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INFERTILITY IN DAIRY COWS – ANATOMICAL CAUSES

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ABSTRACT

Reproductive failure has been recognized today as one of the most serious problem affecting economy of the dairy cattle industry. Complete sterility is probably less important than sub-fertility or infertility, because sterile animals are few and easily identified in comparison with those having transient form of reproductive disorders. It is commonly observed that the individual females may be infertile due to a cause which does not involve other animals in a herd. Congenital or acquired genital abnormalities are important cause of infertility. Recent focus on the genetic basis of female reproductive tract malformations has provided insight into the underlying molecular mechanisms that govern this process crucial to the survival of species. Several genes thought to play a significant role in this developmental pathway have been identified by analysis of knock out mouse models and through identification of genetic syndromes that feature anomalies of the female reproductive tract. Therefore, future studies should continue to focus on unveiling the underlying genetic and molecular mechanisms of the development of the female reproductive tract as many of these embryologically defined genes may play a role in adult reproductive functions also. Studies are also to be conducted to develop approaches for diagnosing the defect at an early stage and minimizing the anatomical causes of reproductive disorders so that the conception rate of the herd can be improved, thus reducing economic loss to the farmers.

Keywords: Infertility, Dairy cattle, Anatomical causes

INTRODUCTION

Fertility is a result of intricate balance between anatomy of the reproductive organs and the physiology. Aspects affecting the balance such as hereditary and congenital factors, anatomical defects, nutritional factors, improper herd management, hormonal disturbances, systemic diseases or specific diseases affecting the reproductive system or even environmental changes may affect

the balance and thus influence fertility. Anatomical causes of infertility include structural abnormalities of the ovaries, oviducts, uterus, cervix, vagina and vulva *viz*., ovarian hypoplasia and aplasia, abnormalities of the tubular genitalia, arrested development of Mullerian ducts, kinked cervix, double cervix, etc. which can be inherited. Defects of the Fallopian tubes have been attributed as one of the most important causes of infertility in all species. Trauma or tears during parturition or artificial insemination can lead to permanent damages to uterus, cervix, vagina or the vulva leading to infertility. Another main problem is the development of adhesion of genitalia with adjacent regions as a result of infections, faulty handling of ovary and reproductive tract including forceful intrauterine infusion of irritating drugs in large volumes.

Profitability of a dairy farm is determined by the reproductive efficiency of the stock. Infertility is one of the major problems confronting the dairy industry in India and causes great economic loss to the dairy farmers and is a frequent reason for culling. Loss of two to three lactations due to poor reproductive efficiency greatly affects the economics of dairy farming. Hence, this review article is envisioned to discuss the anatomical causes leading to infertility in dairy cattle.

EMBRYONIC DEVELOPMENT OF THE GENITALIA

The gonads first appear as ridges that protrude from the dorsal wall of the abdominal cavity of the embryo, adjacent to the developing mesonephros. Germ cells migrate by amoeboid movement from the endoderm of yolk sac to reach these gonadal ridges. If the gonad is destined to develop into a testis (as per the genetic makeup of the animal), cells covering the gonadal ridge grow inward to envelop the germ cells to form solid cellular cords (seminiferous cords) that ultimately become the seminiferous tubules by canalisation at puberty. Germ cells within the seminiferous cords will become the spermatogonia. The supporting or Sertoli cells arise from mesenchymal tissue adjacent to the germ cells and Leydig cells develop in the intertubular areas. As development of the embryonic testis proceeds, a band of connective tissue (tunica albuginea) develops between the superficial cells and the testis cords (Roly *et al*., 2018).

In contrast, cortical development signifies ovarian formation. The cellular cords containing germ cells (oogonia) will undergo re-organisation, so that each germ cell gets covered by a layer of flat supporting cells forming primordial follicles. Oogonia differentiate into primary oocytes before birth and they commence meiosis but

remain in the prophase of Meiosis I until ovulation following puberty. In cattle, the primitive gonad becomes recognizable as testis or ovary at 41 days of gestational age. The full allotment of primary oocytes is present in the neonatal ovary.

Lack of both testosterone and testis-derived Anti-Mullerian Hormone in female embryos allows regression of the Wolffian duct and differentiation of the Mullerian or paramesonephric duct into the female reproductive tract. Cranial region of each paramesonephric duct forms the Fallopian tube that remains open at the anterior most portion. Caudal to the level of inguinal fold, the duct forms uterine horn. At a more caudal level, the two paramesonephric ducts fuse to form a single tube, which corresponds to the body of uterus, cervix and cranial third of the vagina. The fused single tube ends blindly in contact with the urogenital sinus. The degree of fusion of the two paramesonephric ducts is species specific and among domestic animals, fusion is maximum in equines and minimum in carnivores. As an extreme case, rodents and rabbit have double cervices that open into a single vagina. Caudal two-third of the vagina develops from a solid tubercle (vaginal plate) that develops outwards from the urogenital sinus from the point of contact with blind end of paramesonephric duct. Degeneration of the cells in the central portion of the plate leaves the lumen of the vagina. A hymen may persist at the junction between vagina and vestibule. Vestibule develops from urogenital sinus (Fletcher and Weber, 2013).

Direction and control of normal sexual differentiation is complex. Key genes involved in Mullerian duct formation have been identified through the analysis of animal models and humans with dysfunctional reproductive organs. Cell fate mapping and genetic analyses in mouse and chicken embryos have provided details on the molecular and cellular events underlying Mullerian duct specification, invagination and elongation. It is reported that morphogenesis of the Mullerian duct is controlled by coordinated action of transcription factors and signalling molecules. This process includes a close interaction between epithelial cells and underlying mesenchyme.

CONGENITAL ANATOMICAL CAUSES OF INFERTILITY IN DAIRY CATTLE

Congenital anatomical causes of infertility are often inherited. Common anatomical defects include ovarian (gonadal) hypoplasia and aplasia, anomalies of the tubular genitalia, hermaphroditism, Freemartinism, arrested development of

the Mullerian ducts (White heifer disease) and double cervix. Muneer *et al.* (2010) conducted studies on the incidence of reproductive disorders in Frieswal crossbred cows and found that functional causes constituted the major problem (68.64%), the remaining being infectious (29.73%) and anatomical (1.63%) causes.

Millward *et al*. (2019) observed female reproductive tract of 680 dairy cows in UK and found 141 abnormal tracts with acquired and congenital defects. 54.6 per cent of abnormality was associated with ovaries followed by 25.5 per cent in uterus and 3.54 per cent in the cervix. While comparing dairy breeds and beef animals, the dairy cattle had 1.6 times more abnormal genitalia than beef animals. Connell *et al.* (2013) opined that genes significant to the developmental pathway of female reproductive tract not only played a role in the proper structural development of the tract but also might persist in adult mammals to regulate proper function of the endometrium of the uterus. A range of developmental defects including agenesis, atresia and septation of the reproductive tract were associated with genetic syndromes.

1. Ovarian Hypoplasia

This is the most common type of congenital abnormality in animals. Bovine gonadal hypoplasia can be unilateral or bilateral and total or partial. It is not easy to diagnose the condition and in cases of bilateral ovarian hypoplasia, heifers do not develop secondary sexual characteristics. The animals will be anoestrus and infertile (Akkoyunlu *et al*., 2014). If the condition is unilateral, normal sexual organs and oestrus activity may be observed (Farin and Estill, 1993). Such animals would be fertile, although less so than normal. Bovine ovarian hypoplasia is difficult to diagnose. The small size of the ovary hinders location by per-rectal palpation. According to Vale *et al*. (1984), 17.27 per cent of non-pregnant slaughtered animals out of 5238 in Brazil were suffering from ovarian and other reproductive tract abnormalities. The condition is potentiated by an autosomal recessive gene with incomplete penetrance (Davis *et al*., 1992), and therefore the incidence of gonadal hypoplasia can be reduced by culling such animals from the breeding stock and using only animals (both male and female) with normally developed sexual organs as the breeding stock.

2. Ovarian Aplasia

Aplasia or dysgenesis of ovary has been described in several species of domestic animals. This is associated with many chromosomal abnormalities

(monosomy X or Turner syndrome, trisomy XXX, or Klinefelter syndrome XXY). The ovaries will be very small and there will not be any follicular activity (Tibary, 2021).

3. Aplasia of the Oviduct and Tubal Obstruction

Aplasia of the uterine tube is bilateral and no parts of the oviduct can be seen. The remainder of the genital tract is normal indicating a segmental defect of the Mullerian duct system. In segmental aplasia of uterine tube or oviduct, the tube has a blind end near the uterotubal junction caused by the segmental aplasia. The whole length of the tube is distended. Sometimes, there is duplication of the uterine tube observed wherein, the normal and the accessory one, patent with two distinct uterotubal junctions. The accessory tube is macroscopically normal. Hatipoglu *et al*. (2002) reported that 0.81 per cent of the disorders in the oviduct of 1113 cows examined were due to oviductal abnormalities.

4. Segmental Aplasia of the Mullerian Ducts

The aplasia (obstruction) may be situated in a part of the oviduct, uterine horn, body of the uterus, cervix or vagina. Ovary will be developed normally. Accumulation of secretion anterior to the obstruction happens secondarily leading to hydrosalpinx, hydrometra, mucometra, etc. Segmental aplasia of the uterus may include one horn (*uterus unicornis*), both the horns or only part of one horn (this can cause cystic dilatation of the horn of the uterus cranial to the region of dilatation).

Basile and Megale (1974) examined 6054 heifers in South America and observed segmental aplasia of uterus and cervical abnormalities in 22 per cent of the animals. Hatipoglu *et al*. (2002) observed segmental aplasia in five cases out of 1113 genitalia of cows. The abnormalities were characterized by congenital absence of right uterine horn, body of uterus and cervix. In other cases, vagina was a narrow blind duct. In these cases, the body of uterus was short and anteriorly both the uterine horns became blind sacs, without any connection to the corresponding oviduct. Cervical aplasia is reported in rare cases but not common (Tibary, 2021).

True persistence of the hymen or imperforate hymen is the most frequently described Mullerian duct anomaly in domestic animals (Ladds, 1993). Fluid accumulates in the vagina and uterus and this results in protrusion of the hymen at the vulva while the animal is lying down or straining. Hymen defects are most common in white Shorthorn cattle (‘White heifer disease’).

Uterus unicornis certainly appears to result from abnormal development of the Mullerian/ paramesonephric duct. Early in development these cords are solid, but they develop a lumen about the time of the median fusion of their caudal portions, when the cords become closely associated with the dorsal wall of the urogenital sinus. ***Uterus didelphys*** is a rare congenital anomaly of the female reproductive tract occurring in several species, including cattle, sheep, goats, horses, llamas and humans. The anomaly results from a complete failure of proper fusion of the caudal portion of the Mullerian ducts and is characterized by a double cranial part of the vagina, double cervix and a divided uterine fundus resulting in two single-horned uteri. However, *uterus didelphys* is a normal feature of the female reproductive tract in rabbits and some marsupials. The etiology of the condition is unknown, but it is thought to be hereditary and associated with a recessive gene. Of all the conditions associated with arrest in the development of the Mullerian duct system, the anomalies associated with failure of proper fusion like *uterus didelphys* are rarer than those associated with aplastic or hypoplastic defects like segmental aplasia or 'White heifer disease', with the exception of partial hymenal persistency, which is common.

5. Abnormalities of the Cervix

Failure of the Mullerian ducts to fuse will lead to double external *os* of the cervix. It may appear as a band of tissue posterior to, or in the external *os* of cervix. In some cases, double external *os* openings can be seen, which open into single caudal part of the cervical canal. Rarely, a true double cervix, with a complete septum between the two cervical canals, each opening into its respective uterine horn (*uterus didelphys*), can be seen (Tibary, 2021). Animals with the abnormalities of cervix may conceive normally.

Robertson *et al*. (1996) investigated eight infertile nulliparous heifers in West Highlands of Scotland and found four non-patent and double cervix conditions. Patency of the cervix was examined by introducing an artificial insemination pipette. According to them, cervical abnormalities were associated with inbreeding and observed within a closed breeding herd.

Cervical stenosis and incomplete closure and bending of cervix are also found in dairy cattle. Many of known inherited causes of infertility involve kinked cervix. The hardness of cervix may appear due to trauma or lacerations during calving and artificial insemination followed by infection and fibrosis. Singh *et al.* (2008) studied the etiological factors causing

repeat breeding in cattle and found that 7.1 per cent of animals showed acquired anatomical abnormalities. The anatomical abnormalities observed included kinked and hard cervix, ovaro-bursal adhesions (OBA), combination of OBA and kinked cervix and uterine tumors.

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