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Impact of High Temperature on Oocytes and Embryos: A Review

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ABSTRACT

High temperature is one of the leading factors for decline reproductive performance in livestock and other species as a result of heat stress causing severe economic losses. The embryonic death causes due to heat stress is having multifactorial mechanism in live animal. Heat stress could influence reproductive physiology through modulating blood flow to the reproductive tract, ovarian steroid concentrations and patterns of follicular development. It is difficult for embryos to survive in the increase an oviductal and uterine temperature which is coincident with heat stress. *In vitro* culture of embryos at high temperatures has been reported to affect embryonic development. Similarly, increased *in vitro* culture temperatures can compromise oocyte activity and reduce fertilization rate. Studies have demonstrated that there were lethal effects of heat shock on *in vitro* cultured embryos of cattle at 41.0 - 43.0°C. However, these experimental temperatures are higher than those generally experienced by heat-stressed cows which ultimately reduced their fertility. Furthermore, a lot of research have been conducted in livestock species all indicating that exposure to high temperature is detrimental to oocytes and embryonic developmental processes as it leads to cell damage and may interfere with oocyte maturation, and fertilization process. It concludes that the longer exposure of oocytes and embryos to high temperatures causes more damage to oocytes and embryos.

Introduction

Heat stress is considered as one of the major concerns in reproductive performance of cattle and other livestock species resulting in severe economic losses (Rivera and Hansen, 2001). Several aspects of reproductive physiology are affected by heat stress, such as blood flow to the reproductive system, ovarian steroid concentrations and follicular development (Badinga et al., 1993; Wolfenson et al., 1995; Trout et al., 1998). Several studies have showed that the embryonic development found reduced upon culture of embryos at high temperatures (Edwards and Hansen,

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1996; 1997; Rivera and Hansen, 2001). Similarly, oocyte function and fertilization rate was found compromised after increasing culture temperatures (Baumgartner and Chrisman, 1987; Edwards and Hansen, 1996). The harmful effects of high temperature on cultured embryos of cattle at 41.0-43.0°C has been demonstrated (Ealy and Hansen, 1994; Edwards and Hansen, 1996; 1997). However, these experimental temperatures are higher than those generally observed in heat-stressed cows which ultimately reduced fertility. For example, it was observed a reduction in fertility from 48% in control animals to 0% for heifers exposed to 32.2°C for 72 h immediately after mating; however, the mean rectal temperature of the heat-stressed heifers was 40.0°C (Edwards et al., 2005).

Several studies observed that the fertility of many farm animals such as cattle (Badinga et al., 1985; Cavestany et al., 1985; Wang et al., 2009), pigs (Omtvedt et al., 1971), sheep (Dutt, 1963) and buffalo (Vijayalakshmy et al., 2020) found lower in the summer than in any other season. It was also reported that heat stress caused infertility not only by affecting hormonal secretion (Wolfenson et al., 2000) and embryonic development (Edwards and Hansen, 1997; Rivera and Hansen, 2001) but also by damaging oocytes. Oocytes collected from cows during the summer season showed reduced ability to develop into blastocysts post fertilization *in vitro* (Rutledge et al., 1999; Al-Katanani et al., 2002). Exposure of heifers to heat stress between the onset of estrus and insemination increased the proportion of arrested and abnormal embryos (Putney et al., 1989), which suggests that the progression of oocyte maturation is susceptible to high temperatures. In fact, it has also been demonstrated that exposure of bovine oocytes to high temperature during *in vitro* maturation decreased their subsequent cleavage and blastocyst formation rates (Roth and Hansen, 2004; Abdelnour et al., 2020).

Maturation of oocyte involves both cytoplasmic and nuclear events. The nuclear maturation comprises the resumption of the first meiotic division followed by the progression of meiosis to the metaphase II stage, while cytoplasmic maturation contains a series of processes that are necessary for the oocyte to attain the capacity to support the male pronucleus formation, monospermic fertilization, and early embryonic development (Eppig et al., 1996) as summarized in Fig 1 and 2. Earlier, it was demonstrated that the oocytes and embryos were found sensitivity to heat stress due to insufficient production of heat

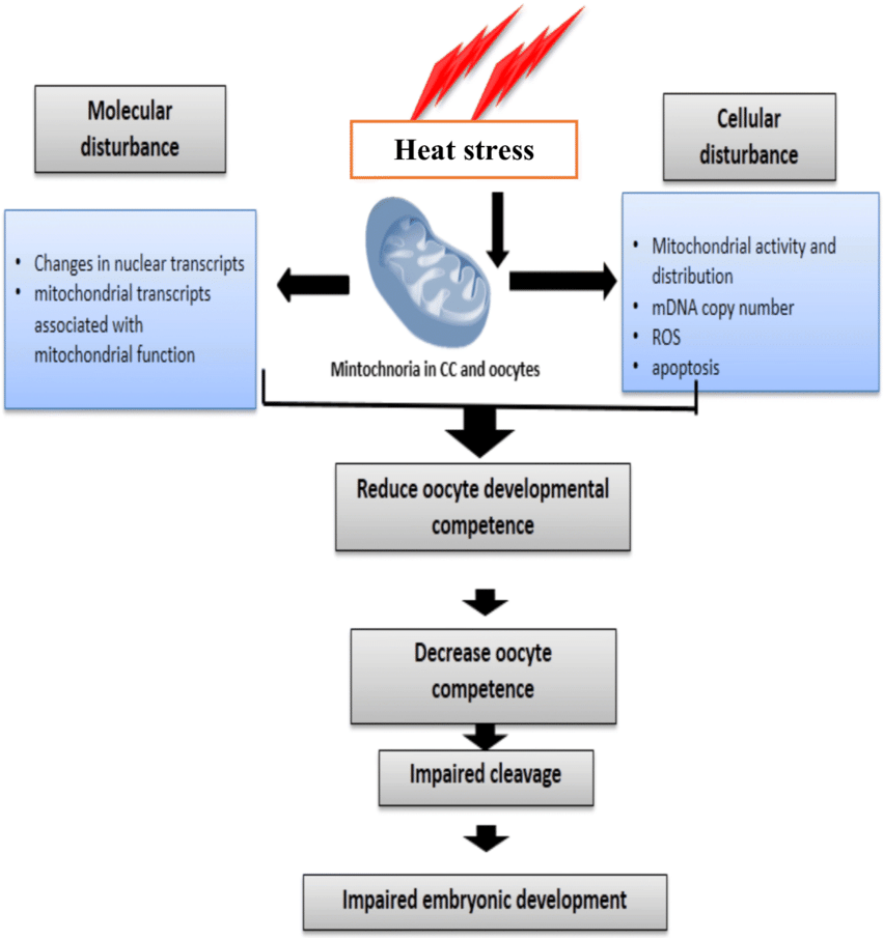

Fig 1. Impact of heat stress on mitochondria function of oocyte and cumulus cells (Abdelnour et al., 2020).

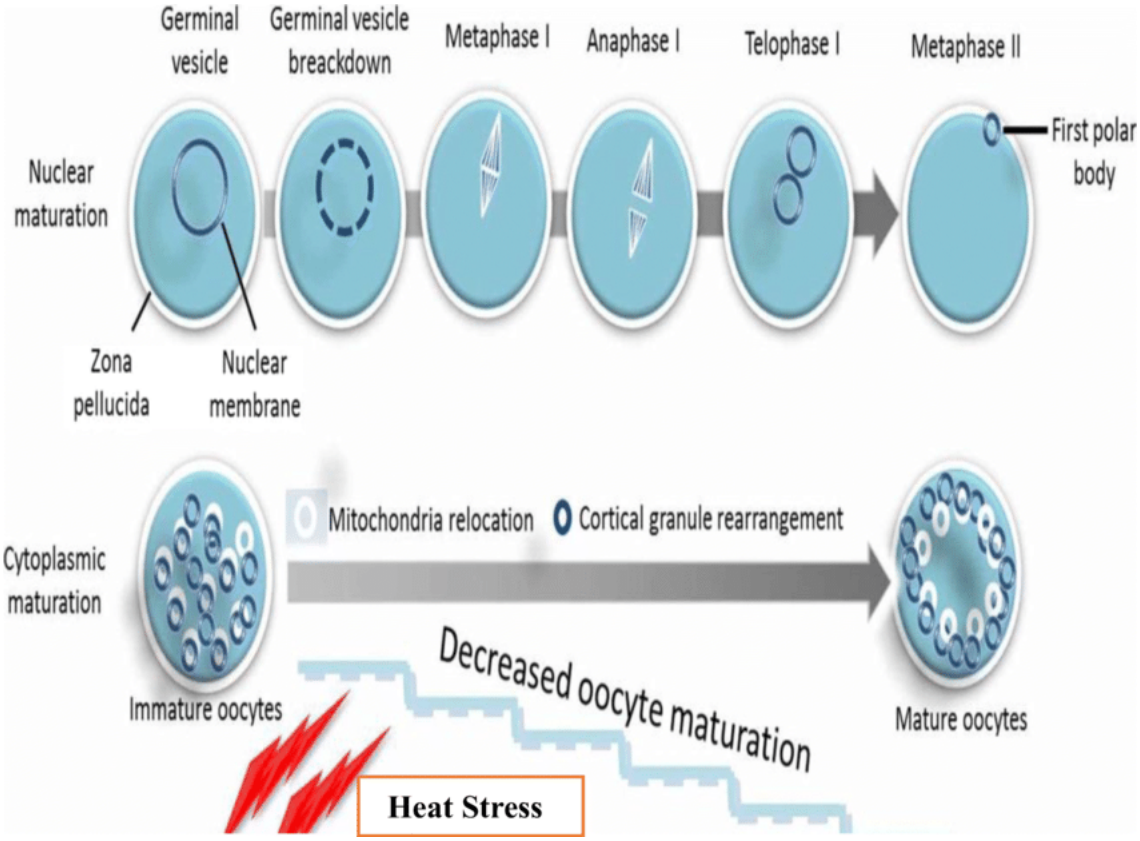

Fig 2. Events showing how nuclear and cytoplasmic maturation is affected by extreme heat (Abdelnour et al., 2020).

shock protein (HSP) (Edwards and Hansen, 1996). Ealy et al. (1993) found that the second day's post-fertilization (8-16 cells stage of embryo) was the most sensitive period, because, from this stage, the embryo begins to acquire resistance against high temperatures. Recent report suggested that the 2 cells embryos are not able to synthesize HSP70 in response to heat stress (Pöhland et al., 2020). However, 2 - 4 cells stage mouse embryos able to support the induced thermo-tolerance. A study conducted on mice showed that HSP synthesis occurs prematurely in 8 cells stages due to full activation of the embryonic genome at this stage (Ealy et al., 1993). The resistance for development of bovine embryos can follow this theory, since its genome is activated between 8 to 16 cell stages. Contrary, Saeki et al. (1999) reported that the 1 cell stage also able to syntheses HSP due to existence of maternal transcription of messenger RNA (mRNA).

A study conducted by Alves et al. (2013), in which they exposed the oocytes at 40°C during maturation and they observed that the significant reduction in cleavage rate (31.46% ± 2%), morula formation rate (35.64% ± 2%) and blastocysts formation rate (0.0%) than the cleavage rate (68.23% ± 2%), morula formation rate (50.16% ± 2%) and blastocysts formation rate (43.28% ± 1%) in control group. Similarly, it was observed that the exposure of oocytes to heat stress at 40°C and 41°C for 12 hours blocked or reduced the development to 35% and 18% blastocysts stage at respective temperature (Edwards and Hansen, 1996; Edwards and Henson, 1997). In addition, the exposure of bovine oocytes to thermal stress during the first 12 h of maturation reduced cleavage rate as well as blastocyst formation rate (Fig 1 and 2; Roth and Hansen, 2004). Tseng et al. (2006) also reported a similar result that rates for blastocyst formation of pig oocytes were reduced after post-maturation heat shock.

Another study showed that oocytes exposed to heat stress for one hour at 40°C or 42°C had no deleterious effects on blastocysts formation after the IVF (Ju et al., 1999). But, when the temperature was increased to 43°C, the developmental competencies of treated oocytes were severely reduced following an exposure of 45 minutes (Ju et al., 1999). It was recommended that the temperature and duration of exposure are limiting factors for *in vitro* embryo production (Ealy et al., 1995; Ju et al., 1999). Krininger III et al. (2003) suggested that the exposure of heat shock or the intensity of temperature and duration of exposure to oocytes leads to reduced cleavage rate and blastocysts formation rate. Some studies demonstrated

that the 2-cells stage bovine embryos, when subjected to heat stress at 40°C for 3 hours, developed to the blastocysts stage normally (Ealy et al., 1995; Tseng et al., 2004). The same authors observed that embryo development decreased when subjected to heat stress at 41°C and 42°C for a long period of time (12 hours). These effects were also reported in porcine embryos by Ju and Tseng (2004), where they noticed that the effects of conditions produced by high temperatures on the viability and developmental competence of oocytes and embryos depended on the intensity of temperature and duration of exposure to the heat stress.

Consequences of extreme heat on estrus and endocrine activity in female reproduction

The length and passion of estrus in dairy cows is shortened by heat stress (Trout et al., 1998) and increased anestrus and silent ovulation (Gwazdauskas et al., 1981). It is difficult to detect estrus as a result of these changes; thereby the number of pregnancies is reduced due to low success rate in artificial inseminations. Reproductive performance in beef cows is affected by heat stress. Reproductive functions are greatly affected by heat stress as well as endocrine activities in females. Increased temperature disrupts hormonal secretion by reducing luteinizing hormone (LH), follicle-stimulating hormone (FSH, Gilad et al., 1993) and progesterone (Burke et al., 2001) in cows and estradiol (E2) in goats (Ozawa et al., 2005). Due to decreases the secretion of progesterone by heat stress results in diminished LH surge in sheep (Hill and Alliston, 1981), alters the luteal phase and ovulation in humans (Carpenter and Nunneley, 1988), reduces estradiol levels and concentration of estradiol within follicules, aromatase activity and in goats the level of LH receptor associated with late ovulation (Ozawa et al., 2005). Gonadotropin receptors and the amount of aromatase activity in granulosa cells as well as the concentration of estradiol in follicular fluid collected from rat follicle are all lessened (Shimizu et al., 2005). An *in vitro* study conducted revealed that there was a reduction in follicular steroidogenesis, androstenedione and estradiol of follicle wall exposed to high temperatures (Bridges et al., 2005). However, less effect was observed on levels of insulin-like growth factor binding protein, E2 and progesterone in dominant follicles upon exposure of dairy cows to extreme heat in spite of the rise in rectal temperature (Guzeloglu et al., 2001). These differences in responses to extreme heat depends on the duration of exposure, stage of estrous cycle, nutritional status, and other environmental factors especially wind and humidity (De Rensis and Scaramuzzi, 2003). There is clear difference in ovarian function in lactating cows as compared to that in dry cow as well as in heifers, since milking activity in lactating cows leads to production of more heat (Sartori et al., 2002).

High temperatures influence development of follicles and quality of oocyte

Heat stress undesirably has damaging effects on ovaries by preventing follicular growth and altering oocyte number and quality. It decreases level of inhibin thereby speeding up the decrease in size of the first wave dominant follicle and the emergence of the second dominant follicle (Roth et al., 2000). For oocyte growth and quality, the condition inside the follicle is very important. In dairy cows, the developmental competence and number of oocytes after *in vitro* fertilization is greatly affected by high ambient temperatures but have less effect on beef cows (Hansen et al., 2001). It was reported that exposure of cows to high temperature decreases estradiol production and viability of granulosa cells as well as declined androstenedione production by thecal cells (Roth et al., 2001). Blood glucose level and non-esterified fatty acid (NEFA) affect follicles under heat stress conditions. Report have shown that bovine follicular fluid having ~85% glucose of the plasma glucose level in the winter season which found significantly decreases in summer in follicular fluid (Shehab-El-Deen et al., 2010). In contrast, level of NEFA did not affected in follicular fluid in spite of a significant increase in plasma level by heat stress (Shehab-El-Deen et al., 2010). Taken together, these results indicate that the follicles condition is affected by body blood nutrition or biochemical components which vary in the summer season. However, oxygen is probably not a factor because its concentration in the follicular fluid does not vary in heat and non-heat stressed conditions (de Castro et al., 2008). Although rectal temperatures are often considered as representative of core body (and thereby tissue) temperatures, ovarian temperatures are found 1-1.5°C cooler than rectal temperatures in several species, including cattle, goat, pigs, rabbits and humans (Grinsted et al., 1985; Grøndahl et al., 1996). Maternal heat stress did not affect the blood oxygen pressure in the ovarian vein of swine (Wettemann et al., 1988). On the contrary, ovarian, cervical and oviductal blood flows decreased by 20–30% by heat-stressed rabbit while vulval blood flow rose by 40%, regardless of pregnancy or lactation status (Lublin and Wolfenson, 1996). These studies indicate that it is needed to study the effect of body temperature and local blood flow associated with local temperature and distribution of nutrition to follicles for oocyte growth. However,

it is unclear how follicular temperature is affected in heat-stressed ovaries. Further studies are needed to determine how heat stress affects local reproductive organs to clarify the follicular and oocyte growth. The impact of high temperatures on female reproductive functions is summarized in Fig. 3.

Effects of heat stress on oocyte growth, fertilization and early embryonic development

Several *in vivo* and *in vitro* studies have documented the effects of heat stress on maturation and developmental competence of oocytes. Exposing females to heat stress after fertilization caused decreases in the quality and quantity of embryos after super-ovulation in cow (Ealy and Drost, 1993) and in mice (Ozawa et al., 2002; Ozawa et al., 2004; Roth et al., 2008). Heat stress also caused decreases in fetal growth in pigs (Wettemann et al., 1988), mice (Roth et al., 2008) and beef cows (Biggers et al., 1987). Exposing GV stage oocytes to high temperature inhibits the rate of MII stage oocytes in mice (Wang et al., 2009) and cows (Payton et al., 2004; Sugiyama et al., 2007; Zhandi et al., 2009). Although, experimental heat stress coincident with ovulation and oocyte maturation may or may not have an effect on the capacity of oocytes to be fertilized, the resultant embryos are more likely to develop slowly or abnormally. Exposures of oocytes to heat stress during *in vitro* maturation caused nuclear and cytoskeletal alterations in mice (Wang et al., 2009), pigs (Ju and Tseng, 2004) and cows (Payton et al., 2004, Roth and Hansen, 2005). Heat stress also induces cumulus–oocyte complexes (COCs) to undergo apoptosis. Fig 4 shows the increase in the number of TUNEL-positive cells in cumulus cells surrounding bovine oocytes when COCs were exposed to heat stress during *in vitro* maturation.

Heat stress also induced apoptosis in bovine oocytes (Roth and Hansen, 2004; Zhandi et al., 2009; Soto and Smith, 2009) and an increase in phosphatidylserine, an indicator of apoptosis in porcine oocytes (Tseng et al., 2006). On the other hand, short exposures of heat stress

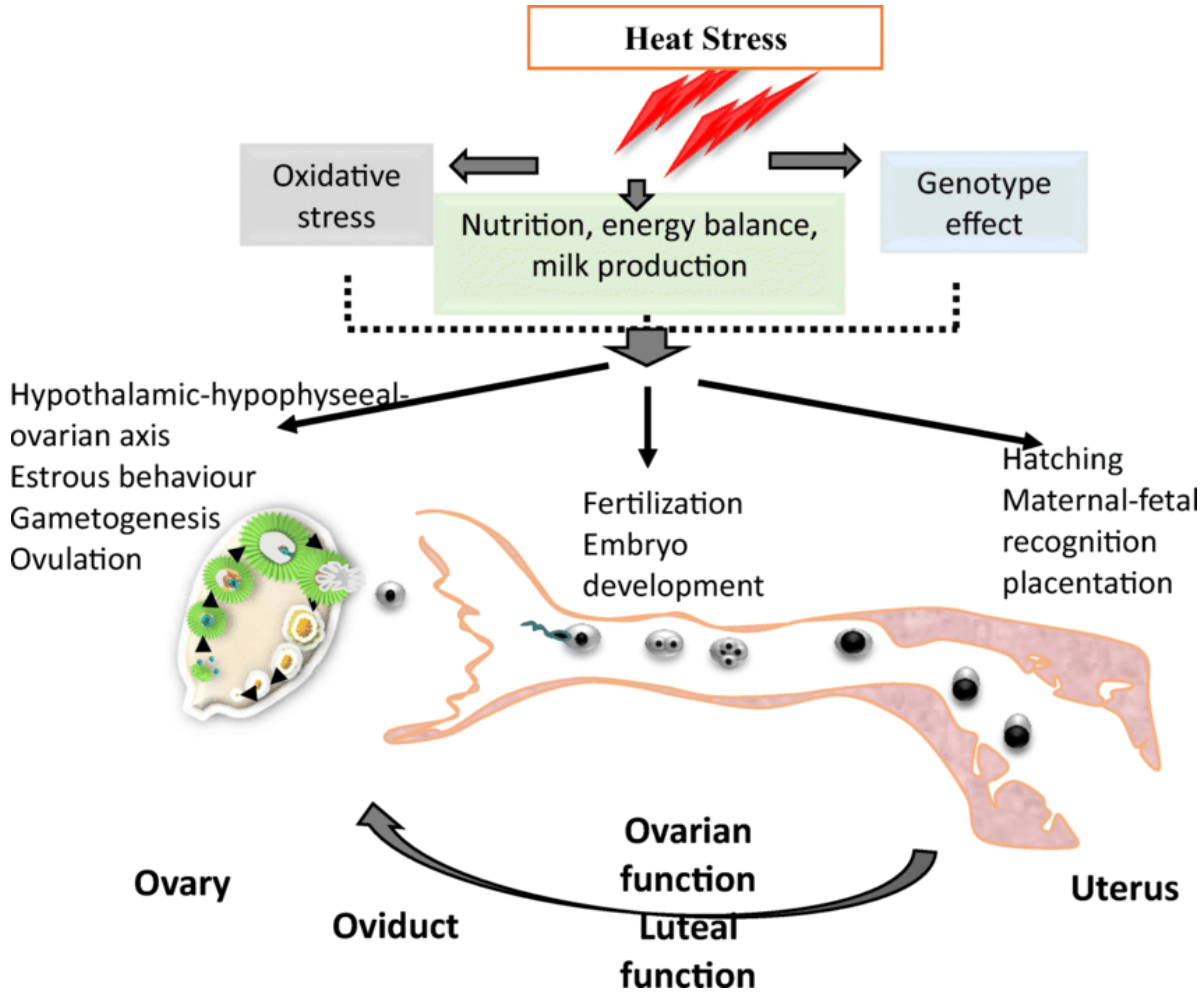

Fig 3. Summary of the impact of heat stress on female reproductive functions (Abdelnour et al., 2020).

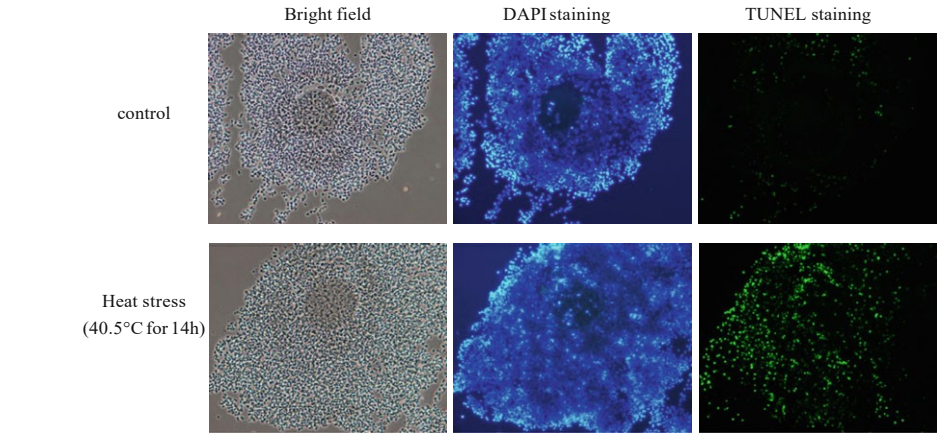

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Fig. 4. Apoptosis induced by heat stress in matured cumulus–oocyte complexes (COCs) of cattle. After COCs were collected from follicles, they were matured for 20 h in maturation medium and were exposed to 40.5˚C for 14 h followed by fixation and TUNEL staining (Takahashi, 2011).

seem to be having less impact on *in vitro* maturation of oocyte (Schrock et al., 2007; Edwards et al., 2009). Contrary results of heat stress on *in vitro* or *in vivo* oocyte maturation need to be carefully analysis. Heat stress at the time of fertilization also decreased subsequent embryonic development, which suggests that heat stress has detrimental effects on both oocytes and sperms (Sugiyama et al., 2007). Apart from female, heat stress also affects males to reduce the number of sperm count with intact acrosomes at the time of ejaculation (Murase et al., 2007). Embryos between fertilization and implantation undergo dynamic growth, cell proliferation, cell differentiation, and many changes in gene expression. Therefore, if the maternal body is exposed to heat stress during this period, it is likely that the pre-implantation development is severely affected directly by heat stress itself or indirectly by the deleterious change of reproductive tracts. The stage at which embryos become susceptible to heat stress has been studied. *In vivo* maternal heat stress inhibited embryo development at an early stage in mice (Ozawa et al., 2002; Ozawa et al., 2004) and cows (Ealy et al., 1993). *In vitro* and *in vivo* studies have clearly shown that the sensitivity of bovine embryos to heat stress is stage-specific (Ealy et al., 1993; Krininger et al., 2003; Sakatani et al., 2004). In cows, *in vivo* and *in vitro* experiments showed that embryo development is significantly inhibited by heat stress approximately 48-72 h after fertilization, which corresponds to the 8-16 cell stage (Sakatani et al., 2004). After this stage, heat stress exposure has less effect on the rate of development and cell proliferation (Sakatani et al., 2004). In mouse and cow embryos, the stage that is most sensitive to heat stress is approximately the time of zygotic genome activation (ZGA), which occurs at the 2-cell stage in mice (Schultz, 1993) and at the 4- to 8-cell stage in cows (De Sousa et al.,1998). Both during and after ZGA, heat stress can also change the chromatin structure of embryonic cells (Edwards, 1998), which might disturb gene expression. In addition to inducing apoptosis in maturing oocytes, heat stress also induces apoptosis in embryonic cells in cows (Soto and Smith, 2009; Paula-Lopes and Hansen, 2002a; Paula-Lopes and Hansen, 2002b), pigs (Isom et al., 2007; Jin et al., 2007) and rabbits (Makarevich et al., 2007). The knowledge of when an embryo is most sensitive to heat stress can be used to select the best time for embryo transfer by preventing the early embryonic loss after artificial insemination in cows (Putney et al., 1989; Drost et al., 1999).

In conclusion, therefore, further studies need to be carried out to elucidate the genes that are involved in both cellular and physiological responses to heat stress which would help to control and improve mammalian reproduction.

Competing Interest

There is no conflict of interest among the authors.

References

Abdelnour SA, Yang CY, Swelum AA, Abd El-Hack ME, Khafaga AF, Abdo M, Shang JH, Lu YQ. Molecular, functional, and cellular alterations of oocytes and cumulus cells induced by heat stress and shock in animals. Environ Sci Pollut Res Int. 2020;27(31):38472-38490. doi: 10.1007/s11356-020-10302-4.

Al-Katanani YM, Paula-Lopes FF, Hansen PJ. Effect of season and exposure to heat stress on oocyte competence in Holstein cows. J Dairy Sci. 2002;85(2):390-6. doi: 10.3168/jds.s0022-0302(02)74086-1.

Alves MF, Roseli FG, Danielle LP, Eduardo GP, Flavio S, Roberta KRQ, Magali D'A, Marcos AA. Effect of heat stress on the maturation, fertilization and development rates of in vitro produced bovine embryos. J Anim Sci. 2013; 3:174-178.

Badinga L, Collier RJ, Thatcher WW, Wilcox CJ. Effects of climatic and management factors on conception rate of dairy cattle in subtropical environment. J Dairy Sci. 1985;68(1):78-85. doi: 10.3168/jds.S0022-0302(85)80800-6.

Badinga L, Thatcher WW, Diaz T, Drost M, Wolfenson D. Effect of environmental heat stress on follicular development and steroidogenesis in lactating Holstein cows. Theriogenology. 1993;39(4):797-810. doi: 10.1016/0093-691x(93)90419-6.

Baumgartner AP, Chrisman CL. Embryonic mortality caused by maternal heat stress during mouse oocyte maturation. Anim Reprod Sci. 1987; 14: 309–316. doi: 10.1016/0378-4320(87)90021-2.

Biggers BG, Geisert RD, Wetteman RP, Buchanan DS. Effect of heat stress on early embryonic development in the beef cow. J Anim Sci. 1987; 64(5):1512-8. doi: 10.2527/jas1987.6451512x.

Bridges PJ, Brusie MA, Fortune JE. Elevated temperature (heat stress) in vitro reduces androstenedione and estradiol and increases progesterone secretion by follicular cells from bovine dominant follicles. Domest Anim Endocrinol. 2005; 29(3):508-22. doi: 10.1016/j.domaniend.2005.02.017.

Burke JM, Spiers DE, Kojima FN, Perry GA, Salfen BE, Wood SL, Patterson DJ, Smith MF, Lucy MC, Jackson WG, Piper EL. Interaction of endophyte-infected fescue and heat stress on ovarian function in the beef heifer. Biol Reprod. 2001;65(1):260-8. doi: 10.1095/biolreprod65.1.260.

Carpenter AJ, Nunneley SA. Endogenous hormones subtly alter women's response to heat stress. J Appl Physiol. 1988;65(5):2313-7. doi: 10.1152/jappl.1988.65.5.2313.

Cavestany D, el-Wishy AB, Foote RH. Effect of season and high environmental temperature on fertility of Holstein cattle. J Dairy Sci. 1985;68(6):1471-8. doi: 10.3168/jds.S0022-0302(85)80985-1.

de Castro E Paula LA, Andrzejewski J, Julian D, Spicer LJ, Hansen PJ. Oxygen and steroid concentrations in preovulatory follicles of lactating dairy cows exposed to acute heat stress. Theriogenology. 2008; 69(7):805-13. doi: 10.1016/j.theriogenology.2007.12.008.

De Rensis F, Scaramuzzi RJ. Heat stress and seasonal effects on reproduction in the dairy cow-a review. Theriogenology. 2003;60(6):1139-51. doi: 10.1016/s0093-691x(03)00126-2.

De Sousa PA, Watson AJ, Schultz GA, Bilodeau-Goeseels S. Oogenetic and zygotic gene expression directing early bovine embryogenesis: a review. Mol Reprod Dev. 1998; 51(1):112-21. doi: 10.1002/(SICI)1098-2795(199809)51:1<112::AID-MRD14>3.0.CO;2-9.

Drost M, Ambrose JD, Thatcher MJ, Cantrell CK, Wolfsdorf KE, Hasler JF, Thatcher WW. Conception rates after artificial insemination or embryo transfer in lactating dairy cows during summer in Florida. Theriogenology. 1999;52(7):1161-7. doi: 10.1016/S0093-691X(99)00208-3.

Dutt RH. Critical period for early embryo mortality in ewes exposed to high ambient temperature. J Anim Sci. 1963; 22: 713–719.

Ealy AD, Drost M, Hansen PJ. Developmental changes in embryonic resistance to adverse effects of maternal heat stress in cows. J Dairy Sci. 1993; 76(10):2899-905. doi: 10.3168/jds.S0022-0302(93)77629-8.

Ealy AD, Hansen PJ. Induced thermotolerance during early development of murine and bovine embryos. J Cell Physiol. 1994; 160(3):463-8. doi: 10.1002/jcp.1041600309.

Ealy AD, Howell JL, Monterroso VH, Aréchiga CF, Hansen PJ. Developmental changes in sensitivity of bovine embryos to heat shock and use of antioxidants as thermoprotectants. J Anim Sci. 1995;73(5):1401-7. doi: 10.2527/1995.7351401x.

Edwards JL, Saxton AM, Lawrence JL, Payton RR, Dunlap JR. Exposure to a physiologically relevant elevated temperature hastens in vitro maturation in bovine oocytes. J Dairy Sci. 2005;88(12):4326-33. doi: 10.3168/jds.S0022-0302(05)73119-2.

Edwards JL, Bogart AN, Rispoli LA, Saxton AM, Schrick FN. Developmental competence of bovine embryos from heat-stressed ova. J Dairy Sci. 2009;92(2):563-70. doi: 10.3168/jds.2008-1495.

Edwards JL, Hansen PJ. Differential responses of bovine oocytes and preimplantation embryos to heat shock. Mol Reprod Dev. 1997;46(2):138-45. doi: 10.1002/(SICI)1098-2795(199702)46:2<138::AID-MRD4>3.0.CO;2-R.

Edwards JL, Hansen PJ. Elevated temperature increases heat shock protein 70 synthesis in bovine two-cell embryos and compromises function of maturing oocytes. Biol Reprod. 1996; 55(2):341-6. doi: 10.1095/biolreprod55.2.341.

Edwards MJ. Apoptosis, the heat shock response, hyperthermia, birth defects, disease and cancer. Where are the common links? Cell Stress Chaperones. 1998;3(4):213-20. doi: 10.1379/1466-1268(1998)003<0213:athsrh>2.3.co;2.

Eppig JJ, O'Brien M, Wigglesworth K. Mammalian oocyte growth and development in vitro. Mol Reprod Dev. 1996;44(2):260-73. doi: 10.1002/(SICI)1098-2795(199606)44:2<260::AID-MRD17>3.0.CO;2-6.

Gilad E, Meidan R, Berman A, Graber Y, Wolfenson D. Effect of heat stress on tonic and GnRH-induced gonadotrophin secretion in relation to concentration of oestradiol in

plasma of cyclic cows. J Reprod Fertil. 1993;99(2):315-21. doi: 10.1530/jrf.0.0990315.

Grinsted J, Kjer JJ, Blendstrup K, Pedersen JF. Is low temperature of the follicular fluid prior to ovulation necessary for normal oocyte development? Fertil Steril. 1985 Jan;43(1):34-9. doi: 10.1016/s0015-0282(16)48314-7.

Grøndahl C, Greve T, Schmidt M, Hunter RHF. Bovine preovulatory follicles are cooler than ovarian stroma and deep rectal temperature. Theriogenology, 1996; 45: 289.

Guzeloglu A, Ambrose JD, Kassa T, Diaz T, Thatcher MJ, Thatcher WW. Long-term follicular dynamics and biochemical characteristics of dominant follicles in dairy cows subjected to acute heat stress. Anim Reprod Sci. 2001;66(1-2):15-34. doi: 10.1016/s0378-4320(01)00082-3.

Gwazdauskas FC, Thatcher WW, Kiddy CA, Paape MJ, Wilcox CJ. Hormonal patterns during heat stress following PGF(2) alpha-tham salt induced luteal regression in heifers. Theriogenology. 1981;16(3):271-85. doi: 10.1016/0093-691x(81)90012-1.

Hansen PJ, Drost M, Rivera RM, Paula-Lopes FF, al-Katanani YM, Krininger CE 3rd, Chase CC Jr. Adverse impact of heat stress on embryo production: causes and strategies for mitigation. Theriogenology. 2001;55(1):91-103. doi: 10.1016/s0093-691x(00)00448-9.

Hill TG, Alliston CW. Effects of thermal stress on plasma concentrations of luteinizing hormone, progesterone, prolactin and testosterone in the cycling ewe. Theriogenology. 1981;15(2):201-9. doi: 10.1016/s0093-691x(81)80008-8.

Jin YX, Lee JY, Choi SH, Kim T, Cui XS, Kim NH. Heat shock induces apoptosis related gene expression and apoptosis in porcine parthenotes developing in vitro. Anim Reprod Sci. 2007;100(1-2):118-27. doi: 10.1016/j.anireprosci.2006.06.017.

Ju JC, Parks JE, Yang X. Thermotolerance of IVM-derived bovine oocytes and embryos after short-term heat shock. Mol Reprod Dev. 1999;53(3):336-40. doi: 10.1002/(SICI)1098-2795(199907)53:3<336::AID-MRD9>3.0.CO;2-M.

Ju JC, Tseng JK. Nuclear and cytoskeletal alterations of in vitro matured porcine oocytes under hyperthermia. Mol Reprod Dev. 2004;68(1):125-33. doi: 10.1002/mrd.20054.

Krininger CE 3rd, Block J, Al-Katanani YM, Rivera RM, Chase CC Jr, Hansen PJ. Differences between Brahman and Holstein cows in response to estrus synchronization, superovulation and resistance of embryos to heat shock. Anim Reprod Sci. 2003;78(1-2):13-24. doi: 10.1016/s0378-4320(03)00045-9.

Lublin A, Wolfenson D. Lactation and pregnancy effects on blood flow to mammary and reproductive systems in heat-stressed rabbits. Comp Biochem Physiol A Physiol. 1996;115(4):277-85. doi: 10.1016/s0300-9629(96)00060-6.

Makarevich AV, Olexiková L, Chrenek P, Kubovicová E, Fréharová K, Pivko J. The effect of hyperthermia in vitro on vitality of rabbit preimplantation embryos. Physiol Res. 2007;56(6):789-96.

Murase T, Imaeda N, Yamada H, Miyazawa K. Seasonal changes in semen characteristics, composition of seminal plasma and frequency of acrosome reaction induced by calcium and calcium ionophore A23187 in Large White boars. J Reprod Dev. 2007;53(4):853-65. doi: 10.1262/jrd.19026.

Omtvedt IT, Nelson RE, Edwards RL, Stephens DF, Turman EJ. Influence of heat stress during early, mid and late pregnancy of gilts. J Anim Sci. 1971;32(2):312-7. doi: 10.2527/jas1971.322312x.

Ozawa M, Hirabayashi M, Kanai Y. Developmental competence and oxidative state of mouse zygotes heat-stressed maternally or in vitro. Reproduction. 2002;124(5):683-9. doi: 10.1530/rep.0.1240683.

Ozawa M, Matsuzuka T, Hirabayashi M, Kanai Y. Redox status of the oviduct and CDC2 activity in 2-cell stage embryos in heat-stressed mice. Biol Reprod. 2004;71(1):291-6. doi: 10.1095/biolreprod.103.022152.

Ozawa M, Tabayashi D, Latief TA, Shimizu T, Oshima I, Kanai Y. Alterations in follicular dynamics and steroidogenic abilities induced by heat stress during follicular recruitment in goats. Reproduction. 2005;129(5):621-30. doi: 10.1530/rep.1.00456.

Payton RR, Romar R, Coy P, Saxton AM, Lawrence JL, Edwards JL. Susceptibility of bovine germinal vesicle-stage oocytes from antral follicles to direct effects of heat stress in vitro. Biol Reprod. 2004;71(4):1303-8. doi: 10.1095/biolreprod.104.029892.

Pöhland R, Souza-Cácares MB, Datta TK, Vanselow J, Martins MIM, da Silva WAL, Cardoso CJT, Melo-Sterza FA. Influence of long-term thermal stress on the in vitro maturation on embryo development and Heat Shock Protein abundance in zebu cattle. Anim Reprod. 2020;17(3):e20190085. doi: 10.1590/1984-3143-AR2019-0085.

Putney DJ, Drost M, Thatcher WW. Influence of summer heat stress on pregnancy rates of lactating dairy cattle following embryo transfer or artificial insemination. Theriogenology. 1989;31(4):765-78. doi: 10.1016/0093-691x(89)90022-8.

Rivera RM, Hansen PJ. Development of cultured bovine embryos after exposure to high temperatures in the physiological range. Reproduction. 2001;121(1):107-15.

Roth Z, Aroyo A, Yavin S, Arav A. The antioxidant epigallocatechin gallate (EGCG) moderates the deleterious effects of maternal hyperthermia on follicle-enclosed oocytes in mice. Theriogenology. 2008;70(6):887-97. doi: 10.1016/j.theriogenology.2008.05.053.

Roth Z, Hansen PJ. Disruption of nuclear maturation and rearrangement of cytoskeletal elements in bovine oocytes exposed to heat shock during maturation. Reproduction. 2005;129(2):235-44. doi: 10.1530/rep.1.00394.

Roth Z, Hansen PJ. Involvement of apoptosis in disruption of developmental competence of bovine oocytes by heat shock during maturation. Biol Reprod. 2004;71(6):1898-906. doi: 10.1095/biolreprod.104.031690.

Roth Z, Meidan R, Braw-Tal R, Wolfenson D. Immediate and delayed effects of heat stress on follicular development and its association with plasma FSH and inhibin concentration in cows. J Reprod Fertil. 2000;120(1):83-90.

Roth Z, Meidan R, Shaham-Albalancy A, Braw-Tal R, Wolfenson D. Delayed effect of heat stress on steroid production in medium-sized and preovulatory bovine follicles. Reproduction. 2001;121(5):745-51.

Rutledge JJ, Monson RL, Northey DL, Leibfried-Rutledge M L. Seasonality of cattle embryo production in temperate region. Theriogenology. 1999; 51: 330. doi:10.1016/S0093-691X(99)91889-7

Saeki K, Matsumoto K, Kaneko T, Hosol Y, Kato H, Iritani A. Onset of RNA synthesis in early bovine embryos detected by reverse transcripition polymerase chain reaction following introduction of exogenous gene into their pronuclei. Theriogenology. 1999; 51:192.

Sakatani M, Kobayashi S, Takahashi M. Effects of heat shock on in vitro development and intracellular oxidative state of bovine pre-implantation embryos. Mol Reprod Dev. 2004;67(1):77-82. doi: 10.1002/mrd.20014.

Sartori R, Sartor-Bergfelt R, Mertens SA, Guenther JN, Parrish JJ, Wiltbank MC. Fertilization and early embryonic development in heifers and lactating cows in summer and lactating and dry cows in winter. J Dairy Sci. 2002;85(11):2803-12. doi: 10.3168/jds.S0022-0302(02)74367-1.

Schrock GE, Saxton AM, Schrick FN, Edwards JL. Early in vitro fertilization improves development of bovine ova heat stressed during in vitro maturation. J Dairy Sci. 2007;90(9):4297-303. doi: 10.3168/jds.2007-0002.

Schultz RM. Regulation of zygotic gene activation in the mouse. Bioessays. 1993;15(8):531-8. doi: 10.1002/bies.950150806.

Shehab-El-Deen MA, Leroy JL, Fadel MS, Saleh SY, Maes D, Van Soom A. Biochemical changes in the follicular fluid of the dominant follicle of high producing dairy cows exposed to heat stress early post-partum. Anim Reprod Sci. 2010;117(3-4):189-200. doi: 10.1016/j.anireprosci.2009.04.013.

Shimizu T, Ohshima I, Ozawa M, Takahashi S, Tajima A, Shiota M, Miyazaki H, Kanai Y. Heat stress diminishes gonadotropin receptor expression and enhances susceptibility to apoptosis of rat granulosa cells. Reproduction. 2005;129(4):463-72. doi: 10.1530/rep.1.00502.

Soto P, Smith LC. BH4 peptide derived from Bcl-xL and Bax-inhibitor peptide suppresses apoptotic mitochondrial changes in heat stressed bovine oocytes. Mol Reprod Dev. 2009;76(7):637-46. doi: 10.1002/mrd.20986.

Sugiyama S, McGowan M, Phillips N, Kafi M, Young M. Effects of increased ambient temperature during IVM and/or IVF on the in vitro development of bovine zygotes. Reprod Domest Anim. 2007;42(3):271-4. doi: 10.1111/j.1439-0531.2006.00776.x.

Trout JP, McDowell LR, Hansen PJ. Characteristics of the estrous cycle and antioxidant status of lactating Holstein cows exposed to heat stress. J Dairy Sci. 1998;81(5):1244-50. doi: 10.3168/jds.S0022-0302(98)75685-1.

Tseng JK, Chen CH, Chou PC, Yeh SP, Ju JC. Influences of follicular size on parthenogenetic activation and in vitro heat shock on the cytoskeleton in cattle oocytes. Reprod Domest Anim. 2004;39(3):146-53. doi: 10.1111/j.1439-0531.2004.00493.x.

Tseng JK, Tang PC, Ju JC. In vitro thermal stress induces apoptosis and reduces development of porcine parthenotes. Theriogenology. 2006;66(5):1073-82. doi: 10.1016/j.theriogenology.2006.03.003.

Vijayalakshmy K, Verma R, Rahman H, Yadav HP, Virmani M, Kumar D, Choudhiry V. Factors influencing seasonal anestrus in buffaloes and strategies to overcome the summer anestrus in buffaloes, Biological Rhythm Research, 2020;51(6):907-914. doi: 10.1080/09291016.2018.1558740.

Wang JZ, Sui HS, Miao DQ, Liu N, Zhou P, Ge L, Tan JH. Effects of heat stress during in vitro maturation on cytoplasmic versus nuclear components of mouse oocytes. Reproduction. 2009;137(2):181-9. doi: 10.1530/REP-08-0339.

Wettemann RP, Bazer FW, Thatcher WW, Caton D, Roberts RM. Conceptus development, uterine response, blood gases and endocrine function of gilts exposed to increased ambient temperature during early pregnancy. Theriogenology. 1988;30(1):57-74. doi: 10.1016/0093-691x(88)90263-4.

Wolfenson D, Roth Z, Meidan R. Impaired reproduction in heat-stressed cattle: basic and applied aspects. Anim Reprod Sci. 2000;60-61:535-47. doi: 10.1016/s0378-4320(00)00102-0.

Wolfenson D, Thatcher WW, Badinga L, Savio JD, Meidan R, Lew BJ, Braw-Tal R, Berman A. Effect of heat stress on follicular development during the estrous cycle in lactating dairy cattle. Biol Reprod. 1995;52(5):1106-13. doi: 10.1095/biolreprod52.5.1106.

Zhandi M, Towhidi A, Nasr-Esfahani MH, Eftekhari-Yazdi P, Zare-Shahneh A. Unexpected detrimental effect of Insulin like growth factor-1 on bovine oocyte developmental competence under heat stress. J Assist Reprod Genet. 2009;26(11-12):605-11. doi: 10.1007/s10815-009-9364-0.