhances decidual uterine artery, fetal middlecerebral artery, descending aorta and umbilical artery within one day after the dispensation37.Maternal dexamethasone when given during the early stages of embryogenesis have been shown to impair the functions of hormone cortisol on binucleate cells phenotypes from inactive form to active form leading to apoptosis and autophagy affecting placental vasculogenesis.3839.This explains the reason for smaller placenta in animal treated with dexamethasone than those not treated in animal studies. Furthermore , glucorticoids impairs placental embryogenesis, growth and proliferation, vasculogenesis and angiogenesis and glucose transport by altering VEGF, VEGFR1 and VEGFR2 .4041,42Prenatal dexamethasone also lower progesterone production and secretion hormone hence impairing the placenta sufficiency resulting to low placental weight. Moreover decline in progesterone hormone in early pregnancy upsurge prostaglandin synthetase activity and prostaglandin F2 generation leading to the abortions and miscarriages.42. Research studies done on sheep have shown that, dexamethasone administration during third trimester can cause fetal death due to impaired placental agenesis and malfunction. 39. Feng et al 2018 found out that prenatal dexamethasone exposure on day 16 to 18 of embryogenesislead to decrease of lake of the neonatal primordial follicle by induction apoptosis, also led to reduced fetal body weight and intrauterine growth retaration43.

V. Conclusion

Use of varied doses of prenatal dexamethasone at different gestation period, have numerous adverse effects especially when given throughout gestation periods and high and medium dexamethasone doses compared when given during the last trimesters in low or medium doses. This concludes that embryo and fetal growth and development are negatively impaired by chronic and high doses of glucorticoids.

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