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Review Article

Historical Background and Significance of Embryo Transfer Technology in Cattle with its Relevant Applications

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ABSTRACT

In recent decades, many significant improvements have taken place accompanying different assisted reproductive biotechnologies like estrous synchronization, artificial insemination, superovulation, cloning, embryo recovery and its transfer, *in vitro* fertilization, cryopreservation and transgenesis. Among these technologies, embryo transfer has achieved a great importance having produced numerous offspring from a genetically superior female. After the first successful transfer of mammalian embryos in 1890, it was approximately 60 years before significant progress became quite noticeable in the basic technology of embryo transfer in cattle. In embryo transfer process, embryo is collected from superior quality donor cattle and transferred to other recipient female cattle for complete development unless the gestation accomplishes. This technology involves the selection of donor and recipient animals, management for better breeding evaluation, embryo production, collection and transfer of embryo within a narrow window of suitable estrous time. In cattle, embryo transfer technology is widely used to amplify the reproductive rates of genetically improved superior females, planed mating, twinning, disease control, better pregnancy rate in repeat breeder cattle and increment of production of farm and reproductive rates. However, embryo transfer is widely used owing to its potential benefits. Hormonal protocol and synchronization improvements increase the embryo production rates via superovulation. This review details the embryo production technique, transfer of embryo from donor to recipient and the factor that are necessary for transfer of embryo from donor to recipient for production of offspring. Previously limited information existing regarding embryo transfer and its significance in farm animals therefore, in future this review might be helpful in improving the reproductive potential of farm animals.

INTRODUCTION

Selective breeding program and assisted reproductive technologies have been the key factors regarding dairying profitability having enhanced genetic potential (Loi *et al*., 2016). The genetically increased milk and meat yield attracts the demand for transplant animals; hence the breeding for productive animals escalates (Loi *et al*., 2016). In 20th century breeds improved assisted reproductive technologies like artificial insemination, multiple ovulation and ET (MOET) and multiple newer technologies that include *in vitro* embryo production, cloning, and transgenesis (Choudhary *et al*., 2016; Moore and Hsler, 2017). A well-developed reproductive technology embryo transfer (ET) is proved a beneficial to enhance production and replication of genetic superior animals with exploitation of genetic superior female cattle (Batista *et al*., 2016; Roper *et al*., 2018; Rico *et al*., 2012). Another study reported that annually more than one million embryos are produced globally. ET included different

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procedure like selection of donor cattle, its superovulation, artificial insemination of donor by sexed semen, recovery of embryo, cryopreservation of embryo, preparation of recipient cattle and transfer of good quality embryo in low genetic potential cattle (Hasler, 2014).

Among the assisted reproductive technologies, the beneficial techniques to increase animal production are the multiple ovulation and ET (Faizah *et al*., 2011; Oguejiofor, 2019).

For more betterment in cattle herds, ET is helpful to generate more embryos of predetermined sex and known genotype (Moore and Hasler, 2017). Superior females are preferred to mate through assisted reproductive technologies (*in vitro* fertilization, ET, and superovulation) to potentiate genetic improvement (Gaddis *et al*., 2017). After *in-vivo* or *in-vitro* fertilization, the commercial animal embryo production has become an international business (Kidie, 2006). Amidst the genomic era, interest of breeding techniques of developed artificial insemination by hygienic measures and ET technology plays the vital role for production in livestock enterprises (Humblot *et al*., 2010; Wray-Cahen *et al*., 2022). In 1940s and 1950s, superovulation and ET technique were pioneered (Hasler, 2014; Moore and Hasler, 2017). ET technology is the third most important and commonly used reproductive technology after artificial insemination (AI), and oestrous synchronization in large animals (Cowan, 2010; Mebratu *et al*., 2020). It is an important approach for the fortification of genetically superior offspring of animals and enhancing livestock production (Frade *et al*., 2014; Dochi, 2019; Alkan *et al*., 2020).

The ET protocol is the collection of embryo from donor (superior genetic) animal and transferring in the recipient (having lesser genetic quality) at proper timing (Block *et al*., 2010; Stroud, 2012).

Major hurdles for ET are high cost, low laboratory efficiency, low survivability of embryo by cryopreservation and calf produced by ET; cost-effective reproductive technology has restricted usage on farms but has proved to be beneficial (Campanile *et al*., 2010; Bonilla *et al*., 2014). In cattle, the number of follicles initiation per follicular wave is more than buffalo (Palanisammi et al., 2020). Hence, the ET technique is mostly practiced in cattle. While, in buffalos embryo production and transfer technology is important as like as *in vitro* ET (Neglia *et al*., 2011; Baruselli *et al*., 2013). Success rate around 90% of developed artificial insemination technique is achieved and this technique is used to control offspring gender by using sex semen for embryo production (Borchersen *et al*., 2009; Viana *et al*., 2017). In ET method, different steps followed from donor superovulation for more embryo production and recipient preparation for ET is costly and effective (Viana *et al*., 2017). In last two decades, embryo production in donor cattle and its transfer into recipient is increased (Baruselli *et al*., 2010; Watanabe *et al*., 2018).

This review details the embryo production technique, its transsfer from donor to recipient and the factor that interlinked for embryo production in donor and its transfer to recipient for offspring production. Different factors that effect on this, which are considered for the improvement of effectiveness of ET technology in buffalo and cattle. Perhaps, this review provides historically pioneer attempts at ET along with the swift changes within up to date. Having discussed ET at its peak, also it covers the futuristic steps for ET.

BENEFITS OF ET TECHNOLOGY

Timed ET, ovum pickup, and superovulation are playing an important role to reduce generation interval, and increase genetic improvement in cattle. Previous studies showed that synchronization is a good process for ovulation to assist reproductive technologies (Stewart *et al*., 2011; Das *et al*., 2022). In last decade, the insemination and the transfer technique of frozen-thawed semen or embryo were increased due to good fertility rate achievement (Cowan, 2010). In different studies, it is shown that ET is a safe technique and it does not transmit infectious diseases. Therefore, it has been indicated that use of ET is a salvage genetic material in case of disease outbreak and it is a valuable choice in demonstration of disease-free-herds (Wrathall *et al*., 2004; Mebratu *et al*., 2020). For high production of beef and dairy cattle, ET brings great number of calves/year/female (Wrathall *et al*., 2004). Many discriminations are observed in different phases of development on foreign and domestic studies of ET and their viability in cattle (Danchuk *et al*., 2020; Bollman *et al*., 2020; Roman *et al*., 2020; Grymak *et al*., 2020). The usage of ET technology is increasing in cattle by more offspring production in short lifespan. Normally, cows are monotococus, their ovaries have potential to ovulate routinely one ova and two ova rarely, and only single offspring can be obtained from cow per annum (Crowe *et al*., 2021). An effective technique of assisted reproductive technology called superovulation followed by timed AI is efficient to create large numbers of embryos in donor cattle (Mapletoft *et al*., 2009; Stroud and IETS, 2011).

In Vitro Embryo Production

For the genetic improvement in animal, *in-vitro* embryo production (IVP) shows an important enhancement for dairy and livestock production. *In vitro* embryo

Table I. Historical background of embryo transfer (ET).

Events	Year	Citation
ET in rabbit doe	1890, 2003, 2020	(Heape, 1891; Betteridge, 2003; Mebratu, 2020).
4 pregnancies in cattle by ET in Texas	1949	(Umbaugh, 1949).
First calf born by surgical ET	1951	(Willett *et al*., 1951; Mapletoft, 2013).
In Cambridge (England) Rowson and his college work on ET and get success in cattle and pig	1950-70	(Foote, 1970).
In-vitro fertilization and cloning technique increases after ET technology	Since 1970s	(Kennady *et al.,* 2018).
ET technology developed in North America	1970	(Hasler, 2014; Moore, 2017) .
First calf birth through ET by E.L. Willet *et al*.,	1973	(Betteridge, 2000).
Establishment of International ET Society (IETS)	1974	(Theiber, 1992).
In 1980 non-surgical ET technique was first time developed on farm	1980	(Gordon, 2003; Wright 1981; John, 2008).
In cattle breeder ET technology used	1980	(SEIDEL, 1981).
Non-surgical (trans cervical catheterization in uterine horn) ET method developed in commercial level	1980	(Gordon, 2003; Wright, 1981; John, 2008; Mapletoft, 2018).
First young one produced through frozen-thawed embryo in mouse, cattle, rabbit, sheep, goat, horse, cat	1971, 1973, 1974, 1974, 1976, 1982, 1988	(Gordon, 2003; Kidie, 2019).
Multiple ovulation and ET (MOET) was first time introduced at University of Guelph in 1987. This concept showed that this technique is helpful for reduction of generation intervals, increased selection intensity and improved genetics	1987	(Smith, 1988).
World Veterinary Congress proposed symposium International Embryo Movement Symposium (IETS) in Montreal	1987	(Smith, 1988).
Pioneer award to Heapes by IETS	1990	(Biggers, 1991).
First calf birth at University of Wincosin by E.L. Willer *et al* through ET in cattle	2000	(Betteridge, 2000).
In South America invitro embryo production and developed	Since 2000s	(Hasler, 2014; Blondin, 2017)
538,312 embryo produced, out of which 52% were transfered by the freezing technique on farm and 15% produced by *in vitro* technique.	2002	(Theiber, 2003).
790,000 ET red (240,000 *in vivo* produced and 550,000 in-vitro produced embryo)	2004	(Theibier, 2005).
614,464 invitro bovine embryo produced and 464,582 ETred in globe	2014	(Perry, 2015).
More than 992,289 *in vitro* bovine embryo produced in the whole world	2017	(Viana, 2018).

production (IVEP) from oocytes recoup by ovum pick-up is being increased, improved, and reported in last 20 years (Raghu *et al*., 2002; Souza-Fabjan *et al*., 2021). *In vitro* embryo production and transfer to recipient animal is costly but owing to better results, use of this technique is increasing (Sirard, 2018). For maturation of oocyte, fertilization, and embryo culture alter technique occur after first *in vitro* calf production (Ferre *et al*., 2020; Hansen, 2020)

Various studies have basis on improving the efficiency of in-vitro ET technique and different factors like follicular size, oocyte diameter for *in vitro* embryo production (Viana, 2018). The phase of the follicular wave genetic group and the animal category are influencing the ET technique (Ferreira *et al*., 2011; Viana, 2018). Since the last decade, Brazil has become highly developed in ET technology, and produced 57% *in vitro* embryo (IVP) of total world (Adifa *et al*., 2010).

Twinning in cattle

Embryo production is the best alternative source for the production of twin fetuses in monotococus animals such as cattle (Roman *et al*., 2020). Naturally, a single cow in her life can produce 8-10 calves with one calf per annum ratio. However, using improved ET technology, approximately 32 embryos can be obtained by single genetically superior cattle annually. The microsurgical ET technique is beneficial in pure breed herds of cattle for the production of identical twins (Muchemi, 2011; Turner, 2019). Indeed, the twinning method is expensive nonetheless; it escalates herd animals by 60%. Cloning is necessary for producing identical twins before transferring the embryo to recipient cattle (Lopez *et al*., 2017). While genetic selection through twining becomes unreliable. An alternative source of ET happens fruitful in the case of twining to produce more offspring in a short period (Kidie, 2019). Since the last three decades, the twinning rate (due to the production of multiple ova in a single estrous) in dairy cattle is increasing with the milk production (Garcia-Ispeirto, 2019). Sometimes, twining in cattle causes the death of twin fetuses after delivery, reproductive disorder, freemartin condition, and stillbirth (Andre *et al*., 2012; Philips and Jahinke, 2016; Fufa *et al*., 2016).

Applications of ET

Selection of donor

Donor selection has an immense role in the ET procedure. For donor selection, three basic attributes are mostly used to select donor cattle, such as reproductive ability, genetic superiority, the high value of progeny market (Mikkola, 2007; Besenfelder *et al*., 2020). Nutritional status, body condition score, genetic qualities, parity of animal, housing environment of donor, good reproductive age and performance, parity, the timing of superovulation, and the previous fertility record have key role in donor selection (Valenza *et al*., 2012; Burnett *et al*., 2018). Good health of donor cattle is necessary for better superovulation, enhancing fertility levels (Burnett *et al*., 2018). Good nutrition is necessary in donor cattle to maintain hormonal balance for fertilization in salpinx tube and embryo development from zygote at ampulla-isthmus junction before entering in the uterus by the proper hormonal balance that is maintain by good nutrition (Nicholas and Smith, 1983; Burnett *et al*., 2018). In donors, anovulation, fertilization failure, or early embryonic mortality have a great effect on the vitality of the embryo. In lactating donor dairy cattle, about 3.4-6.7% chances of anovulation occur during estrous (Peixoto *et al*., 2006). To mimic fertilization, *in vitro* embryo production, suitable culture media, and provision of a good environment is necessary as in oviduct (Bo and Mapletoft, 2020).

Two selection strategies for donors are proposed by scientists; one of these two is juvenile scheme (donors are heifer and they are selected according to pedigree) selection of male and female during puberty on the interpretation of female ancestor. While the second is “adult scheme” (donors are a high milk-producing animal) that depends on the selection of male on the interpretation of female ancestor (Peixoto *et al*., 2006; Bo and Mapletoft, 2020), and these strategies are very helpful for the selection of donor.

Table II. First young born after transfer of frozen thawed embryos (Gordon 2003, Kidie 2019).

Species	Researchers	Years
Mouse	Whittingham *et al.*	1971
Cow	Wilmut and Rowson	1973
Rabbit	Bank and Maure	1974
Sheep	Willadsen	1974
Rat	Whittingham	1975
Horse	Bilton and Moore	1976
Goat	Yamamoto *et al*	1982
Human	Zeilmaker *et al*	1984
Hmaster	Ridha and Dukelow	1985
Cat	Dresser *et al*	1988
Pig	Hayashi *et al*	1989
Rhesus monkey	Wolf *et al.*	1989

Superovulation in donor animal

Since late 1940s, ET was introduce by the best protocol of superovulation for dramatic embryo production and ET to recipient animals (Moore and Hasler, 2017). To achieve high blastocyst yield and pregnancy rate, several researchers are trying to amend super-ovulatory protocol (Mapletoft *et al*., 2002; Khan *et al*., 2022). The superovulation technique proved to be efficient for the generation of bulk embryos in donor cattle (Jaton *et al*., 2016). In the Canadian Holstein population, significant heritability of the great number of viable embryos produced from superovulation has been reported (Watanabe *et al*., 2017). *Bos taurus* cattle breed produced less number of follicles as compared to *Bos indicus* cattle in single ovulation while superovulation is helpful to produce enormous ova (Wolfenson and Roth, 2019). Gonadotropin-releasing hormone (GnRH) stimulates releasing of FSH and LH to regulate the ovarian functions (follicular growth, ovulation, corpus luteum development) (Batista *et al*., 2014). Anti-Mullerian hormone concentration in cattle breeds and the number of antral follicles in the ovarian cortex display vital role in embryo production via superovulation (Baldrighi *et al*., 2014; Souza *et al*., 2014). The high level of circulating anti-Mullerian hormone (AMH) and a huge number of antral follicles in the ovary result in much fruitful superovulation (Batista *et al*., 2014). Variations in the success of ET program are possible due to the variability of super ovulatory response (Forde *et al*., 2012).

Hormonal Therapy for Super Ovulation in Donor Cattle

Use of external hormone for superovulation can cause alteration in endometrium lining, salpinx tube, and follicular fluid (Forde *et al*., 2012; Santos *et al*., 2018; Fontes *et al*., 2019). FSH supports the super stimulation process and proves to be essential for follicular growth and maturation (Oliveira *et al*., 2014; Sanderson and Martinaz, 2020). Normally, saline diluents are used with FSH for superovulation. The use of slow-releasing diluent of FSH has increased the efficiency of superovulation without increasing embryo production levels. Despite high saline diluents with FSH is comparable with the use of hyaluronic acid as diluents in FSH for superovulation (Dias *et al*., 2013a).

Various reports clearly show that the progesterone and estrogen releasing devices are very helpful for effective follicular growth and superovulation (Dias *et al*., 2013a; Crosier *et al*., 2017; Fontes *et al*., 2019). FSH and eCG protocol are used for superovulation that escalate the estradiol concentration in blood plasma and salpinx tube (Santos *et al*., 2018; Oliveira *et al*., 2014; Barajas *et al*., 2019). In different studies, a beneficial effect of FSH with eCG for superovulation has been observed (Mattos *et al*., 2011; Barajas *et al*., 2019). eCG mimics FSH that provides support to growing follicles, owing to better results, eCG replaces the FSH protocols (Stroud and Hasler, 2006). Different studies reported that the progesterone and estrogen releasing devices are very helpful for effective superovulation (Dias *et al*., 2013a).

Factors affecting the superovulation

Different factors effect on the superovulation in cattle. The best time for AI in super ovulated cattle is 12-24 after showing first sign of estrous, single insemination is widely accepted but twice insemination is quite preferable for superovulation (Peter, 2019). The date of a donor's last estrus with the appropriate heat dates is an important tool for the ability of superovulation (Dias *et al*., 2013a). Age, breed, parity and reproductive ability of donor whereas climate, nutrition of animal and FSH preparation are also dependent for superovulation in cattle (Besenfelder *et al*., 2020). In hot season, owing to heat stress embryonic reduction occurs via superovulation (Gadisa *et al*., 2019). Embryonic chromosomal anomaly is observed by using MOET as compared to *in vitro* embryo production (Hansen, 2020).

Selection of recipient

Selection of diseased free (mainly reproductive disease) recipient cattle is necessary to receive embryo and perform great number of pregnancy (Selk, 2010). Recipient selection has an essential role in the success of ET. Cattle having sound health, reproductive ability, milking yield, and good mothering ability is preferable as the recipient (Wu and Zan, 2012). In recipeint cattle, presence of well deveopled corpus luteum (Cl) after estrous have great role in intrauterine embryo development in good progesterone serum concentration (Mattos et al., 2011; Hansen, 2020).

Reproductive performance, nutritional status, parity, and body condition score checkup is necessary for selecting recipient cattle of a mixed breed, *Bos tauras, Bos indicus* (Gadisa et al., 2019; Selk, 2010). In some researches, a heifer seems fit as a recipient for ET, while some researchers prefer selected cows for ET. In Danish, selected 65% of recipients for the ET technique were milk-producing dairy cows (Wu and Zan, 2012).

Table III. Conception rate in repeat breeder cows after AI or ET (Arkadiusz, 2021).

Work	Conception rate of AI	Conception rate of ET	References
Surgically transferred of fresh embryo in cattle	-	70%	(Tanabe *et al.,* 1985)
Frozen-thawed embryos used with timed ET after using control internal drug releasing device	heat 7.7% *vs* TAI 18.5%	53.8%	(Son *et al.,* 2007)
Frozen-thawed invitro fertilized embryos used with the following AI	20.4%	41.5%	(Dochi *et al.,* 2008)
Frozen-thawed embryos (92%) and fresh embryos (8%) following AI after natural heat	30%	52.6	(Canu *et al.,* 2010)
Frozen-thawed *in vitro* fertilized embryos following AI	-	46.9%	(Yaginuma *et al.,* 2019)

A proper estrous period is necessary for recipient cattle, whereas less pregnancy rate is observable in recipient cattle with an improper estrous period (Santos *et al*., 2018). For the recipient, a good progesterone level >16.9ng/ml and functional corpus luteum are necessary to maintain pregnancy in recipient cattle following ET (Abdelatty *et al*., 2018). Progesterone concentration in blood decreases below 1ng/ml reduces conception rate (Mattos *et al*., 2011). Fluctuation of pregnancy rate is observable in the recipient by using frozen and fresh embryos (Rodrigues *et al*., 2018).

Hormonal protocol in recipient animal for estrous synchronization

Synchronization by spontaneous and induced prostaglandin treatment of the recipient is necessary for ET. Uterine environment and optimal interaction of embryo in recipient cattle are necessary for embryo development (Baldrighi *et al*., 2014). Estrous period and estradiol blood concentration are influential for the change of uterine environment and viability of pregnancy by the growth of embryo (Rodrigues *et al*., 2018). In preliminarily cycling recipient cattle use of synchronizing products (estradiol, ECG, prostaglandin) helps to prepare the suitable uterine environment for embryo development and pregnancy viability (Genzebu, 2015; Macmillan *et al*., 2020). In the reproductive tract of recipient cattle estrogen, progesterone receptors and another growth factor such as insulin-like growth factor (IGF1) are necessary to prepare the uterine environment for embryo reception and for further pregnancy establishment (Bridges *et al*., 2013). To achieve high pregnancy rates, external progesterone supplementation through daily injection, insertion of controlled internal drug releasing (CIDR), or progesterone-releasing intravaginal device (PRID) have been reported (Núñez-Olivera *et al*., 2020; Siqueira *et al*., 2009).

Factors affecting the recipient for ET

In the recipient heifers and cows, many factors affect pregnancy by transfer of *in vivo* and *in vitro* produced embryos in cattle, and different studies have elucidated these factors (Gomez-Seco *et al*., 2017). Optimal management of recipient cattle is necessary for the success of ET program (Mebratu *et al*., 2020). In recipient cattle, corpus luteum is the transient gland present on the ovary results to maintain better pregnancy (Pugliesi, *et al*., 2013; O'Hara *et al*., 2014). The endocrine system has a great effect to prepare a suitable uterine environment and progesterone hormone level for embryo development in recipient uterus animals (Núñez-Olivera *et al*., 2020). Many researchers have used the NSAID protocol with flunixin meglumine as inhibitor, for PGf2α-synthesis to regress corpus luteum in the pregnant uterus in recipient (Wallace *et al*., 2011). Embryo survival rate and uterine tone can have dramatic reduction by protein accumulation due to the placing of large fluid in recipient uterine body (Wahjuningsih and Djati, 2013).

Cryopreservation of Embryo

Today embryo is transferred in recipient after freezing and thawing method (Hasler, 2014). An important technique of cryopreservation is fruitful to preserve embryos for future ET and transport to other states (Moore and Hasler, 2017). In cryopreservation, suitable cryopreserved are used for survival and viability of *in vitro* produced embryos (Kasimanickam *et al*., 2019). The slow freezing and controlled-rate freezing method are put in practice for cryopreservation of bovine embryos. In this method, an embryo is loaded in straw after dilution in suitable diluents and gradually cooled at 0.3-0.5 °C and the temperature gradually decreases up to -30 to -65°C, and then the straw plunged in liquid nitrogen -196 °C temperature (Martins *et al*., 2018b). Wahjuningsih and Djati (2013) have used sucrose with dimethyl sulphoxide solution having saline as diluent to cryopreserve embryo. Embryos can be stored at room temperature for one day for direct transfer from the donor to the recipients. For periods of 24 to 72 hours, the embryos must be stored at 4°C in PBS, medium 199, or medium L15, each supplemented with 50% FBS and these are adequate for maintaining the viability of the embryo between donor and recipient (Abdelatty *et al*., 2018). In North America during 2002, more than half of total embryo were freeze in ethylene glycol for future use direct transfer in animals (Abdelatty *et al*., 2018).

Result of Embryo After Cryopreservation

In embryo of *Bos taurus* cattle is less sensitive in comparison with *Bos indicus* in cryopreserved (Marinho *et al*., 2015). A previous study reported that the high pregnancy rate appears while using fresh embryos as compared to the frozen/thawed embryo (Ferraz *et al*., 2017). The negative effect on fertility and embryo quality can be decreased by the cryopreservation technique (Huang *et al*., 2019). The success of ET not only depends on the cryopreservation technique of the donor embryo but also depends on recipient animals (Ferraz *et al*., 2016). By cryopreservation, poor survivability of blastocyst of a produced embryo is observed (Estrada-Cortes *et al*., 2019). Minute changes of embryonic morphology are considerable having used cryopreservation and the pregnancy success is somehow altered (Febretrisiana and Pamungkas, 2017; Mori *et al*., 2015). Thawing is necessary for stored frozen embryo and improper thawing can decrease the viability of embryo cells and can cause low pregnancy success (Mori *et al*., 2015). After storage in cryoprotectant and transporting to long distances, approximately, 65% frozen-thawed embryos survive (Estrada-Cortes *et al*., 2019).

Pregnancy Rates and Factor Affecting after Frozen ET

Different factors affect the pregnancy rates in cattle by the widespread use of ET technology on commercial scale (Vieira *et al*., 2014). In these factors quality of embryo, season, fresh or thawed embryo used, parity of donor and recipient mother, nutritional status, technicality, site, and time of embryo deposition in uterine horn have gigantic influence (Moore and Hasler, 2017). The technique of using frozen embryos is common, but 10-15% less pregnancy rate occur by using frozen embryos beside the fresh embryos (Luo *et al*., 2021). The highest pregnancy rate is achievable having used the highest quality embryo (Gadisa *et al*., 2019).

Experienced professionals have reported that 60% and 70% pregnancy rates occur having processed thawed embryo and fresh embryo, respectively (Block *et al*., 2010). Better pregnancy rate in recipient cattle are achieved by human chorionic gonadotropin (Hcg) gonadotrpin releasing hormone treatmnent in first week of estrous cycle (Pereira *et al*., 2016). And also effectiveness of luteotropic hormone is seen in increasing pregnancy rate after ET in recipient cattle (Vieira *et al*., 2014).

In 2017, it was reported that 50% of global embryos were produced in 2014 and pregnancy rates of *in vivo* derived embryo were higher than *in vitro* derived embryo (55.9% compared with 19.8%) (Block *et al*., 2010; Gadisa, 2019). In the recipient dairy heifers, mostly embryo losses have been seen between 32-60 days of pregnancy (Pereira *et al*., 2016). While 0-34% of pregnancy losses seen in recipient cows having in-vitro fertilized ET (Ealy *et al*., 2019). Great pregnancy loss occurs during early pregnancy diagnosis after ET in recipient cattle (Souza *et al*., 2014). Pregnancy loss can occur due to less match of endometrial cell and conceptus rate (Viana *et al*., 2017). The post-estrous uterine development asynchrony of donor and recipient mother affects pregnancy rate (Ferraz *et al*., 2016).

Use of Sexed Semen for ET

For optimal breeding, the conventional use of sexed semen for embryo production is increasing day by day (Garcia-Guerra *et al*., 2016). For embryo production, the use of sexed semen is more beneficial and has a clear advantage for the end-user. Embryo by sexed semen helps produce animal according to need like milk or meat producing animal (Stewart et al., 2011; Tribulo *et al*., 2012). For increasing efficiency of animal production, great potential and increasing ratio in cattle is observable via utilizing sex-sorted semen for embryo production (Ulbrich *et al*., 2010; Heikkila and Peippo, 2012). In dairy cattle, pregnancy cost decreases by the use of embryos produced through sexed semen for in-vitro embryo production (Maxwell *et al*., 2004, Dire, 2020).

Effect of heat stress on embryo

Gametes (sperm and egg) are thermolabile because they form and remain active at an optimum temperature in uterine environment that is below normal body temperature; heat stress degrades and blood flow regulates it (Schenk *et al*., 2006; Smith *et al*., 2018). Heat stress have great effect on the pregnancy rate. In heat stress conditions, hormonal levels disrupt as the ovarian function changes, resultantly, embryo rejection occurs. Lately, it's been reported that lactating cows inseminated through AI under a thermal stress environment have 18% chances of infertility (Baruselli *et al*., 2020). According to AI, ET has a great chance of viability and survival in the hot climate. ET at blastocyst stage have thermal stress resistance, meanwhile, ET in heat stress condition has high fertility rate (Whitfield, 2016; Cotter, 2017). High environmental ambient temperature and relative humidity affect on the homeo thermic status of animal that indirectly effect on the uterine environment that can caused detrimental effects on the embryo production and its mortality (Nabenishi *et al*., 2017). In heat stress, body temperatures increases that caused releasing of the prostaglandin hormone and negative impact occurs on corpus luteum that can cause the embryonic loss and reduces the pregnancy loss (Kim *et al*., 2014; Sakatani, 2017; Besbaci *et al*., 2021).

Embryo transfer in repeat breeder

Repeat breeders are the animals that are not conceiving by three or more artificial insemination and natural breeding (Dochi *et al*., 2008; Tiwari *et al*., 2019). Many authors reported that better pregnancy rate is achieving by ET in repeat breeder cattle. In repeat breeder cattle, uterine environment effects on the oocyte and embryo development. While, ET in repeat breeder has deleterious effect on pregnancy (Ahmed *et al*., 2016). In the repeat breeder cattle, great pregnancy success achieved through ET following AI (Mori *et al*., 2015).

CONCLUSIONS

The constantly increasing human population influences the food chain thus demand for excessive production escalates, since then, ET is one of the major drivers to balance the animal productivity in order to balance the supply-and-demand chain. This advanced technology has enhanced the parity, improvised conception rate, and reduced pregnancy failures/complications. This review details the embryo production technique, transfer of embryo from donor to recipient and the factor that are necessary for transfer of embryo from donor embryo production to offspring. Perhaps, this review provides historically pioneer attempts at ET along with the swift changes within up-to-date. Having discussed ET at its peak, also it covers the futuristic steps for ET.

Statement of conflicts of interest

The authors have declared no conflict of interest.

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