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FETAL PROGRAMMING: POTENTIAL TOOL FOR IMPROVING REPRODUCTIVE PERFORMANCE OF RABBITS – A REVIEW

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Poor maternal nutrition during pregnancy cause poor foetal growth, poor foetal mammary gland development and susceptibility to oxidative stress damages all causing poor reproductive performance in adulthood. Inadequate supply of nutrients for metabolic use of animals during pregnancy stages is the most prominent route of this problem at both pre and post natal lives of animals. Rabbits because of their ability to survive on forage and non-conventional animal feeds resources coupled with poor commercial production value attached to rabbits in some countries; are left out of fetal programming science. However, foetal programming at early, mid and late pregnancy as well as early post-birth periods in rabbit, can be a vital means of improving rabbit reproductive performance because these are the periods of gonads development and acquisition of important reproductive traits by the offspring. Fetal programming is a potential reproductive technology for improving rabbit reproductive performance because it is now clear that full range of altered offspring phenotypes includes impaired reproductive function occurred as results of failures during foetal development. In rats, sheep and non human primates, reproductive capacity is altered by challenges experienced during critical periods of foetal development and early post-birth period. This paper will discuss fetal programming practice as a potential reproductive technology for improving reproductive performance and overall productive life-time in rabbit. It also gave an overview of the current state of fetal programming research focusing on improving rabbit reproductive performance through exploration of functional properties in microalgae.

Keywords: Fetal Programming, Rabbit, Reproductive performance and Microalgae.

Feeding and nutritional practices during pregnancy play major roles in cellular, organ and system development as well as lifetime health status and overall productive performance of both humans and animals. This is a scientific position confirmed through epidemiological studies on early life intrauterine environment. Maternal nutrition during pregnancy has effect on reproductive system development and functions for both male and female offspring. Good and poor planes of nutrition are respectively capable of leading to good and poor reproductive performances in offsprings at adulthood (Godfrey and Barker, 2000; Asmad, 2014). During early stage of pregnancy, embryonic metabolic activity and rapid developmental changes in the foetus for growth demand good nutrition; else, growth of the foetus becomes impaired (Ehrhardt and Bell, 1995 and Redmer *et al*, 2004). Poor maternal nutrition during pregnancy cause poor foetal growth, poor foetal mammary gland development and susceptibility to oxidative stress damages (Bielli *et al*, 2001; Jenkinson, 2003 and Bernal *et al*, 2010).

In the long-term, poor and or good maternal nutrition during pregnancy negatively or positively impact on offspring growth, ovarian cell development capability, reproductive output, susceptibility to reproductive related ailments and overall animal productivity. Rabbit because of their ability to survive on forage and non-conventional animal feed resources as well as the poor commercial production value attached to rabbits in some countries; they are left out of foetal programming science. Therefore, to improve rabbit reproductive performance; this article identified foetal programming as a reproductive technology capable of contributing to rabbit reproductive capacity.

***Pre* and *post* natal development of rabbit reproductive system**

In the pre-natal stage (during foetal development phase), the reproductive system of rabbit commences. In both male and female rabbit, 16^{th} day of fertilization is the time of sexual differentiation and development. In male rabbit, oval shaped testes descend from abdominal cavity at about two months after birth. The process of sperm production (spermatogenesis) begins at days 40 – 50 after birth and the testes becomes active at day 84 of existence while spermatozoa can be found in ejaculate at about 110 days old. However, sexual maturity is defined as the moment when daily sperm production ceases to increase in ejaculates which has both biological and environmental determinants such as breeds, nutrition, management practices and environmental variables like temperature and relative humidity (Lebas *et al.*, 1997).

In female rabbit, the process of sexual development commence on day 16^{th} after fertilization similar to what is obtainable in male rabbits. Ovary which is the most primary sexual organ begins maturation from 21^{st} day of foetal growth and continues till birth. Reproductively, a female rabbit matures within 10 – 12 weeks of its lifetime although this period can be regarded as onset of puberty because mating during this time may not necessarily lead to conception as rabbit may not ovulate at onset of puberty. Breed differences, management practices and general body development are factors capable of affecting reproductive maturity of female rabbits.

Female rabbit because of their special ovulation patterns can be on heat for almost all the time and hence has higher and special reproductive capacity compare with other domestic animals. They are spontaneous ovulators whose ovulation takes place within 12 hours after mating; however; without mating, rabbit may not come on heat and naturally ovulate but follicles produced go into regression and are then replaced by production of new ones. Female rabbits can also be put into mating while lactating which is another unique feature of female rabbit (Moret, 1980).

Influence of maternal nutrition during *early*, *mid* and *late* gestation periods on growth and development of reproductive system

Maternal reproductive structure where foetal development takes place is uterine; and it is an environment essential for foetal growth and development during gestation and post-birth period. Productivity at adulthood is programmed in the uterus, therefore factors including maternal nutrition, endocrine functions and *intra*-uterine physical conditions are all factors affecting foetal growth and in the post-birth period. Hence deliberate process of manipulating foetal condition in the uterus for better post-birth performance and higher productivity in adulthood is termed “Foetal Programming”. During this period, permanent physiological changes can be infused in the animal throughout its life-time (Gardner *et al*., 2009; De Boo and Harding, 2006 and Armitage *et al*., 2004).

Maternal nutrition is a leading factor affecting foetal development because availability or non-availability of nutrients for use of the fetus coupled with effectiveness of the placenta connecting the intra-uterine environment and the fetus determines foetal access to nutrients, and nutrients utilization for foetal growth and development. Inadequate maternal nutrition results into poor reproductive performance in future adult life especially in animals with inadequate nutrition during early and mid gestation periods because this is the period of placenta development. Poor placenta development is implicated in reduced reproductive capacity in both male and female offspring. Higher susceptibility to oxidative stress damage, DNA damage and alteration as well as poor development and functioning of gonad tissues were also reported to be associated with poor maternal nutrition (Igwebuike, 2010; Rhind, 2004).

Inadequate maternal nutrition in rabbit does during early pregnancy results into fast and rapid weight gain during a re-feeding phase.

The compensatory growth after inadequate nutrition in early pregnancy is possible, because despite the inadequate nutrition, maternal energy balance is still positive. The fast weight gain is also supported with lower leptin concentration which is an anabolic indicator for compensatory growth in the animals. Early maternal inadequate nutrition was also reported not to affect offspring performance because it does not affect milk production in rabbit (Rommers *et al*., 2004; Brecchia *et al.,* 2006; Manal *et al*., 2010; and Brecchia *et al.,* 2012).

However in mid and late pregnancy, inadequate maternal nutrition in rabbits was reported to negatively affect rabbit performance and also cause poor milk production. Energy which is the most important nutrient during gestation can be implicated for the negative effects because increase energy for metabolic activities in both the dam and the fetus if not satisfied can result into malnutrition in the dam which consequently can cause reduction in fetus number and weight at birth, as well as impaired post-natal life and growth. This was evident in the work of Brecchia *et al.* (2012) which reported reduced litter size for the rabbit does under feed restriction as well as poor reproductive performance of the offspring.

According to Asmad *et al*. (2012), in a meta-analysis studies carried out on foetal nutritional effects on growth and reproductive performance of sheep reported that male sheep offspring undernourished during gestation had significantly slower growth and lower testosterone levels which are pointers to poor reproductive performance at adulthood. The authors pointed out that insufficiency of feed resources during winter period, which is the time most sheep get pregnant in the temperate region can be the reason for the foetal malnutrition. Lambs who were malnourished at foetal stage were also reported to have reduced birth weight while lamb malnourished during lactation were also reported to have reduced testis weight, reduced testosterone concentration and poor live weight gain after birth.

Although Rae *et al* (2002) reported no differences in testis weight and functions in either well-fed or malnourished animals during foetal development but nutrient restriction or inadequacy in their study was protein compared to studies which reported differences in testis weight and functions whereby the inadequate nutrient was energy. It can therefore be deduce from these separate submissions, that nutrients restriction types during foetal growth and development is a very important factor in foetal nourishment because of its consequences on future reproductive performance of the animals.

Potential roles of fetal programming on post foetal growth and semen qualities in rabbits

Maternal malnutrition affect foetal growth rate and is also capable of leading to negative kindling output; in the post birth adult life, it affect rabbit growth performance because rabbit growth rates depends on two major factors including birth weight and litter size (Symeon *et al*., 2015). Since it is possible for malnourished rabbit does to have poor litter size or kindle offspring with poor birth weight as evident in the study of Brecchia *et al*. (2012), where feed restriction at late gestation period resulted into kindling of rabbit fryers with lower birth weight; foetal programming has potential as a reproductive tool for providing solution to this problem. At the early pregnancy stage provision of balanced diets for consumption of the rabbit does will definitely ensure proper implantation and hence inhibit possibility of abortion or dead foetus. Dietary introduction of antioxidants in pregnant rabbit does will also contribute to elimination of free radical influence capable of restricting foetal growth and development. Rabbit with good growth rate will progressively attain sexual maturity within economic and cost effective period.

Quality of semen is a major factor determining reproductive performance of male rabbit in adulthood. Male rabbit are described to have low fertility; an attribute associated with their small testis size and lower daily production of spermatozoa when compared with other mammals (Russell *et* *al*., 1990). Fetal programming is a technology capable of being used for the manipulation of this attribute (inadequate nutrition during late gestation) which can cause poor sperm qualities (Toledo *et al*., 2011). While rabbit capacity for sperm production commence during late gestation, the provision of adequate nutrition during late gestation through proper supply of required nutrients will contribute positively to reproductive performance in adulthood. The technology has potential of impacting on semen quality because nutrition during pregnancy can lead to improved or alterations of metabolism and development into adulthood (Rae *et al*., 2002; Asmad *et al*., 2011; Roble *et al*., 2017).

Microalgae for foetal programming: an overview of our ongoing exploration

Several efforts towards overcoming the challenge of poor rabbit reproductive performance have culminated to identification of oxidative stress as the culprit behind poor productivity. In farm animals including rabbits, oxidative stress impairs health either directly or indirectly. Direct damage effects include peroxidative breakdown of lipids and macro-molecules while indirect effects includes residual effects of cellular membrane and cell components breakdown. Oxidative stress cause economic loss in food producing animals; affect different systemic activities ranging from reproduction to nutrition, coordination, growth, and bodily structural maintenance. Presently, synthetic antioxidants used for management of oxidative damage in animals are Butylated Hydroxyl Anisole and Butylated Hydroxyl Toluene which are becoming non-desirable sources of antioxidants due to health complications and the physiological disruptive roles they play in the body system.

This is why we are currently exploring the influence of natural antioxidants in *Chlorella vulgaris* (one of the most common algae known to contain many antioxidants including carotenoids, asthaxantin, phycobilins and phenols) for the purpose of promoting reproductive performance of rabbits and establishment of the algae as a functional feed resources for livestock production suitable for foetal programming. Summarily, it is envisioned that *Chlorella* usage will lead to improve reproductive performance of rabbit for increasing meat production through the reduction of oxidative damage in rabbit making it possible for rabbit to meet up with its potential as a good source of meat.

CONCLUSION

Poor maternal nutrition during pregnancy not only affect the dam but also impact negatively on the foetal growth and post-birth performance of the offspring. Apart from malnutrition in terms of inadequate nutrition for animals; non-availability of nutrients capable of protecting animals against metabolic failure such as oxidative stress can contribute to offspring poor performance. We hypothesized that if oxidative stress damages is limited in rabbits during the physiological reproductive stages (pre-pubertal, gestation and lactation), this will lead to improvement in foetal reproductive development, excellent birth conditions (birth weight), early post-birth performance, weaning survival, early attainment of puberty and overall life time performance. This we proposed as a potential application of foetal programming for improving rabbit reproductive performance.

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