Review Article

Biochemical and Hormonal Alterations during Different Stages of Follicular Development in Livestock: A Review

Nirupama Dalai[1*], Shashank Shekhar[2], A. P. K. Mahapatra[1], A. K. Kundu[1], Geeta R. Jena[3] and Dhirendra Kumar[4]

[1]Department of Veterinary Physiology, CVSc & A.H., OUAT, Bhubaneswar- 751003, INDIA
[2]Technical Service Officer, Venkey's (India) Ltd., Bhubanswar, INDIA
[3]Department of Veterinary Medicine, CVSc & A.H., OUAT, Bhubaneswar, INDIA
[4]Scientist, CARI, Bhubaneswar, INDIA

***Corresponding author:** niru.vets@gmail.com

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Abstract

Follicular fluid is a vascular compartment within the mammalian ovary, separated per follicular stroma by the follicular wall that constitutes "blood-follicle barrier". The follicular fluids also contain molecules implicated in follicular cell proliferation and differentiation. Follicular fluid consists of various nutrients, growth factors, hormones, electrolytes and enzymes and plays a key role in the physiological, biochemical and metabolic aspects of the maturation process of the oocyte. The knowledge regarding the biochemical composition of the follicular fluid can provide useful information about the requirements for cell and oocyte growth and maturation which may be used as a provisional guide for formulating suitable culture media for in vitro cell culture and oocyte maturation in a particular species. Varying degree of steroid hormonal concentration in the follicular fluid is related to size, growth of follicle, stage of estrous cycle and healthy and atretic state of the ovarian follicles. Thyroid hormones due to their general metabolic and permissive effects are essential for normal ovarian activity in mammalian species.

Key words: Follicular Fluid, Oocyte, Biochemical Metabolites, Steroids

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Introduction

Follicular fluid originates mainly from the peripheral plasma by transudation across the follicle basement lamina and accumulates in the antrum formed by the coalescence of small pockets of fluids (Tabatabaei, K. and Mamoei, M., 2011). Gerard *et al*. (2002) stated that follicular fluid is in part exudates serum and is also partially composed of locally produced substances, which are related to the metabolic activity of the

follicular cells. The rate at which the follicular antrum expands and follicular fluid accumulates differs between dominant and subordinate protein (Fortune *et al.,* 1991 and Beg *et al.,* 2001).The follicular fluids also contain molecules implicated in follicular cell proliferation and differentiation (Adashi, 1994). Hafez and Hafez (2000) suggested that the follicular fluid is a serum transudate modified by follicular metabolic activities, contains specific constituents such as steroids and glycoprotein synthesized by the cells of follicle wall and plays a key role in the physiological, biochemical and metabolic aspects of the nuclear and cytoplasmic maturation of oocyte. The constituents of follicular fluid are considered as a regulating factor in follicular development and steroidogenesis. Das and Khan (2010) stated that follicular fluid consist of various nutrients, growth factors, hormones, electrolytes and enzymes and plays a key role in the physiological, biochemical and metabolic aspects of the maturation process of the oocyte. The oocyte developmental competence which includes mRNA transcription (Kastrop *et al.*, 1990 and Farin and Yang, 1992), protein translation (Sirard *et al.*,1989), post-translational modification of protein (Kruip and Dieleman, 1982) and ultrastructural changes (Hyttel *et al.*, 1986 and Pavlok *et al.*, 1992) also affected by follicle size (Lonergan *et al.*,1994 and Marchal *et al.,* 2002). The knowledge regarding the biochemical composition of the follicular fluid can provide useful information about the requirements for cell and oocyte growth and maturation (Al-Gubory and Martinet, 1987 and Avery *et al.,* 2003) which may be used as a provisional guide for formulating suitable culture media for in vitro cell culture and oocyte maturation in a particular species (Dewit *et al.,* 2001). Gupta *et al.* (2005) reported that as the oocyte and granulose cells grow and get mature in a biochemical environment that changes from small to large follicles, the metabolite, ion and enzymatic characteristics of follicular fluid and follicle or oocyte development are highly correlated.

Minerals such as phosphorous (P), calcium (Ca), manganese (Mn), iodine (I), copper (Cu), selenium (Se) and zinc (Zn) are all involved in governing successful reproductive process (Wilde, 2006). Bearden *et al.* (1997) stated that follicular fluids for many years been known to contain steroids. Subsequently, thyroid hormones govern the control of growth, differentiation and metabolism in nearly all somatic tissues (Grummer and Carroll, 1988).

Biochemical Changes during Follicular Development

The follicular fluid forms the biochemical environment of the oocyte before ovulation (Chang *et al.,* 1976, Gosden *et al.,* 1988 and Jozwik *et al.,* 2001). The metabolic activity together with barrier properties of follicular wall is changing significantly during the growth phase of the follicles (Bagavandoss *et al.,* 1983, Wise, T., 1987, Zamboni, 1974; Edwards, 1974, and Gosden *et al.,* 1988). Therefore, a different biochemical composition of the follicular fluid in different-sized follicles can be expected. The characteristics of porcine follicular fluid harvested from different sized ovarian follicles and

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developmental competences of enclosed oocytes in relation to their sizes were reported by Chakraberty *et al.* (2012). The decline infertility in high yielding dairy cattle is mainly a problem of inferior oocyte and embryo quality, rather than being the result of a disruption in gonadotropin secretion (O'Callaghan, and Boland, 1999). Several in vitro studies showed that metabolites, such as glucose, urea and β-hydroxy butyrate may influence the competence of bovine oocytes to mature and after fertilization, to grow to the blastocyst stage (Hashimoto *et al.,* 2000a, de Wit and Kruip, 2001 and Gomez, 1997). The follicular fluids form the biochemical environment of the oocyte before ovulation (Gosden *et al.,* 1988 and Jozwik *et al.,* 2001). Several studies revealed that the total protein concentrations of the follicular fluid were significantly higher in larger follicle than the small and medium one in buffaloes (Eissa, 1996 and Alkalby *et al.,* 2012), bovine (Mette *et al.,* 1976 and Leroy *et al.,* 2004), ovine (Nandi *et al.,* 2007) and goats (Sidhu *et al.,* 1985). Apart from these there are also some evidences where the total protein concentration decreased as the follicle sizes increased has been reported in sheep and goats (Singh *et al.,* 1999), buffalo (Thangavel *et al.,* 2004) and in cattle (Wise, 1987). Arshad *et al.* (2005) stated that albumin may be required for binding some chemicals as well as minerals inside the follicular fluid for various physiological functions including growth and maturation of follicles. Globulin has a significant importance in the body due to its immunity producing activity and might be necessary for protecting the follicle from external environments (Rufai *et al.,* 2013). Anderson *et al.* (1976) reported that the albumin content of follicular fluid was inversely related to follicular size. Increased level of cholesterol with increase in follicular size were reported in goat (Bardoloi *et al.,* 2000, Thakur *et al.,* 2003 and Mishra *et al.,* 2003), cattle (Brantmeier *et al.,* 1987), sheep (Rufai *et al.,* 2013), buffaloes (Arshad *et al.,* 2005). Cholesterol is the precursor for steroid synthesis and thus increase in steroid production leads to increased levels of follicular cholesterol (Wise, 1987). However, the decreased level of cholesterol with increase in follicular size were reported in pigs (Huang *et al.,* 2004), buffalo (Thangavel and Nayeem, 2004) and in camel (Rahman *et al.,* 2008). The decrease in cholesterol level in larger follicle might be attributed to the conversion of cholesterol to steroid hormones, estrogen and progesterone during steroidogenesis (Nandi *et al.,* 2007).

As a major source of energy for the ovary glucose plays an important role in ovarian metabolism. Several studies showed that as the follicle size increases glucose level in the fluid also increases in cows and buffaloes (Leroy *et al.,* 2004, Arshad *et al.,* 2005, Landau *et al.,* 2004, Nandi *et al.,* 2008 and Razzaque *et al.,* 2012), sheep (Rufai *et al.,* 2013), sow (Chang *et al.,* 1976) and goats (Thakur *et al.,* 2003). An increase in the volume of follicular fluid and increased permeability of the blood follicle barrier during follicular growth (Bagavandoss *et al.,* 1983) could be attributed to higher glucose levels in large size follicles (Gosden *et al.,* 1988). However increased glucose level in small follicle than that of larger one has also been reported in buffalo (Alkalby *et al.,* 2012) and in dromedary camels (Rahman *et al.,* 2008)

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and suggested that small follicles have the ability to filter and reserve the high blood concentrations of glucose for utilization in their development to mature graffian follicles.

Hormonal Changes during Follicular Development

Bearden and Fuquay (1997) stated that follicular fluid is rich in steroid reproductive hormones including testosterone, estradiol and progesterone. Follicular fluids and steroid hormones are commonly used in the culture media as supplements for oocyte maturation and thus steroid concentration in the follicular fluid need to be quantified (Hooda and Yadav, 2002). Varying degree of steroid hormonal concentration in the follicular fluid is related to size, growth of follicle, stage of estrous cycle and healthy and atretic state of the ovarian follicles (Thangavel and Nayeem, 2004; Kor and Moradi, 2013 and Kor *et al.*, 2013) and the presence of steroid hormone in the serum and follicular fluid was one of the major factors controlling follicular development (Yu *et al.*, 2005).

The higher concentration of estrogen and progesterone concentrations in larger follicles as compared to smaller ones has been described in buffaloes (Eissa, 1996 and Alkalby *et al.*, 2012). The significant positive correlation between follicular estrogen and progesterone is consistent with possibility that follicular progesterone serves as a precursor to androgen and subsequently estrogen production by follicles of buffaloes (Alkalby *et al.*, 2012). Increased estrogen concentration in larger follicles than the small follicles has been well described in cattle (Wise, 1987; Henderson *et al.*, 1982; Kruip and Dieleman, 1982; Spicer and Geisert, 1992 and Hiromi *et al.*, 2009), in mares (Meinecke *et al.*, 1987) and in camels (Rahman *et al.*, 2008 Ali *et al.*, 2011 and EI-Shahat *et al.*, 2013). The higher concentration of progesterone in larger follicles suggests that leutinization of granulosa cells occur in dromedary camels (EI-Shahat *et al.*, 2013). However the negative correlations between follicular size and progesterone concentrations have been noticed in bovine (Wise, 1987 and Henderson *et al.*, 1982) and in mares (Meinecke *et al.*, 1987).

Thyroid hormones due to their general metabolic and permissive effects are essential for normal ovarian activity in mammalian species (Kor and Moradi, 2013). Abnormal thyroid hormone levels have been reported to lead to infertility or reduced reproductive function (Fortune, 1994). Maruo *et al.* (1992) showed that thyroid hormone synergizes FSH to induce the differentiation of granulose cells from porcine follicles. Increased concentration of T4 in larger follicles than the T3 is noticed in buffaloes (Alkalby *et al.*, 2012), in camels (Rahman *et al.*, 2008) and in cows (Ashkar *et al.*, 2010). The thyroid hormones may have stimulatory effects on ovarian function in cattle, acting at the level of granulose cells (Spicer *et al.*, 2001).

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Conclusion

The follicular fluid composition provides a useful indication of the requirements for oocyte and follicular cell growth in vitro and may be used as tool for the formulation of cell culture conditions. Its chemical composition is an indicator of the secretary activities and metabolism of follicular cells. The hormonal and biochemical metabolites concentration in follicular fluids fluctuate considerably with the stage of cycle, follicle size and follicle status.

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