UNIVERSITI TEKNOLOGI MARA

PHYSICAL, MORPHOLOGICAL AND BIOCHEMICAL EFFECTS OF PRENATAL ULTRASOUND EXPOSURE ON RABBIT FETUS

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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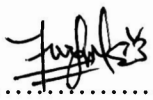
Signature of Student	:	 .....
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ABSTRACT

Ultrasound is extensively used in various clinical specialties throughout the developed world since it was perceived to lack in bioeffects. Somehow, through the advances in the capability of ultrasound equipment that triggered greater image processing power, the revision of potential bioeffects is needed to be corroborated. Hence, this study is designed to determine the physical, morphological and biochemical effects on fetus development. This *in-vivo* experimental study involved twelve pregnant rabbits, exposed to ultrasound exposure durations of 30, 60 and 90 minutes in the middle of the stipulated gestational stages (1st stage; gestational day (GD) 6-7, 2nd stage; GD 17-18, 3rd stage; GD 28-29). Acoustic output parameters were kept constant (frequency = 7.09 MHz, intensity (I_{SPTA}) = 49.4 W/cm^2, power = 56.0 W, thermal index (TI) = 0.2 and mechanical index (MI) = 1.0). The rabbits were euthanized and data were analyzed using SPSS 21. Total 136 fetuses (1st stage, n = 34 (25%); 2nd stage, n = 28 (21%); 3rd stage, n = 74 (54%)) were analyzed for physical, structural and ultrastructural morphological, biochemical and haematological analyses. Physical analysis found to have significant differences in fetal weight between exposed and control groups at all stages ($P < 0.001$, $P = 0.01$, $P < 0.001$, respectively) with a negative correlation between different exposure durations and fetal weight at 1st and 3rd stages ($P = 0.02$, $r = -0.40$, $P = 0.04$, $r = -0.23$, respectively). There were also significant differences in brain volume and surface at all stages of gestation ($P < 0.05$). Ultrastructural morphological analysis showed statistically significant in apoptotic neurons and glial cells (AC) count at 1st and 2nd stages ($P < 0.05$) with positive good and fair correlation ($P < 0.001$, $r = 0.53$; $P < 0.001$, $r = 0.47$, respectively). While, biochemical investigation reported that significant differences in AC at all stages ($P < 0.001$) with mean AC depicted lowest in control groups, in congruent to structural morphological analysis where neuronal cell death (NCD) count were significant at all stages ($P < 0.001$) and mean NCD least in control groups. Haematological analysis reported that significant differences in red blood cell (RBC) count, white blood cell (WBC) count, haemoglobin (Hb) concentration, platelet (PLT) count and lymphocytes (LYM) count ($P < 0.001$, $P = 0.04$, $P < 0.001$, $P < 0.001$, $P = 0.01$ respectively). There were negative correlation of exposure with RBC, Hb and PLT ($P = 0.01$, $r = -0.38$; $P = 0.04$, $r = -0.27$; $P = 0.02$, $r = -0.32$, respectively), yet a positive correlation with LYM ($P = 0.03$, $r = 0.30$). Results suggested that ultrasound might interfere with the sensitive stages of developing fetus by both thermal and mechanical effects that probably induced hyperthermia and heat stress to the fetus *in-utero* hence, plausibly interrupted the biological cells. Further empirical research is needed to endeavor for being sufficient to draw a conclusive safety statement of prenatal ultrasound and contributing to the current body of knowledge.

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CHAPTER ONE
INTRODUCTION

1.1 BACKGROUND OF THE STUDY

This chapter presents the background and the problems of the research, and also the scope, aim and objectives of the study. It ends with an outline of the thesis, which briefly describes each of the following chapters.

Following the invention and development of an ultrasound machine in the late 1950's, it has been used for diagnostic purposes in clinical practices throughout the developed world in various specialties, especially in the care of women and child for decades (Chau, 2002; Haar, 2011; Kieler, Cnattingius, Haglund, Palmgren, & Axelsson, 2001) and at most extensively in the field of obstetrics and gynecology (Abramowicz, Lewin, & Goldberg, 2008; Chau, 2002; Kieler et al., 2001; M. W. Miller, Brayman, & Abramowicz, 1998). Prenatal ultrasound is found to reduce perinatal mortality due to its ability in early detection of fetal malformations during pregnancy in a controlled trial study on human (Saari-Kemppainen, Karjalainen, Ylöstalo, & Heinonen, 1990). It is applied during the assessment of normality or abnormality of the first trimester of pregnancy, determination of gestational age and fetal number, detection of fetal structural abnormalities and continuous assessment of fetal growth and well-being throughout gestations during pregnancy (Abramowicz et al., 2008; McHugo, 2000).

Another application in the hyperparathyroidism ultrasound therapy treatment is possible in lowering the serum parathyroid hormone level (Kovatcheva et al., 2010) and in ablating benign thyroid nodules to eliminate the need for a thyroidectomy surgical procedure (Esnault et al., 2011). These therapeutic applications of ultrasound may use higher acoustic output and exposure as compared to diagnostic ultrasound (Duck, 2008; Haar, 2011). Meanwhile, Deyne & Kirsh-Volders (1995) found that the lytic effects of cells are induced to facilitate phagocytosis and promote scars healing through ultrasound heating. Furthermore, Clement (2004) stated that it is also able to kill tissues through coagulative necrosis while focused beam allows to concentrate on destroying a small volume of tissue without affecting the neighboring structures. Apparently,