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PHYSIOLOGICAL AND MORPHOLOGICAL EFFECTS OF ULTRASOUND INTERVENTION DURING PREGNANCY ON NEWBORN RABBITS WITH PARATHYROID HORMONE DYSREGULATION

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ABSTRACT

Ultrasound bioeffect definition is usually used in the pejorative manner, implying that it is unwarranted, and lead to harmful effects. However in reality, these bioeffects when applied in the correct manner and condition propagates beneficial effects in several medical conditions. Present ex-vivo experimental studies were undertaken to examine the effects of ultrasound intervention during pregnancy over newborn rabbits' hormonal, biochemical, physical, and bone development in maternal hyperparathyroidism (HPT) and hypoparathyroidism (HyPT) with and without ultrasound intervention. There were two different maternal conditions which were HPT and HyPT that compared to normal condition. The HPT consisted of a positive control group devoid of any ultrasound intervention and three experimental groups that received parathyroid ultrasound intervention once at different durations and gestational stages. Similarly, in HyPT also comprise of a negative control group devoid of any ultrasound intervention and three experimental groups that received obstetric ultrasound intervention once at different durations and gestational stages. The intervention were given once during pregnancy in the experimental groups for 30 min, 60 min, and 90 min at the 1st (embryonic day (ED) 6), 2nd (ED 17) and 3rd (ED 28) gestational stage accordingly, using *Philips HD3* 2D B-mode system. Acoustic output parameters were kept constant. Total 136 newborns (control, n=12; HPT, n=62; HyPT, n=62) were euthanized and analysed. In compared to normal condition, maternal HPT caused a significant reduction ($p<0.05$) in positive control group newborn parathyroid hormone (PTH), serum calcium (SCa), body weight (BW) crown-to-rump length (CRL), bi-parietal diameter (BPD), femoral length (FL), femoral diaphysis diameter (FDD), trabecular bone volume fraction (BV/TV), trabecular number (Tb.N), cortical area (Ct.Ar), diaphysis mineral-to-matrix ration (M/M), diaphysis proteoglycan content (PGC), osteochondral junction M/M, osteochondral junction PGC. A significant increase ($p<0.05$) in trabecular separation (Tb.Sp), cortical thickness (Ct.Th), cortical porosity (Ct.Po), bone mineral density (BMD), tissue mineral density (TMD) and hypertrophic zone (HZ) length were noted in positive control group newborn. Compared to positive control groups, parathyroid ultrasound intervention in 2nd gestational stage had significant improved ($p<0.05$) newborn PTH, SCa, BW, BPD, FL, FDD, BV/TV, Tb.N, Tb.Sp, Ct.Ar, Ct.Th, Ct.Po, BMD, TMD, osteochondral junction M/M, PGC and HZ length. In compared to normal condition, maternal HyPT caused a significant reduction ($p<0.05$) in negative control group newborn SCa, BW, CRL, BPD, FL, FDD, BV/TV, Tb.N, Ct.Ar, Ct.Th, TMD, diaphysis M/M, C/M, PGC and osteochondral junction M/M, C/M, PGC. A significant increase ($p<0.05$) in the newborn PTH, Tb.Sp, Ct.Po, and BMD were documented in negative control group newborn. Compared to negative control groups, obstetric ultrasound intervention in 2nd gestational stage had significant improved ($p<0.05$) newborn PTH, SCa, BW, FL, FDD, BV/TV, Tb.Sp, Ct.Ar, Ct.Th, Ct.Po, BMD, TMD, diaphysis M/M, C/M, PGC, and osteochondral junction M/M, C/M, PGC. Outcome of present study postulated the effects of ultrasound intervention during pregnancy over newborn development in maternal parathyroid dysregulation. It is anticipated that this experimental data on newborn rabbit following ultrasound intervention can assist into further insights to the possible favourable effect of ultrasound during pregnancy, a phase which has not been explored fairly to its extremity.

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CHAPTER ONE
INTRODUCTION

This chapter enlightens the rationale, significance, and aim of the study. It includes the background of the study, problem statements, research objectives, and the scope of the study.

1.1 PROBLEM STATEMENTS

Hyperparathyroidism (HPT) is defined as an unregulated overproduction of parathyroid hormone (PTH) resulting in abnormal calcium homeostasis. HPT is considered a benign disease of the elderly but when it occurs during pregnancy, it is a life threatening disease. HPT is no longer a rare disease because there has been a great increase in the rate of HPT in recent years [1]. According to Schnatz and Curry, 25% of HPT cases are diagnosed in woman during their child bearing age [2]. During gestational phase, PTH does not cross the placenta but maternal parathyroid dysfunction may affect fetal parathyroid glands development [3, 4].

Maternal HPT causes an increase in serum calcium (SCa) level which leads to intrauterine hypercalcemia thus restraining the development of fetal parathyroid glands [5-8]. High calcium level condition exposed during 1st and 2nd trimester may suppress the complete parathyroid glands development and as a consequence, hypoparathyrodism (HyPT) will occur in postnatal life [8-12]. It has been reported that even mild hypercalcemia in mother can cause fetal parathyroid suppression [9] resulting in neonatal calcium deficiency or permanent neonatal HyPT in worse cases [10]. Calcium is a vital mineral for newborn infant [13]. A reduction in SCa level during intrauterine life will result in life threatening hypocalcemic crisis in early days of life.

Maternal and neonatal complications due to HPT during pregnancy has been reported as high as 67% and 80% respectively [1]. Maternal complication can set in during the early stage of pregnancy and recurrent miscarriage is likely to occur [14, 15]. During pregnancy, HPT will increase the risk of pregnancy loss 3-5 folds higher than expected as it usually occurs in late 1st trimester or early 2nd trimester [14]. Miscarriages can be detected at all elevated calcium levels but frequently seen in cases of calcium