CLINICAL STUDIES ON PSEUDOPREGNANCY IN DOGS

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CERTIFICATE

This is to certify that the thesis entitled ***"CLINICAL STUDIES ON PSEUDOPREGNANCY IN DOGS"*** submitted by **Ms. SHILPA, V. S., ID No. MVHK-1625** in partial fulfilment of the requirements for the award of degree of **MASTER OF VETERINARY SCIENCE** in **VETERINARY GYNAECOLOGY AND OBSTETRICS** of the Karnataka Veterinary, Animal and Fisheries Sciences University, Bidar is a record of bonafide research work carried out by her during the period of her study in this University under my guidance and supervision and this thesis has not previously formed the basis for the award of any degree, diploma, associateship, fellowship or other similar titles.

Bangalore

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LIST OF ABBREVIATIONS/ ACRONYMS

%	Per cent
±	Plus or minus
>	Greater than
<	Lesser than
Kg	Kilograms
BW	Body weight
et al.	*et alia*
Fig.	Figure
ng	Nanogram
µg	Microgram
pg	Picogram
Pvt.	Private
Ltd.	Limited
ml	Millilitre
rpm	Revolutions per minute
sec	Seconds
mm	Millimetre
i.e.	That is
^{0}C	Degree Celsius

INTRODUCTION

I. INTRODUCTION

Pseudopregnancy, pseudocyesis, false pregnancy, phantom pregnancy, copycat pregnancy or nervous lactation is a physiological syndrome characterised by signs of pregnancy in non-pregnant female dogs (Gobello *et al.,* 2001a). The estrous cycle in domestic dog is considered as unique and different from other domestic animals. They are mostly monoestrous and predominantly non-seasonal with several months of anestrus between active reproductive phases (Stabenfeldt and Shille, 1977; Hoffmann *et al.*, 1992; Concannon, 2011). The phenomenon of pseudopregnancy is more of a pseudonym as the signs mimic the period post-whelping or the period of lactation rather than the actual pregnancy.

The dogs develop maternal instinct, behavioural changes and undergo mammary development with lactation. The condition may have had functional importance during evolution when non-bred female wolves had to nurse other females' litters in a pack (Jochle, 1997; Voith, 1980). However, these behaviour changes in domestic dogs can become nuisance to the owners. In the absence of litter to feed, the mammary development and lactation could also complicate with resultant mastitis and/or mammary dermatitis which demands medical attention. The sudden protective and maternal instincts could lead to aggressive behaviour against owners or visitors which is also difficult to manage in housed dogs. Mostly pseudopregnancy is considered as a physiological syndrome which does not demand treatment and the signs reduce or regress over time (Feldman and Nelson, 1996; Gobello *et al.,* 2001a). Development of rare but possible complications and domestic nuisance associated with the condition cannot be ignored and need to be addressed.

The clinical signs associated with pseudopregnancy are mostly behavioural changes like nesting behaviour, mothering of inanimate objects, anxiety, inappetance, aggressiveness, hyperexitability, restlessness, whining, decreased activity and licking of abdomen (Johnston, 1980; Feldman and Nelson, 1996; Gobello *et al.,* 2001a). The other clinical signs are mammary enlargement with milk or serous secretions, vaginal discharges and abdominal contractions (Jochle *et al.,* 1987; Razzaque *et al.,* 2008). Rarely other signs like vomiting, diarrhoea, polyuria, polydipsia, polyphagia and complications like mastitis and mammary dermatitis also occur (Johnston, 1980; Gobello *et al.,* 2001a; Razzaque *et al.,* 2008). Though the set of clinical signs usually fall within this group the intensity of expression were observed to be highly variable (Gobello *et al.,* 2001b; Thangamani *et al.,* 2018). These variations were initially thought to be due to difference in levels of hormones like progesterone and prolactin between individuals with pseudopregnancy. Different experiments by different researchers have shown that there is no significant difference in the levels of these hormones in pregnant, non-pregnant and pseudopregnant dogs. This leads to a possibility that there could be existence of genotypic differences among dogs wherein the expression of prolactin receptors or the sensitivity to the prolactin by the target organs varies between individuals. This could act as the underlying factor causing the variation in intensity of clinical sign in different individuals with a relatively similar hormone profile.

Over time, the intensive dog breeding have focused more on the physical appearance of the breeds of dogs and not the health status or reproductive performance of the dogs. Intensive breeding policies aimed at the supply of pure breed dogs with optimum phenotypic features could propagate various genetic traits or predispose the dogs to exhibit more genotype oriented attributes. Though pseudopregnancy was mentioned as a frequent

finding in domestic dogs by different researcher, literature on the genetic predisposition of dogs to pseudopregnancy or factor that could influence exhibition of pseudopregnancy is scanty. Therefore, the present study was aimed to systematically track down the basic factors that could attribute to exhibition of pseudopregnancy and to study the relative advantages of different treatment protocols followed to manage pseudopregnancy in dogs. Considering all these factors, the objectives for the present study were formed as:

1. To study the prevalence of pseudopregnancy in dogs.
2. To study the factors associated with pseudopregnancy in dogs.
3. To record the various clinical signs exhibited by pseudopregnant dogs.

REVIEW OF LITERATURE

II. REVIEW OF LITERATURE

2.1. Estrous cycle in dogs

The reproductive cycle of female dogs are considered unique in comparison to other domestic animals. The phases of estrous cycle are characterized based on behavioural aspects, clinical signs exhibited, hormonal profile, vaginoscopy and cytological changes of the vaginal epithelium. Based on these, the estrous cycle has been divided into 4 phases viz., proestrus, estrus, diestrus and anestrus (Jochle, 1997; Concannon, 2011).

2.1.1. Proestrus:

The resumption of ovarian activity and follicular development after the obligate anestrus period is marked by signs of proestrus in female dogs. The duration usually varies over a range of 3-20 days with an average of 9 days (Gobello *et al.,* 2001a). During this stage external signs of estrogenization are manifested as vulval oedema, serosanguinous vaginal discharge, attraction of males but refusal of mating, flagging of tail and elevation of tail with swaying of hips in response to touching the peri-anal region. The vaginal discharge is typically bright red and voluminous at onset of proestrus and reduce in colour and volume towards end of estrus (Jaller, 2015). Under the influence of estrogen, vulva slowly enlarges and vaginal epithelium undergoes proliferation and cornification. There is increased secretion of pheromones like p-hydroxybenzoate in the vulval discharge that attracts the males to females in proestrus (Concannon, 2011). A gradual shift from parabasal to intermediate cells occurs in vaginal cytology during this period (Antonov, 2017).

2.1.2. Estrus:

Acceptance of male by the female dogs marks the onset of estrus. The duration of estrus is also prolonged and variable over a range of 5-15 days with an average of 9 days (Gobello *et al.,* 2001a). This fertile period in female dogs is characterized by proactive receptivity to mounting by males and an increased male seeking behaviour (Concannon, 2011). Other signs shown by a female dog in estrus includes crouching or elevating the perineum towards the male with tail shifted on one side, tensing of the rear legs to support the weight of a mounting male, relaxation and softening of vulva, presence of straw or pink coloured vaginal discharge (Feldman and Nelson, 1996; Jaller, 2015). Identification of the optimum time of breeding within this fertile period is mostly aided by use of vaginal cytology along with other techniques. Srinivas *et al.* (2004) has described that the optimum time can often be associated when the percentage of superficial or cornified cells in vaginal smears are above 80% and breeding or artificial insemination should be done in two or three days interval until diestrus occurs.

2.1.3. Diestrus:

Canines have a unique physiologically long diestrus lasting around 50-80 days in both pregnant and non-pregnant female dogs. The onset of this phase is marked by the female rejecting mating, vaginal discharge gradually becoming scanty and reduction in size of vulva from the proestral stage. This phase is more accurately defined by vaginal cytology recognised by appearance of parabasal cells, neutrophils and the number of superficial and squamous cells decreased by at least 20% from the previous phase (Srinivas *et al.,* 2004; Antonov, 2017). Johnston *et al.* (2001) suggested that identification

of day of onset of diestrus by serial vaginal cytologic examination can be used to predict date of whelping more accurately than mating behaviour.

2.1.4. Anestrus:

Canine estrous cycle is marked by a period of obligatory anestrus of around 80-240 days (Jochle, 1997; Concannon, 2011). During anestrus the reproductive organs undergo a period of quiescence. There is absence of any significant ovarian activity owing to low frequency of GnRH pulses. During this period the female dogs are not attractive to males and are not receptive to mating. Vulva is usually small without any discharge. The cytology during this phase shows sparse number of parabasal cells (Concannon, 2011). If the dog was pregnant in the cycle this stage is the period of uterine involution and lactation. However, in non-pregnant dogs the stage is not clinically differentiable. The duration is also said to vary according to breed, health, age, time of year, environment and multiple other factors (Feldman and Nelson, 2004; Jaller, 2015).

2.2. Endocrinology of canine estrous cycle

Complex sequences of events interconnecting brain and reproductive organs that repeat itself in cyclic pattern are under endocrinological regulation. Canine estrous cycle has a unique endocrinology compared to other domestic animals. Hypothalamus and anterior pituitary are the two main parts of brain that exert impact on reproductive system mediated through different hormones. Hypothalamus is the master center for reproduction controlling the estrous cycle through its main mediator the gonadotropin releasing hormone (GnRH). The release of GnRH is under the influence of a number of factors including duration and intensity of light, body condition, age and the feedback mechanism of other hormones. The secretion of GnRH is pulsatile with a short half-life of 2-5 minutes

due to rapid cleavage by protease (Gobello, 2007). Gonadotrophs in anterior pituitary are specialized cells that have receptors for GnRH. In response to GnRH, two large protein hormones (gonadotropins), namely luteinizing hormone (LH) and follicle stimulating hormone (FSH) will be secreted into blood. The pulsatile release of GnRH from hypothalamus is reflected as pulsatile release of LH and FSH. The FSH acts on the granulosa cells of ovaries and helps in follicular development and production of a steroid hormone, estrogen. The LH acts on the luteal cells and helps in ovulation, leutinization of the granulosa cells and aids in the production of another steroid hormone the progesterone.

Anestrus, a period of low frequency GnRH release and associated reproductive quiescence, is followed by resumption of cyclical activity. It is considered obligate lasting around a minimum of 7 weeks after the progesterone values comes down to 1-2 ng/ml (Kowalewski, 2014). The low frequency of pulsating GnRH results in pulses of LH and FSH at intervals greater than 7 hours. The estradiol concentration is also variable but generally around 5-10 pg/ml. (Concannon, 2011). When the pulse of GnRH increases, reflected as increased frequency of FSH and LH pulses of intervals less than 2 hours, it causes increased follicular activity. The increased frequency of LH leads to follicular selection and development of dominant follicles. These follicles produce estrogen in higher concentration resulting in manifestation of proestrus (Concannon, 2011). With the presence of dominant follicles in the ovary, estrogen is the predominant hormone of proestrus and the values increases to 40-120 pg/ml. Progesterone values in serum during early proestrus are at basal levels (<0.5 ng/ml) but start rising at the end of proestrus due to pre-ovulatory leutinization of follicles in canines (Wildt *et al.,* 1979; Jaller, 2015).

Endocrinologically proestrus ends and estrus starts with preovulatory LH surge. This preovulatory LH surge is considered as the central event of the cycle or day 0, with

spontaneous ovulation of primary oocytes from partially luteinized follicles occurring around 48-60 hours after LH surge. Oocytes undergo maturation during the next two or three days in the oviduct (Concannon *et al.,* 1977). The behavioural estrus or acceptance of male by the female is mediated by the sharp decline in estrogen accompanied by increase in progesterone concentration. The progesterone values increases from 1-3 ng/ml to reach peak values of 10-25 ng/ml. (Concannon, 2011).

The luteal phase following estrus is called diestrus and the period is associated with the function of the corpus luteum and progesterone secretion. After day 30, progesterone secretion is dependent on pituitary secretion of prolactin and luteinizing hormone (Concannon *et al.,* 1987; Arbeiter *et al.,* 1988).The peak progesterone concentrations of 15-80 ng/ml are achieved at around 20-30 days. After this period it decreases gradually and reaches the basal values of 1-2 ng/ml by day 55-90 post LH surge. Ozyurtlu *et al.* (2006) described that period of diestrus should be considered as long as serum progesterone levels are greater than 1 ng/ml. The corpus luteum of diestrus has a physiologically long life span which is common in pregnant and non-pregnant dogs. This may be due to absence of any luteolysin from the uterus in non-pregnant dogs (Olson *et al*., 1984; Okkens *et al*., 1985).

2.2.1. Progesterone:

Progesterone is a uniquely potent steroid in female dogs. It can without estrogen pre-treatment, cause endometrial hyperplasia and mammary hyperplasia. Endogenous progesterone is important for behavioural estrus and helps in prolonging the life span of corpus luteum as it is luteotrophic. The unique feature of canine follicles that undergo preovulatory leutinization causes rise in peripheral progesterone concentration to around

5ng/ml at the time of ovulation (Concannon and Lein, 1989) and then further increases up to 30 days after ovulation.

The progesterone from corpus luteum of diestrus can produce stimulation of mammary tissue resulting in mammary enlargement with or without milk or milk like secretions making diestrus physiologically distinct and recognisable phase even in non-pregnant dogs. This mammary development may persist 1 or 2 months after progesterone reaches its basal levels (Concannon, 1986). Progesterone also lead to increase secretion of growth hormone from mammary tissue as well as pituitary that leads to increase gluconeogenesis manifested as pregnancy diabetes (Mol *et al.,* 1996; Stroving *et al.,* 1997; Concannon, 2011). Major difference between pregnant and non-pregnant female dogs is the elevation of relaxin from day 25 (Concannon *et al.,* 1996; Onclin and Verstegan, 1997; Concannon, 2010). The concentration of progesterone produced is related to the amount of luteal tissue formed in that cycle. Adult dogs and heavier dogs were reported to have more luteal tissue and were associated with higher progesterone concentration than young and low body weight dogs. Accordingly, the rate of progesterone decline is slower in dogs with heavier luteal tissue (Marinelli *et al.,* 2008). Further, Thomassen *et al.* (2006) mentioned that the young and primiparous dogs are more predisposed to low litter size owing to reduced number of ovulations in these animals. Reduced number of ovulation leads to reduced luteal tissue and a more rapid progesterone decline (Concannon *et al.,* 1977; Marinelli *et al.,* 2008).

The concentration of progesterone in pregnant and non-pregnant female dogs was thought to be significantly different (Schaefers- Okkens, 1996). In non-pregnant female dogs the progesterone was said to peak around 5-10 days and then subside gradually. Whereas in pregnant female dogs a second rise in progesterone concentration

to 40-50 ng/ml around 20-25 days after LH peak was reported by Smith and Mc Donald (1974). Ozyurtlu *et al.* (2006) have reported that the second rise in the pregnant female dog is not significantly important and the serum progesterone concentrations reach 15-80 ng/ml in 15-30 days in all female dogs. Smith and Mc Donald (1974) and Ozyurtlu *et al.* (2006) have reported that there was no significant difference in progesterone concentrations between non-pregnant and pseudopregnant dogs.

2.2.2. Estrogens

Corpora lutea of canines also play a role in secreting estrogens during the luteal phase of estrus cycle. Papa and Hoffmann (2011) described a time-dependant aromatase enzyme expression in luteal cells justifying the estrogen production by these cells. Estrogen acts as luteotrophic in canines by exerting an autocrine and/or paracrine action on luteal cells to up regulate the progesterone and prolactin receptors (Kowalewski, 2014). Kowalewski *et al.* (2009) described the paracrine action of estrogen on luteal cells by describing the estrogen alpha and beta receptors on luteal cells. Further, he also described the use of anti-estrogens to induce preterm luteolysis supporting the luteotrophic action of estrogens in canines. Onclin *et al.* (2002) observed similarity in progesterone and estrogen secretion patterns in both pregnant and non-pregnant dogs. Pre-partum drop in concentration of estrogen recorded in pregnant dogs further implicated that corpus lutea was the source of estrogen in canines.

2.2.3. Prolactin

Prolactin is a major luteotrophic factor in canines. Prolactin can be seen as early as 2 weeks, however peak concentrations observed from day 30-35 until parturition (Concannon *et al.*, 1996; Onclin and Verstegan, 1997; Concannon, 2010). The prolactin

levels further increases to 50ng/ml during time of parturition (De Coster *et al.*, 1983). Verstegan and Onclin (1995) and Concannon *et al.* (2009) suggested that the progesterone negatively affects prolactin secretion along with its physiological suppression by dopamine. A drop in progesterone concentration in pre-partum period causes acute elevation of prolactin concentration as described by De Coster *et al.* (1983). In non-pregnant female dogs also, a 2-3 fold increase from the initial levels of prolactin around the time of physiological luteolysis was recorded causing clinical manifestations of lactation known as pseudopregnancy (Concannon, 2011; Kowalewski, 2014). Progesterone withdrawal associated increase in prolactin concentration and activity is also observed during administration of progesterone antagonists, ovariectomy during luteal phase and prostaglandin induced luteolysis (Concannon, 2011). Kowalewski (2014) has also mentioned about a pregnancy associated increase in prolactin secretion in relation to the relaxin levels. Relaxin secreted from the syncytiotrophoblast unit around 25-30 days of gestation stimulates secretion of prolactin owing to the higher concentration of the same in pregnant dogs than non-pregnant dogs.

The mechanism of action of prolactin could be by increasing cholesterol uptake by luteal cells, increase in lipoprotein uptake, increase LH receptors in luteal cells, increase progesterone receptors and down regulation of PGF receptors (Concannon, 2011). Prolactin also plays an important role in exhibition of maternal behaviour and inducing lactation. Administration of dopaminergic agonist, which lowers the circulating prolactin concentration, had a complete luteolytic effect during the second half of luteal phase (Concannon, 1993). Administration of GnRH antagonists or LH antiserum during last half of luteal phase causes luteolysis (Onclin *et al.*, 2000; Concannon, 1993; Concannon, 2011).

2.2.4. Pregnant v/s Non-pregnant endocrinology

The endocrinology of female dogs is unique and similar in both pregnant and non-pregnant female dogs. The female dogs have a physiological luteal phase with the life span of CL similar in both pregnant and non-pregnant cycles. So diestrus in dogs could be referred to as pseudopregnancy, as progesterone concentrations remain increased with or without pregnancy (Wilson *et al.*, 2012). Concannon, (2011) described that non-pregnant dogs have a spontaneously prolonged luteal phase, often longer and with a more protracted decline in serum progesterone than in pregnancy as there is no uterine luteolytic mechanism. Smith and Mc Donald (1974) investigated the patterns of LH and progesterone secretion during the estrous cycle, pseudopregnancy and pregnancy. According to this study, the pattern of release of LH and progesterone were similar in both pregnant and non-pregnant dogs. Although the levels of progesterone were generally lower in pseudopregnant females than in non-pregnant females that were not clinically pseudopregnant but the difference were not significant. Schaefers-Okkens, (1996) reported that in pregnant female dogs there could be a secondary increase in circulating progesterone concentrations between the 25^{th} and 40^{th} day of gestation that may reflect a pregnancy-specific mechanism that results from additional stimulation of progesterone production. Ozyurtlu and Alacam (2005) studied around 30 female dogs and came to conclusion that the serum progesterone concentrations in pregnant female dogs were higher and statistically more significant ($P< 0.01$) than those in overt and covert pseudopregnant female dogs. However, serum progesterone concentrations were similar in overt and covert pseudopregnant female dogs.

Reimer *et al.* (1978) said that no significant differences could be found in prolactin concentrations between pregnant and non-pregnant beagle dogs. Hoffmann *et al.* (1992)

and Harvey *et al.* (1999) have described that the serum prolactin levels in overtly and covertly pseudopregnant female dogs are not significantly different. High prolactin levels do not seem to be necessary for overt pseudopregnancy presence as spayed dogs exhibited clinical sigs with lower serum prolactin values (Gobello *et al.,* 2001c). Tsutsui *et al.* (2007) explained that in most cases of overt pseudopregnancy, the plasma prolactin levels were elevated above normal owing to an apparent premature and/or more abrupt than normal decline in progesterone occurs and triggers prolactin release similar to effects of progesterone withdrawal at parturition. Gunzel-Apel *et al.* (2009) described that the mean concentrations of progesterone and prolactin were not different in non-pregnant German Shepherd dogs and Beagles except at days 50-60, when progesterone concentration were found to be higher in Beagles ($P< 0.05$). Mean progesterone concentration in pregnant Beagles at days 50-60 after ovulation were higher ($P<0.05$) than in German Shepherd dogs at that time. Prolactin concentrations were higher in Beagles throughout pregnancy compared with those in the German shepherd dogs. Still Beagles were reported to have fewer predispositions to overt pseudopregnancy than German Shepherd breed of dogs (Concannon, 2011). This indicates a genetic variation which could also play a role in different response in different animals to same levels of hormones.

Marinelli *et al.* (2008) studied the factors affecting progesterone production in corpora lutea from pregnant and diestrus female dogs by conducting comparison of luteal tissue characteristics and progesterone content along with investigation on effect of animal age, weight and ovulation rate on individual corpus luteum parameters. It was described that none of the luteal parameters differed between pregnant and non-pregnant female dogs, even when the stage of luteal phase was considered. This further justified the fact that the pattern of hormone secretions was similar in both pregnant and non-pregnant

dogs. However, the age and weight of the female dogs significantly influenced the luteal tissue characteristics with heavier and older female dogs having more corpora lutea tissue.

2.3. Mechanism of luteolysis

Corpora lutea is one of the key organs in regulating the estrous cycle of dogs due to its role as the major source of progesterone both during pregnancy and in non-pregnant dogs. Mechanism of luteolysis in dogs is different from other domestic animals. There is no luteolysin secretion from uterus to cause acute luteal regression in canines. Prostaglandins (PGF) are luteolytic when administered exogenously however they are not produced endogenously in sufficient quantities to cause luteolysis at least in non-pregnant dogs (Concannon, 2010). Kowalewski (2014) has discussed on two possible mechanisms of luteolysis in canines. Considering the fact that there is an acute decline in progesterone concentration during pre-partum period, an active luteolytic mechanism could be present in pregnant animals whereas a passive apoptotic mechanism leads to luteolysis in non-pregnant dogs. Kowalewski *et al.* (2009) has described a significant drop in luteal steroidogenic acute regulatory protein (STAR) expression along with elevated PGF2α concentrations. These endogenous pre-partum prostaglandins originate in the up-regulated expression of PGFS2 receptors within the utero-placental unit (Luz *et al*., 2006; Kowalewski, 2014). Kowalewski (2014) also associated increased expression of endothelial receptors type A, a vasoconstrictive factor, at the cellular levels localised in the luteal capillary endothelium in active luteolysis cascade in pre-partum luteolysis. Hoffmann *et al.* (1992) has described that ovarian cyclicity is maintained even after hysterectomy in dogs justifying the statement that there is an inherent control mechanism regulating the physiological lifespan of corpora lutea in both pregnant and non-pregnant female dogs. In canines, there is slow luteal regression over a period of 1-2 months with

no evident decrease in LH and Prolactin receptors on the luteal cells (Fernandes *et al.*, 1987; Concannon, 2010; Kowalewski, 2014). Kowalewski *et al.* (2009) suggested that during mid-luteal phase, STAR expression decreases and endoplasmic reticulum of luteal cells exhibited whirl-like structures on the periphery followed by clear signs of structural regression by day 45 after ovulation. There is evidence of increasing intracellular distances, collagen fibres, connective tissues, lipid droplets in cytoplasm and decrease in capillary density, all suggestive of cellular degeneration. However, Kowalewski (2014) noted absence of active luteolytic principle in corpora lutea of non-pregnant dogs. So evidence focuses on a low but significant apoptotic activity leading to luteolysis (Luz *et al.*, 2006; Concannon, 2010).

2.4. Pseudopregnancy:

Pseudocyesis (PSC), pseudopregnancy, false pregnancy, copycat pregnancy, phantom pregnancy or nervous lactation is a physiological syndrome, characterized by clinical signs similar to a post-partum period in a non-pregnant female dog at the end of diestrus (Feldman and Nelson, 1996; Gobello *et al.*, 2001a). Allen (1986) said that the condition was the luteal phase of non-fertile ovulatory cycle in female dogs and the signs were actually similar to those of the post-partum period. According to Voith (1980) and Jochle (1997) pseudopregnancy could have had an evolutionary importance when non-pregnant female of canidae family used to nurse other females' litter within a pack. Thangamani *et al.* (2018) reviewed that both pregnant and non-pregnant female dogs could have similar signs but the intensity of signs varies between individuals.

2.4.1. Prevalence

Johnston (1980) had mentioned pseudopregnancy as a frequent finding in dogs with a prevalence of 50-75%. Castex and Gobello (2002) studied the prevalence of the condition in the non-descript and pure bred dogs presented to their clinic and recorded a prevalence of 50-75% in accordance with earlier reports. Study on individual breed population revealed variations from this prevalence rate. Concannon *et al.* (2009) mentioned that incidence of pseudopregnancy in Beagle breeds were less than 5%. The incidence rate is therefore not well documented and can be between 2-20% when the mild signs are not concluded (Concannon, 2011). This incidence rate of clinical pseudopregnancy may be influenced by age, breed, parity and environmental factors (Razzaque *et al.,* 2008). In canines, breeds with physiologically short luteal phase like German shepherds were reported to be more sensitive to expression of overt pseudopregnancy due to rapid fall in progesterone levels and associated increased sensitivity to progesterone (Gobello *et al.,* 2001c). Concannon *et al.* (2009) has mentioned that Beagles are less disposed to this condition and incidence in this breed was recorded to be less than 5%.

2.4.2. Aetiophysiology

Marshall and Halnan (1917) initially postulated overproduction of progesterone or abnormal persistence of corpora lutea as cause of pseudopregnancy in female dogs. However, it was then described that luteal function is almost identical in pregnant and non-pregnant dogs. So occurrence could be a result of increased concentrations of prolactin or an increased sensitivity to prolactin induced by a more rapid than normal decline of progesterone levels in the late luteal phase (Smith and McDonald, 1974; Graf *et*

al., 1977; Gerres *et al*., 1988; Concannon and Lein, 1989). This leads to non-pregnant dogs exhibiting signs of pregnancy usually at the end of diestrus (Gobello *et al.,* 2001a). Spaying or ovariectomy during the luteal phase could be the surgery induced cause of pseudopregnancy (Gobello *et al.,* 2001c; Thangamani *et al.,* 2018). Drastic hormonal changes due to PGF induced luteolysis or anti-progestin treatments that rapidly decline the serum progesterone level could also induce false pregnancy in some female dogs (Allen, 1986; Johnston, 1986; Gobello *et al.,* 2001b; Concannon, 2010). Despite all these causes even the normal hormonal changes is sufficient to cause pseudopregnancy in non-pregnant female dogs (Thangamani *et al.,* 2018).

2.4.3. Clinical Signs:

Concannon (1986) described that all non-pregnant female dogs in mid to late diestrus and between 6 to 20 weeks after estrus could be considered to be in physiological pseudopregnancy. The manifestations of pseudopregnancy was reported to include behavioural changes marked by restlessness, anorexia, decreased activity, aggression, licking of abdomen and maternal behaviour such as nesting, mothering inanimate objects and adopting puppies of other female dogs. The clinical signs may also include physical signs like weight gain, abdominal distension, mammary enlargement, lactation and sometimes even abdominal contractions mimicking whelping (Mialot *et al*., 1984; Feldman and Nelson, 1996). These signs usually appear in non-pregnant female dogs at the end of diestrus (Gobello *et al.,* 2001a). Lactation in pseudopregnant dogs is often encouraged by self-nursing or by adoption of unrelated neonates. This lactation apparently results from the development of not only intra-acinar but also intra canalicular mammary secretion in predisposed female dogs (Johnston, 1980; Razzaque *et al*., 2008). The abdominal distension in non-pregnant dogs could be due to relaxation of abdominal

muscles. Weight gain associated with pseudopregnancy is also attributed to the elevated growth hormone levels in the luteal phase in dogs (Kooistra and Okkens, 2002; Concannon *et al.,* 2009).

Vomiting, anorexia, diarrhoea, polyuria, polydipsia and polyphagia have also been reported. (Johnston, 1980; Gobello *et al*., 2001a; Razzaque *et al*., 2008; Thangamani *et al.,* 2018). This effect is attributed to increased growth hormones during the progesterone dominant luteal phase of canine estrous cycle which causes insulin resistance (Kooistra and Okkens, 2002; Concannon *et al.,* 2009). Insulin resistance causes a condition similar to pregnancy diabetes in non-pregnant dogs and causes these clinical signs. Complications of false pregnancy, like mastitis and mammary dermatitis were not reported as common findings. The wide variation in the intensity of clinical signs in different female dogs could be attributed to prolactin bioactivity (Gobello *et al*., 2001c).

2.4.4. Diagnosis:

Pseudopregnancy is diagnosed based on the presence and extend of clinical signs. Pregnancy must be ruled out by abdominal palpation, radiography or ultrasonography in all female dogs even without history of mating. Mismating or misalliances in female dogs should not be ruled out as history may not reveal correct breeding history. Other diseases like pyometra or recent pregnancy and abortion must also be ruled out. Pseudopregnancy may coexist with other diseases of reproductive system and should not be ignored (Gobello *et al*., 2001a; Razzaque *et al*., 2008).

2.4.5. Treatment:

In female dogs, when the signs are exacerbated to a level of clinical significance, there will be need for treatment. If complications don’t appear, the signs of

pseudopregnancy were reported to subside within 2-4 weeks. Susceptible female dogs were associated with high recurrence rates in successive estrous cycles. (Johnston, 1986; Gobello *et al*., 2001c; Razzaque *et al*., 2008)

Pseudopregnancy is a self-limiting physiological syndrome, so mild cases need no treatment. Licking, milking, or hot or cold packing the glands were all reported as important stimuli for lactation and therefore need to be avoided. Licking or self-nursing could be avoided by use of Elizabethan collars. Water removal for 5-7 nights will force water conservation and also helps termination of lactation (Mialot *et al.*, 1984; Feldman and Nelson, 1996). To counteract severe behavioural signs use of non-phenothiazine tranquilizers was reported (Voith, 1983). Sex steroids were also used in the treatment of pseudopregnancy as they exert a negative feedback in high doses on the hypothalamic-pituitary axis thereby inhibiting prolactin secretion (Johnston, 1980; Allen, 1986). Concannon, (2011) suggested that progestin administration should be avoided as subsequent progestin withdrawal could result in reoccurrence of symptoms.

Inhibition of prolactin secretion by ergot derivatives was found to be effective in treating pseudopregnancy (Allen, 1986). The most common compounds used to inhibit prolactin secretion are bromocriptine and cabergoline which have a direct action on dopamine receptors of the anterior pituitary gland, and metergoline which is a serotonin antagonist with a dopaminergic effect at high doses could be observed (Jochle *et al*., 1989). Concannon *et al.,* (1987) studied the suppression of luteal function in dogs by bromocriptine that caused a significant decrease in progesterone suggesting that normal luteal function in dogs is dependent upon endogenous levels of prolactin throughout luteal phase. Gobello *et al.,* (2001c) described that the use of bromocriptine and cabergolin can

significantly reduce the prolactin levels than the placebo group however, between the bromocriptine and cabergoline group did not show any significant difference. Use of bromocriptine @10-100µg/Kg BW for 10-14 days and cabergoline @5 µg/Kg BW for 5-10 days were recommended for treatment of pseudopregnancy in dogs. Predisposed female dogs not intended for breeding should be spayed, as ovariectomy is only permanent measure for the problem of pseudopregnancy (Johnston, 1986; Gobello *et al.,* 2001a; Razzaque *et al*., 2008; Thangamani *et al.,* 2018).

2.4.5.1 Bromocriptine

Ergot alkaloids have long been found to have dopaminic action. Dopamine is a natural antagonist in prolactin synthesis. Bromocriptine, a synthetic ergot alkaloid was reported to inhibit prolactin secretion in many species like rat, sheep, humans and dogs (Allen, 1986). A dose rate of 0.1 to 1mg/Kg BW used for 10-14 days is reported to have a significant effect in reducing the clinical signs of pseudopregnancy (Gobello *et al.,* 2001a; Concannon, 2011). Because of its short half-life, the drug must be used twice daily to get clinically significant result (Razzaque *et al.,* 2008). Administration of bromocriptine orally has been associated with vomiting around 1.5 to 2 hrs after ingestion of the tablets. This vomiting can be controlled by using anti-emetic tablets. The side effects can also be reduced by administration of the tablets along with food or use of increasing doses of the tablet (Mialot *et al.,* 1984). Mialot *et al.* (1981) and Janssens (1986) have reported more than 80% successful rate in the use of bromocriptine as an anti-prolactin drug at dose rate of 10µg/ Kg BW twice daily for 10 days. A similar effect on the use of these anti-prolactin drugs was reported by Arbeiter *et al.* (1988) and Jochle *et al.* (1989).

2.4.5.2. Cabergoline

Cabergoline is also an ergot derivative with agonistic action on dopamine receptors. Mechanism of action is similar to bromocriptine but cabergoline is recorded to have a higher level of activity, superior specificity and longer duration of action than bromocriptine (Gobello *et al.,* 2001b). Cabergoline is generally recommended at a dose rate of 5µg/Kg BW for 5-10 days. The lower side effects associated with cabergoline was recorded to be due to its inability to cross the blood-brain barrier (Jochle *et al.,* 1987; Arbeiter *et al.,* 1988; Gobello *et al.,* 2001b). Harvey *et al.* (1997) studied the effect of cabergoline as anti-prolactin drugs. He has reported a 90% success rate with cabergoline at the dose rate of 5µg/ Kg BW in 5 days. Dopamine agonists are recommended for treatment of pseudopregnancy in different reports (Allen, 1986; Razzaque *et al.,* 2008; Castex and Gobello, 2002; Concannon, 2011). Gobello *et al.* (2001b) have also reported that there were no significant differences in the effectiveness between bromocriptine and cabergoline treatment for physical signs of pseudopregnancy.

2.4.5.3. Ondansetrone

Ondansetrone is a centrally acting antiemetic. It belongs to the class of 5-HT3 receptor antagonists. It exerts its effect by antagonising the 5-HT3 receptor on the vagal nerve and centrally in chemoreceptor trigger zone. Vomiting seen during treatment of pseudopregnancy using dopamine agonists needs to be managed by use of anti-emetics which do not block the central dopamine receptors. Drugs like metoclopramides can interfere with the results as they have action on the dopamine receptors (Gobello *et al.,* 2001a)

MATERIALS AND METHODS

III. MATERIAL AND METHODS

The present study was conducted on female dogs presented for pregnancy diagnosis to the Department of Veterinary Gynaecology and Obstetrics, Veterinary College, Bengaluru and other private clinics in and around Hebbal for a period of 8 months from August 2017 to March 2018. The apparently healthy non-pregnant dogs with clinical signs of pseudopregnancy and around 30-90 days from their last estrus period were considered for the present study.

3.1 Experimental design

Of the 282 animals presented for pregnancy diagnosis with or without history of mating, all the non-pregnant dogs with behavioural and clinical signs of pseudopregnancy (51/144) were selected for the study. The dogs that were apparently healthy based on clinical history, physical and clinical examination findings and around 30-90 days from last estrus were considered for the study.

Dogs with overt pseudopregnancy were randomly categorised into three treatment groups with 10 animals in each group and a control group of 10 animals.

3.2. History

A detailed history including breed, age, parity, interval from previous estrus to the date of presentation , breeding history, history of pseudopregnancy in previous cycle were recorded to study the influence of various factors on the prevalence of overt pseudopregnancy.

3.3. Pregnancy Diagnosis

All female dogs presented for pregnancy diagnosis with or without history of mating were subjected to pregnancy diagnosis. The female dogs were initially subjected to abdominal palpation of the flank and lower abdomen. In pregnant dogs gestational sacs were palpated as tense conceptual swellings (6-30 mm in diameter) within the uterine cornua. This helped in an accurate diagnosis between 24-35 days post breeding.

Real time B-mode ultrasound scanning Aloka Prosound α6, Japan was used to confirm pregnancy and to rule out uterine pathologies like pyometra which is also seen during the diestral stage of canine estrous cycle. Animals found to be pregnant or with uterine pathologies were excluded from the study.

3.3. Prevalence of pseudopregnancy

The prevalence of pseudopregnancy was estimated by using the formula

$$\text{Prevalence of pseudopregnancy (\%)} = \frac{\text{Number of pseudopregnancy cases recorded during August 2017 to March 2018}}{\text{Total number of non-pregnant dogs presented during the same period}} \times 100$$

3.4. Physical Examination

The selected animals were subjected for physical examination of integument, colour of visible mucus membrane, rectal temperature, pulse and respiration. Female dogs in poor physical health, congenital or acquired abnormality of vulva or vagina as well as

concurrent pyometra and those with uncertain history regarding the exact date of onset of proestral bleeding were excluded from the present study.

The owners were enquired regarding the presence or absence of behavioural signs, physical changes, maternal behaviour, clinical signs and complications associated with pseudopregnancy observed in their pets and recorded in the questionnaire (Appendix 1).

3.5. Blood Collection

Blood samples were collected from dogs with overt pseudopregnancy on the day of presentation to the clinic to evaluate the serum progesterone levels. Blood samples were collected by venipuncture of the cephalic or lateral saphenous vein into a sterile serum collection vacutainer using a sterile scalp vein set connected to a 2 ml syringe. The collected blood samples were kept at room temperature for one hour for separation of serum. The samples were then centrifuged at 3000 rpm for 10 minutes. A micro pipette was used to separate serum and the separated serum were made into aliquots and stored at -20ºC until analysed.

3.6. Determination of serum progesterone concentration:

The serum progesterone levels were estimated using chemiluminescence method.

3.3. Treatment

The dogs presented with clinical signs of pseudopregnancy were grouped randomly into three treatment groups of 10 animals each and a control group of 10 female dogs.

3.3.1. Group I: Treatment using cabergoline tablets

The animals in this group were treated with cabergoline (Cabgolin® 0.25mg tablets) at the dose rate of 5µg/Kg BW once daily orally for 7 days. The duration of treatment was adjusted between 5 to 10 days based on remission of clinical signs. The exhibition of side effects if any was also recorded.

3.3.2 Group II: Treatment using bromocriptine tablets

The animals in this group were treated with bromocriptine (Brom® 2.5 mg tablets) at the dose rate of 0.01 mg/Kg BW twice daily orally for 10 days. The duration of treatment was adjusted between 7 to 14 days based on remission of clinical signs. The exhibition of side effects if any was also recorded.

3.3.3. Group III: Treatment by managemental changes

The animals in this group were treated by adapting managemental changes to reduce clinical signs of pseudopregnancy. The owners were advised to withdraw water and food during night hours i.e. from 8 pm to 8 am and to apply Elizabethan collar to prevent self-nursing for 14 days. The duration of treatment was adjusted between 12 to 20 days based on remission of clinical signs.

3.3.4. Group IV: Control

10 animals were categorised into this group and the owners were advised not to give any treatment and allowed for natural remission of clinical signs. The duration taken for complete remission was recorded.

3.4. Statistical analysis:

The data generated was tabulated and the mean with standard error was calculated for all parameters. The data generated were analyzed using Chi-square test for study on effect of predisposing factors and one way ANOVA with Tukey's Multiple Comparison test to analyze the effect of treatment on the number of days needed for complete remission of clinical signs using Graph Pad Prism 5.00. The statistical analysis was done as per the procedure described by Snedecor and Cochran (1996).

RESULTS

IV. RESULTS

The aim of present study was to observe and record the prevalence of overt pseudopregnancy, factors that predisposes female dogs to pseudopregnancy; various clinical signs exhibited during overt pseudopregnancy and the comparative efficiency of different treatment protocols. The non-pregnant dogs presented to the Department of Veterinary Gynaecology and Obstetrics, Hebbal, Bengaluru, were used for this study.

4.1. Prevalence of Pseudopregnancy

The present study was conducted for eight months from August 2017 to March 2018. Of the 282 dogs presented for pregnancy diagnosis during the period of study, 144 were found negative for pregnancy. Among the non-pregnant dogs, 51 animals were diagnosed with overt pseudopregnancy. Thus the prevalence of overt pseudopregnancy was recorded as 35.41% (Table 1).

4.2. Factors influencing pseudopregnancy

4.2.1. Age

The age of dogs in the present study ranged from 11 months to 14 years. The female dogs were categorised into four different age groups as less than 2 years, 3-5 years, 6-8 years and above 8 years. The mean age group of the female dogs that exhibited pseudopregnancy were 3.566±0.36 years. Out of the 51 dogs with overt pseudopregnancy, 50% of them belonged to the age group of less than 2 years. The dogs aged between 2-5 years of age were of 36 %. Adult dogs between 5-8 years of age were 7% and those in age group above 8 years were 7% (Table 2 and Fig 1). The statistical analysis revealed that age has a significant effect in prevalence of overt pseudopregnancy ($P<0.05$).

4.2.2. Breed

In the present study, the overt signs of pseudopregnancy were observed in 15 different breeds like Labrador retriever (29.42%), German shepherd (7.84%), Golden Retriever (13.73%), Pug (11.76%), Daschund (1.96%), Doberman (1.96%), Pit Bull (1.96%), Great Dane (1.96%), St. Bernard (3.92%), Pomeranian (3.92%), Rottweiler (1.96%), Spitz (1.96%), Minpin (1.96%), Boxer (1.96%) and non-descript (13.73%) (Table 4). The dogs were grouped as small dogs breeds (<20Kg BW), medium dog breeds (20-40 Kg BW) and large dog breeds (>40Kg BW) based on their body weight to study the effect on prevalence of overt pseudopregnancy. Among the 51 dogs with overt pseudopregnancy, 56.86% were medium sized breeds, 37.26% small sized breeds and 5.88% dogs were large sized breeds (Table 3 and fig 2). The statistical analysis revealed that breed had no significant effect on prevalence of overt pseudopregnancy ($P>0.05$).

4.2.3. Parity

In the present study, female dogs were grouped as nulliparous, primiparous and pluriparous based on parity. Out of the 51 dogs with overt pseudopregnancy 57% were nulliparous, 25% were primiparous and 18% were pluriparous (Table 5 and fig 3). The statistical analysis revealed that parity had a significant effect in prevalence of overt pseudopregnancy ($P<0.05$).

4.2.4. Days from last estrus

The number of days from last estrus was recorded on the day the dog was presented to the clinic with signs of pseudopregnancy. The number of days from last estrus to the day the dogs were presented ranged from 30-90 days with an average of 63.70 ± 2.25 days. Out of the 51 dogs with overt pseudopregnancy highest prevalence of 70.58% was observed

after 60 days from last estrus. Lower prevalence was observed at a rate of 13.73% between 30-50 days and 13.73% between 50-60 days from last estrus.

4.2.5. Previous history of pseudopregnancy

In the present study only five out of 51 dogs (9.8%) with overt pseudopregnancy had history of pseudopregnancy in previous cycles.

4.3. Serum progesterone concentrations (ng/ml)

In the present study, serum progesterone concentrations of all dogs with overt pseudopregnancy were evaluated on the day of presentation to the clinic. The serum progesterone levels ranged from 0.012 to 2.76 ng/ml with an average value of 0.95 ± 0.015 ng/ml (Table 7). Out of the 51 dogs with overt pseudopregnancy, 56.86% dogs had serum progesterone values less than 1 ng/ml. 25.5 % dogs had serum progesterone values between 1-2 ng/ml and only 17.64% dogs had serum values above 2 ng/ml (Table 7 and Fig 4).

4.4. Signs exhibited during pseudopregnancy

The signs exhibited by the dogs during overt pseudopregnancy were recorded under different groups as behavioural signs, clinical signs, maternal behaviour, physical signs and complications of overt pseudopregnancy based on the questionnaire answered by the dog owners.

Behavioural changes studied among the 51 dogs with overt pseudopregnancy showed that 31.37% dogs were anxious, 39.21% dogs showed transient inappetance or anorexia, 13.72% dogs developed aggressiveness even towards owners, 27.45% had

hyperexitability, 49.01% dogs were restless, 33.33% dogs had whining, 52.94% dogs showed decreased activity and 58.82% dogs exhibited licking of abdomen (Table 6).

The clinical signs were less common and were exhibited by only less than 50% out of the 51 pseudopregnant dogs studied. Vomiting was exhibited by 23.52% of the dogs and only 1.96% dogs had diarrhoea associated with overt pseudopregnancy. Polydipsia was exhibited by 35.29% of dogs, 25.49% dogs showed polyuria and 17.64% had polyphagia (Table 6).

Maternal behaviours exhibited by the 51 dogs with pseudopregnancy were studied. Nesting was exhibited by 66.67% dogs and 50.98% of dogs showed mothering of inanimate objects like toys and foot wears. No dogs in the present study adopted orphaned or abandoned puppies (Table 6).

Physical changes were the most common symptoms showed by the pseudopregnant dogs. Out of the 51 dogs, mammary enlargement was observed in 96.08% dogs and was associated with secretions of which 56.8% were milk, 19.6% were serous and another 19.6% of partly serous secretions. Abdominal distension was observed in 49% of the dogs and 47% had weight gain after the last estrus. Mucoid vaginal discharge was observed in 9.8% dogs and 1.96% of the dogs exhibited abdominal contractions mimicking whelping (Table 6).

During the current study period, only 3.92% of the dogs exhibited complications like mastitis (1.96%) and mammary dermatitis (1.96%) among the 51 dogs with overt pseudopregnancy (Table 6).

4.5. Effect of treatment

4.5.1. Control Group

The animals in control group were given no treatment and all the dogs had complete recovery (100%) within 23.4 ± 1.25 days from the day of presentation to the clinic (Table 8). The dogs did not develop side effects or complications in the absence of treatment.

4.5.2. Treatment Group 1

Female dogs in this group were treated with cabergolin tablets. The average duration of recovery was recorded to be 6.4 ± 0.65 days (Table 8). Though 30% of the dogs (3/10) developed vomiting and anorexia in the first two days of treatment the signs were mild and controlled by ondansetron tablets. The side effects did not demand the cessation of treatment in any animal of this group.

4.5.3. Treatment Group 2

Female dogs in this group were treated with bromocriptine tablets. The average duration of recovery was recorded to be 9.5 ± 0.73 days (Table 8). Though 50% of the dogs (5/10) developed vomiting and anorexia in the first two days of treatment the signs were controlled by ondansetron tablets. The side effects did not demand the cessation of treatment in any animal of this group.

4.5.4. Treatment Group 3

Female dogs with pseudopregnancy in this group were treated by adapting managemental changes. The average duration of recovery was recorded to be 15 ± 0.77 days (Table 8). The dogs did not develop side effects or complications.

4.5.5. Comparison between groups

The effect of treatment on the number of days required for complete remission of clinical signs was compared using one way ANOVA and Tukey's multiple comparison tests. There was no significant difference between group 1 and group 2; however there was a statistically significant difference between group 1 and group 3. Statistically significant difference existed between group 2 and group 3. Group 1, 2 and 3 differed significantly from the control group (Table 8).

Table 1. Prevalence of pseudopregnancy in female dogs.

No. of female dogs presented for pregnancy diagnosis from August 2017 to March 2018	282
No. of female dogs diagnosed positive for pregnancy	138
No. of female dogs diagnosed negative for pregnancy	144
No. of females with overt signs of pseudopregnancy	51
Prevalence of pseudopregnancy (%)	35.41

Table 2. Effect of age on exhibition of pseudopregnancy in dogs (n=51)

Age group (in years)	No. of dogs with overt pseudopregnancy	No. of non-pregnant dogs without overt pseudopregnancy	Percentage Of overt pseudopregnancy	Mean ± SE
<2 yrs.	25	17	49.02	3.56±0.36
2-5 yrs.	18	14	35.30	
5-8 yrs.	4	35	7.84	
>8 yrs.	4	27	7.84	
Total	51	93	100	
$\chi 2$ 3df= 34.41*				

*Result is statistically significant (P<0.05)

Table 3. Effect of breed size on exhibition of pseudopregnancy in dogs (n=51)

Breed size	No. of dogs with overt pseudopregnancy	No. of non-pregnant dogs without overt pseudopregnancy	Percentage of overt pseudopregnancy
Small dog breeds	19	29	37.26
Medium dog breeds	29	59	56.86
Large dog breeds	3	5	5.88
Total	51	93	100
$\chi 2$ 2df= 0.6127**			

** Result is not statistically significant (P>0.05)

Table 4. Effect of breed type on exhibition of pseudopregnancy in dogs (n=51)

Breed	No. of dogs with overt pseudopregnancy	No. of non-pregnant dogs	Percentage of dogs with overt pseudopregnancy
Labrador Retriever	15	19	29.42
Golden Retriever	7	7	13.73
Non-Descript	7	5	13.73
German Shepherd	4	14	7.84
Pug	6	16	11.76
St. Bernard	2	2	3.92
Pomeranian	2	5	3.92
Other breeds	8	25	15.68
	51	93	100
$\chi 2$ 7df= 9.507 **			

** Result is not statistically significant (P>0.05)

Table 5. Effect of parity on exhibition of pseudopregnancy in dogs (n=51)

Parity	No. of dogs with overt pseudopregnancy	No. of non-pregnant dogs	Percentage of dogs with overt pseudopregnancy
Nulliparous	29	20	56.87
Primiparous	13	32	25.49
Pluriparous	9	41	17.64
Total	51	93	100
$\chi 2$ 2df= 19.57*			

***Result is statistically significant (P<0.05)

Table 6. Different signs exhibited of pseudopregnancy in dogs (n=51)

Signs exhibited		No. of dogs exhibiting these signs	Percentage (%)
Behavioural signs			
Anxiety		16	31.37
Anorexia		20	39.21
Aggressiveness		7	13.72
Hyperexitability		14	27.45
Restlessness		25	49.01
Whining		17	33.33
Decreased activity		27	52.94
Licking of abdomen		30	58.82
Clinical signs			
Vomiting		12	23.52
Diarrhoea		1	1.96
Polyuria		13	25.49
Polydipsia		18	35.29
Polyphagia		9	17.64
Maternal behaviour			
Nesting		34	66.67
Mothering toys/foot wears/other objects		26	50.98
Adopting puppies		0	0
Physical signs			
Abdominal distension		25	49.01
Weight gain		24	47.05
Mammary enlargement		49	96.08
Milk secretion	Serous	10	19.6
	Partly serous	10	19.6
	Milk	29	56.8
Abdominal contractions		1	1.96
Vaginal discharge		5	9.8
Complications			
Mastitis		1	1.96
Mammary dermatitis		1	1.96

Table 7. Serum progesterone concentrations in dogs on the day of presentation to the clinics (n=51).

Serum progesterone concentration (ng/ml)	No. of dogs	Percentage
<1ng/ml	29	56.86
1-2ng/ml	13	25.5
>2ng/ml	9	17.64
Total	51	100

Table 8. Effect of different treatments on complete remission of clinical signs (n=40).

Treatment groups	**Average number of days for recovery**	**Number of dogs exhibiting side effects**
GROUP 1 (n=10)	6.4 ± 0.65^{a}	3
GROUP 2 (n=10)	9.5 ± 0.73^{a}	5
GROUP 3 (n=10)	15 ± 0.77^{b}	0
CONTROL (n=10)	23.4 ± 1.25^{c}	0

Values bearing different superscripts in column differ significantly ($P<0.05$)

Fig 1. Effect of age on exhibition of pseudopregnancy in dogs (n=51).

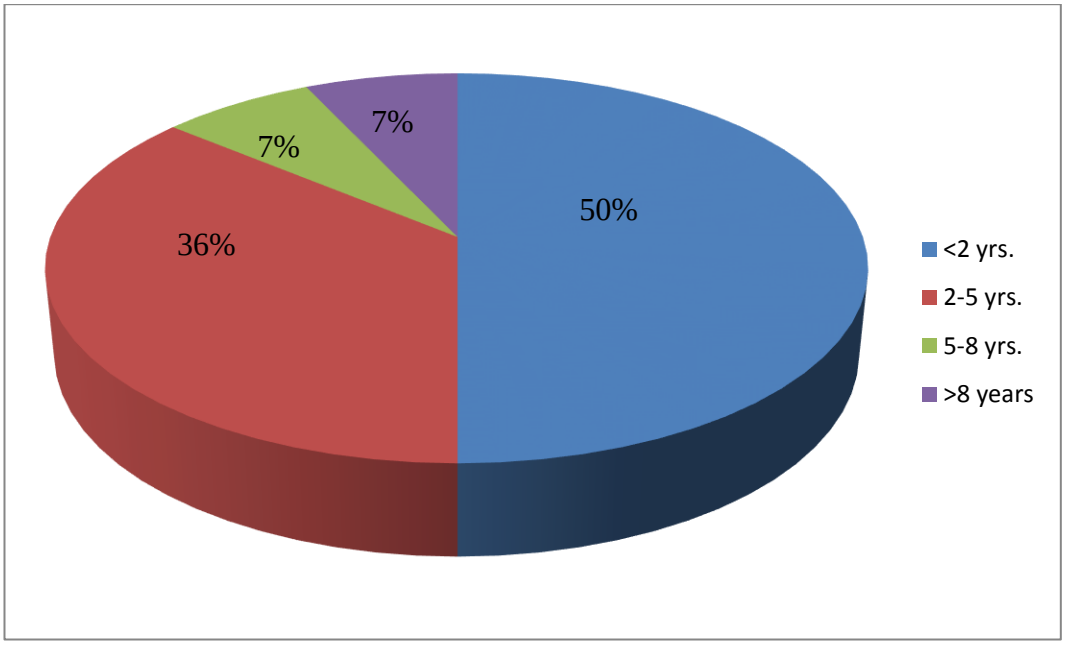


Fig 2. Effect of breed size on exhibition of pseudopregnancy (n=51)

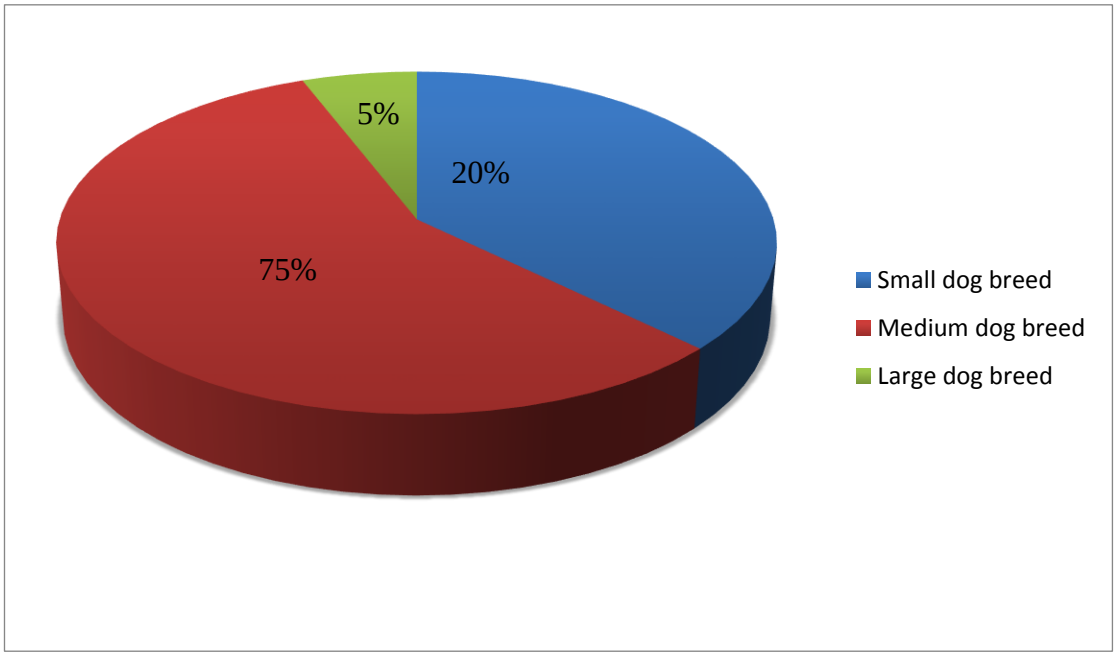


Fig 3. Effect of parity on exhibition of pseudopregnancy in dogs (n=51).

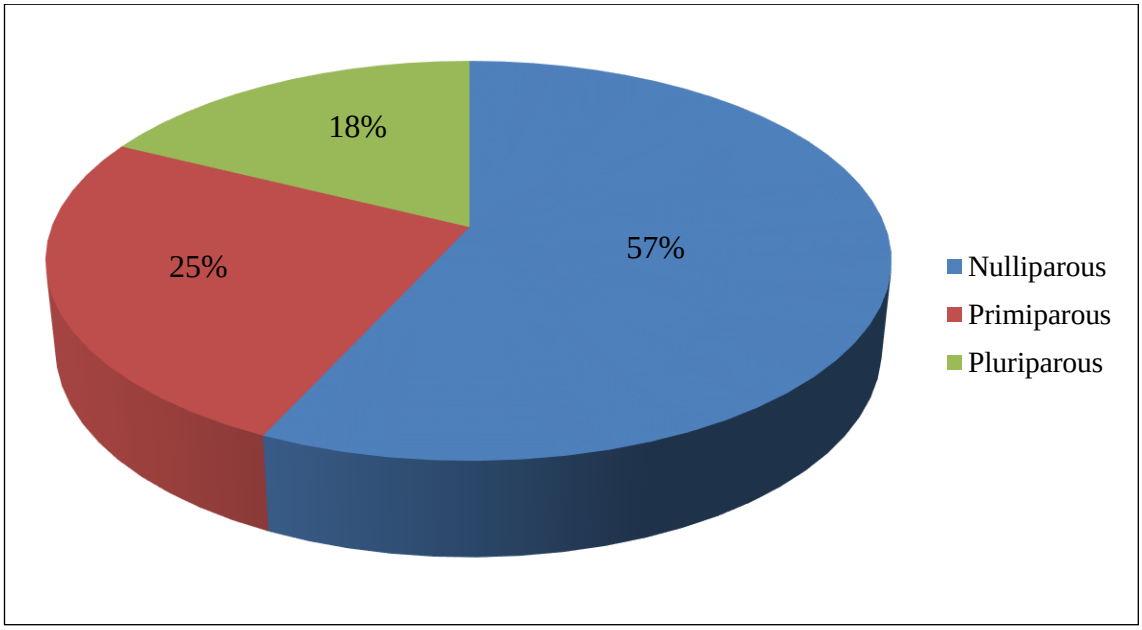
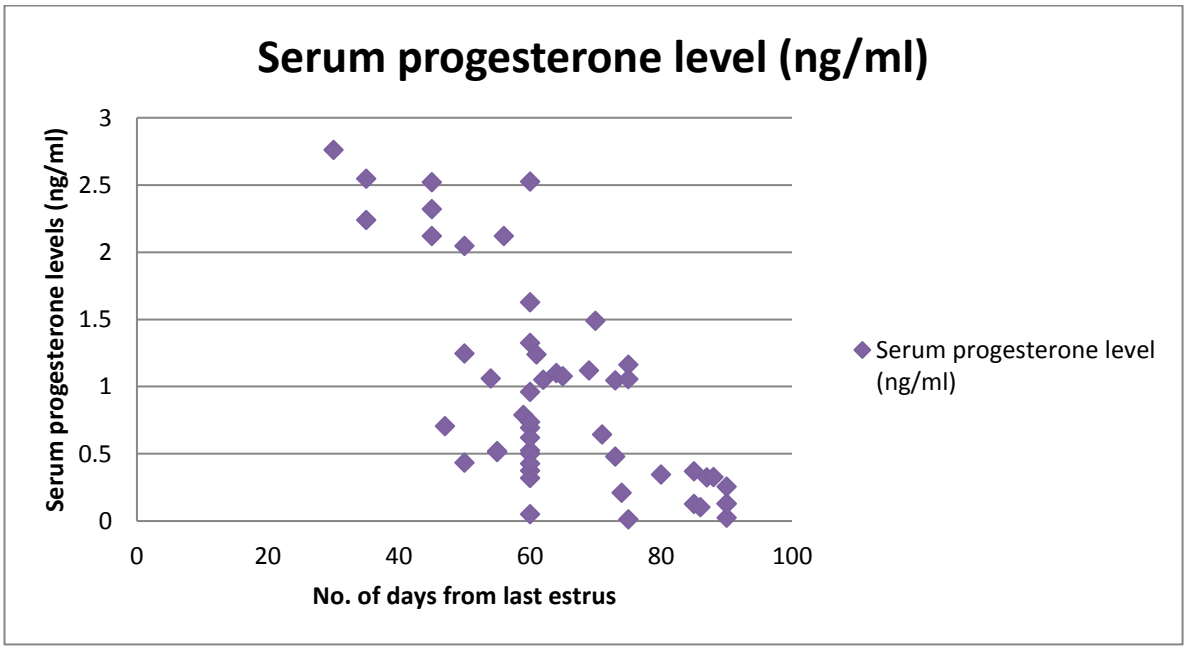


Fig 4. Days from last estrus and serum progesterone concentration (ng/ml)



DISCUSSION

V. DISCUSSION

Canine estrous cycle and the associated mechanisms are unique and have demanded extensive research for ages. Researches are mostly focussed on studying the phenomenon associated with ovulation, predicting fertile period, determination of age of gestation and mechanisms of luteolysis. Even after rigorous research these fields still hold mysteries. Pseudopregnancy, a physiological state where the cycling female dog shows signs mimicking last stages of pregnancy or more commonly post-partum period is a mystery on its own (Allen 1986; Gobello *et al.,* 2001a; Thangamani *et al.,* 2018). The clinical signs are exhibited to varying degrees with wide individual variations. As it is a self-limiting condition, researches have not widely been focussed in identifying the predisposing factors behind the varying degrees of exhibition of signs in dogs with a relatively common endocrinological profile. In some dogs where signs are exacerbated to levels of clinical significance, there is need of treatment and different protocols have been studied.

5.1. Prevalence of pseudopregnancy

The prevalence rate of overt pseudopregnancy was recorded to be 35.41% among the non-pregnant dogs presented during the study period. Different researches have reported different rates of exhibition of overt pseudopregnancy in dogs. Pseudopregnancy has been considered a frequent finding in female dogs with a prevalence of 50-75% (Johnston, 1980; Razzaque *et al.,* 2008; Gobello *et al.,* 2001a; Castex and Gobello, 2002). However, Concannon *et al.* (2009) has reported that the incidence rate is not well documented and can be 5-20% when the mild signs are not included. The findings in the

current study fall between the observations recorded. This could be because of the difference in breeds or age group of dogs studied.

5.2. Factors influencing pseudopregnancy

5.2.1. Age

Out of the 51 pseudopregnant dogs, 50% belonged to the age group of less than two years. The pseudopregnant dogs reported fell into a wide range of age from 11 months to 14 years indicating that the condition can be manifested at any age. However, the mean age was 3.57±0.36 years with highest prevalence among young dogs. Prevalence rate was low in age group of 5-8 years (7%) and more than 8 years (7%). The dogs aged between 2-5 years were of 36 % among the pseudopregnant dogs (Table 2 and fig 1). Statistical analysis revealed that age had a significant effect in prevalence of overt pseudopregnancy ($P<0.05$). Razzaque *et al.* (2008) has reported that age may be a factor influencing the incidence of pseudopregnancy in female dogs but even after extensively going through different research articles, no record on which age group is more susceptible could be found. This observation could suggest a genetic predisposition which will be exhibited as early as the first non-fertile cycle in pre-disposed female dogs but could also be exhibited in later cycles. The underlying cause leading to increased prevalence of the condition in young dogs could be the difference in the amount of luteal tissue formed and the rate of progesterone decline. Marinelli *et al.* (2009) reported that age of the dog can affect the amount of luteal tissue formed. Young dogs have less luteal tissue than older dogs and hence amount of progesterone produced will be less. The mechanism of luteolysis in a non-pregnant dog is by progressive passive apoptosis (Hoffmann *et al.*, 2004; Kowalewski, 2014). So the immature reproductive system and reduced luteal tissue in young dogs could

be the reason of rapid fall in progesterone values and subsequent increased sensitivity to prolactin. This could be a reason why more number of young dogs exhibited overt pseudopregnancy in this current study. The varied frequency with which dogs of different age groups were presented to the clinics could also be a reason for such a result.

5.2.2. Breed

In this study, out of the 51 pseudopregnant dogs, 56.86 % of the dogs were medium sized dog breeds, 37.26% were small sized dog breeds and 5.88% were large sized dog breeds (Table 3 and Fig 2). Of these 29.42% were Labrador retrievers, 13.73% were Golden Retrievers, 11.76% were Pugs, 13.73% were non-descript, 7.48% were German Shepherds, 3.92% were St. Bernard, 3.92% were Pomeranian and 15.68% were other breeds including Pit Bull, Minpin, Great Dane, Daschund, Rottweiler, Boxer, Spitz and Doberman with 1.96% each (Table 4). The statistical analysis revealed that breed had no significant effect on prevalence of overt pseudopregnancy ($P>0.05$). However, earlier work by Gobello *et al.* (2001a) had suggested that breed predisposition exists in exhibition of overt pseudopregnancy and could be linked to particular features of estrous cycle. Breeds with physiologically short luteal phase like German Shepherds could be more sensitive in expression of overt pseudopregnancy due to rapid fall in progesterone levels and associated increased sensitivity to progesterone (Gobello *et al.*, 2001c). The chance of particular breeds being predisposed to clinical pseudopregnancy has been also suggested by Razzaque *et al.* (2008). Concannon *et al.* (2009) mentioned that Beagles are less disposed to this condition and incidence in this breed was recorded to be less than 5%. The disparity of the current result with earlier reports could be due to the difference in frequency distribution with which different breeds were presented to the clinics during the study period. The geographical location of the study and the population of different breeds in the

area could be the reason why a particular breed was presented in more numbers to the clinic.

5.2.3. Parity

The effect of parity on exhibition of overt pseudopregnancy was studied and out of 51 pseudopregnant dogs, highest prevalence (57%) was observed in nulliparous dogs. the lowest prevalence of 18% in pluriparous animals and 25% prevalence in primiparous dogs were reported (Table 5 and fig 3). Razzaque *et al*. (2008) have suggested that parity could also affect the exhibition of clinical pseudopregnancy. Smaller litter size has been associated with young animals and primiparous dogs (Thomassen *et al.,* 2006). Reduced litter size is associated with reduced number of ovulations and in turn reduced luteal tissue (Concannon *et al.,* 1977; Marinelli *et al.,* 2008). The reduced luteal tissue is associated with early luteolysis and hence a rapid drop in progesterone during late diestrus stage. This is associated with increased sensitivity to prolactin and exhibition of pseudopregnancy in predisposed individuals (Gobello *et al.,* 2001c; Concannon, 2011). Comparative study details on the effect of parity on exhibition of pseudopregnancy could not be found for further discussion.

5.2.4. Days from last estrus

In the dogs studied, the number of days from last estrus to the day the dogs were presented ranged from 30-90 days with an average of 63.70 ± 2.25 days. The physiological two month luteal phase in dogs is considered the period of pseudopregnancy due to the similar endocrinology in pregnant and non-pregnant dogs. In the present study, out of the 51 dogs with overt pseudopregnancy highest prevalence of 70.58% was observed after 60 days from last estrus. Lower prevalence was observed at a rate of 13.73% between 30-50

days and 13.73% between 50-60 days from last estrus (Fig 4). Harvey *et al.* (1997) mentioned that the condition can appear at variable times, starting as early as 21 days to as late as 98 days and the varied range is associated with individual variations or genetic factors affecting the rate of progesterone decline. Later studies reported that clinical manifestation of pseudopregnancy could be observed in late luteal phase due to abrupt decline in progesterone usually seen 42-84 days after estrus (Gobello *et al.,* 2001a; Razzaque *et al.,* 2008). Concannon *et al.,* (2009) has reported that the luteal phase of dogs range from 55-75 days with an average of 65 days. The dogs studied were also within this range from last estrus. Marinelli *et al.* (2008) suggested that the circulating serum values of progesterone can be affected by the number of ovulation, body weight of the dam and age of the dam. This difference is attributed to the amount of corpora luteal tissue that develops in each case. Therefore, dogs with less number of ovulations can possibly show an earlier decline in serum progesterone level and associated clinical manifestation of pseudopregnancy in predisposed bitches. Further the delayed exhibition of pseudopregnancy after 60 days in majority of the dogs is suggestive that the condition is more mimicking the post-partum stage or a condition exhibited during the anestrus period in dogs.

5.2.5. Previous history of pseudopregnancy

In the present study only 9.8% of dogs presented had history of pseudopregnancy in the previous cycles. However, earlier reports have suggested a higher recurrence rate of the condition (Johnston, 1986; Feldman and Nelson, 1996; Harvey *et al.,* 1997; Razzaque *et al.,* 2008). But these reports did not mention the percentage of recurrence and suggested genetic predisposition as cause of recurrence. However, the current study showed a low rate of recurrence. Owners being sensitized about the self-limiting property of

pseudopregnancy could be a reason why the cases are rarely presented to clinics when this condition recurs.

5.3. Serum progesterone concentrations (ng/ml)

The serum progesterone values ranged from 0.012 ng/ml to 2.76 ng/ml with a mean value of 0.95±0.015 ng/ml (Table 7). Out of the 51 pseudopregnant dogs studied, 56.86% (29/51) of dogs had serum progesterone concentrations less than 1 ng/ml. 25.5 % (13/51) dogs had values between 1 to 2 ng/ml and only 17.64% (9/51) dogs had serum values above 2 ng/ml (Table 7 and Fig 4). Over production of progesterone or abnormal persistence of corpus luteum in normal cycling dogs were initially postulated to be the cause for pseudopregnancy (Marshall and Halnan, 1917). Further, studies proved that this hypothesis was wrong and the endocrinology was similar in non-pregnant dogs with both overt and covert pseudopregnancy (Smith and McDonald, 1974). However, the fall in progesterone concentration has a positive effect on prolactin release which is the hormone responsible for maternal instinct in mammals (Graf *et al.*, 1977; Allen, 1986). The condition is widely associated with late luteal phase but the signs mimic the period of lactation in a pregnant dog rather than the actual period of pregnancy. This period of lactation is actually the period of endocrinological anestrus. Ozyurtlu *et al.* (2006) has mentioned that the period of diestrus should be considered only as long as blood levels of progesterone are >1 ng/ml. In the present study, majority (56.86%) of dogs had serum progesterone concentration less than one ng/ml suggesting that the condition is expressed when the female dog enters into an endocrinological anestrus period rather than in the late luteal phase. Concannon (2011) suggested that the mean progesterone level were lower in pseudopregnant animals that facilitate increase prolactin secretion or increased prolactin sensitiveness of mammary tissue but no statistically significant difference in concentrations

of either progesterone or prolactin is recorded between overt and covertly pseudopregnant dogs. Similar to this observation 82.36% (42/51) dogs in this study had serum progesterone concentrations lower than 2ng/ml and 17.64% (9/51) dogs had values below 3 ng/ml. This further justifies that the condition is exhibited during endocrinological anestrus rather than late luteal phase. However, Gobello *et al.* (2001c) have mentioned that only predisposed female dog exhibit substantial rise in prolactin when there is an abrupt decrease in progesterone values.

5.4. Signs exhibited during pseudopregnancy

In the present study, the percentage of animals exhibiting different signs was recorded. Out of the 51 pseudopregnant dogs, majority (96.08%) of the dogs had well developed mammary enlargement with serous (19.6%), partly serous (19.6%) or milk (56.8%) secretions. However, 3.92% dogs had only mild mammary enlargement with no secretions but showed other signs like behavioural changes, maternal behaviours and physical changes like abdominal distension. Among the behavioural changes that were recorded, 58.82% dogs exhibited licking of abdomen, 52.94% dogs showed decreased activity, 49.01% dogs were restless, 39.21% dogs showed transient inappetance or anorexia, 33.33% dogs had whining, 31.37% dogs were anxious, 27.45% had hyperexitability and around 13.72% dogs developed aggressiveness even towards owners (Table 6). The behavioural changes could be associated with preparation of the dam to the anticipated whelping. The licking of abdomen or self-nursing could further stimulate lactation. The behavioural changes are attributed to increase in serum prolactin levels (Gobello *et al.*, 2001a)

The clinical signs were less common and were exhibited by only less than 50% of animals. Polydipsia was exhibited by 35.29% of dogs, 25.49% dogs showed polyuria, 23.52% had vomiting, 17.64% had polyphagia and only 1.96% had diarrhoea associated with pseudopregnancy (Table 6). These signs are associated with variations in the growth hormone and insulin levels during diestrus stage in female dogs. The changes are also seen in pregnant dogs and associated with gestational diabetes. This effect is attributed to increased growth hormones during the progesterone dominant luteal phase of canine estrous cycle which causes insulin resistance (Kooistra and Okkens, 2002; Concannon *et al.,* 2009). Such clinical signs associated with pseudopregnancy have also been reported by Jochle *et al.* (1986) and Razzaque *et al.* (2008).

Physical changes were the most common symptom with around 96.08% dogs having mammary enlargement. The next most observed sign was development of abdominal distension in 49.01% of dogs, whereas 47.05% had weight gain. Some dogs had mucoid vaginal discharges (9.8%) and 1.96% of the dogs exhibited abdominal contractions mimicking whelping (Table 6). The mammary enlargement is associated with sequential exposure of the mammary tissue to estrogen and progesterone. In clinical pseudopregnancy this further undergoes hyper-response including lactogenesis and lactopoesis (Concannon, 2011). The abdominal distension in non-pregnant dogs could be due to relaxation of abdominal muscles. Weight gain associate with pseudopregnancy is also attributed to the elevated growth hormone levels in the luteal phase in dogs (Kooistra and Okkens, 2002; Concannon *et al.,* 2009). Feldman and Nelson (1996) and Razzaque *et al.* (2008) have mentioned that along with the physical signs sometimes abdominal contractions mimicking parturition will also be exhibited by the dogs.

Other common signs included maternal behaviour are nesting behaviour in 66.67% of dogs and 50.98% of dogs and care for inanimate objects like toys or foot wear in 50.98% dogs. No dogs were reported to adopt unrelated puppies. This could be due to the reason that the study was conducted in housed dogs that were presented to the clinic and these dogs did not have access orphaned or abandoned puppies for them to adopt. These changes are associated with decrease in progesterone levels and associated rise in prolactin concentrations. Prolactin is the hormone responsible for maternal instincts in mammals. Progesterone has a negative feedback effect on the release of prolactin (Verstegan and Onclin, 1995).

The complications associated with pseudopregnancy like mastitis and mammary dermatitis were only 3.92%. Johnston (1986) and Gobello *et al.* (2001a) have mentioned these as rare and not common signs. The complications are caused by stagnation of milk leading to mastitis and excessive licking leading to mammary dermatitis. The signs exhibited by the dogs during overt pseudopregnancy vary between dogs and intensity of the exhibition of signs also varies between dogs (Feldman and Nelson, 1996; Johnston, 1980). However, the percentage of exhibition of these signs was not recorded in these studies.

The feature peculiar to clinical signs exhibited by animals during pseudopregnancy is that no sign is expressed by 100% of dogs. Presence of increased concentrations of target organ receptors or heightened peripheral sensitivity to prolactin could be the reason for varying intensities of clinical signs (Feldman and Nelson, 1996; Gobello *et al.,* 2001c). The observations were made based on the questionnaire answered by the owners' interpretations.

5.5. Effect of treatment

In the present study, group 1 animals were treated with cabergoline tablets at dose rate of 5µg/Kg BW for 5-10 days. The average duration of recovery in this group was 6.4± 0.65 days (Table 8). Though 30% of the dogs (3/10) developed vomiting and anorexia in the first two days of treatment the signs were mild and controlled by ondansetron tablets. The side effects did not demand the cessation of treatment in any animal of this group.

Female dogs in group 2 were treated with bromocriptine tablets. The average duration of recovery was recorded to be 9.5± 0.73 days (Table 8). Though 50% of the dogs (5/10) developed vomiting and anorexia in the first two days of treatment the signs were controlled by ondansetron tablets. The side effects did not demand the cessation of treatment in any animal of this group.

Both treatment groups showed 100% response but the effect of treatment was not statistically different between the two groups. Harvey *et al.* (1997) studied the effect of cabergoline as anti-prolactin drugs. He has reported 90% success rate with cabergoline at the dose rate of 5µg/ Kg BW in 5 days. Mialot *et al.* (1981) and Janssens (1986) have reported more than 80% success rate with the use of bromocriptine as anti-prolactin drug at dose rate of 10µg/ Kg BW twice daily for 10 days. A similar effect on the use of these anti-prolactin drugs was also reported by Arbeiter *et al.* (1988) and Jochle *et al.* (1989). Dopamine agonists are recommended for treatment of pseudopregnancy in different reports (Allen, 1986; Razzaque *et al.*, 2008; Castex and Gobello, 2002; Concannon, 2011). Gobello *et al.* (2001b) has also reported that there was no significant difference in the effectiveness of bromocriptine and cabergoline in treating the physical signs of pseudopregnancy. A similar result was obtained in the current study also. However, use of

bromocriptine or cabergoline has a significant advantage over conservative treatment practises. Cabergoline is reported to have higher activity and milder side effects than bromocriptine due to its more specific action and its ability to cross blood brain barrier (Arbeiter *et al.,* 1988; Harvey *et al.,* 1997; Gobello *et al.,* 2001b; Razzaque *et al.,* 2008). Though pseudopregnancy is a self-limiting disease, female dogs with exacerbated clinical signs demand treatment and dopamine agonists can be used to treat the condition without severe side effects (Concannon, 2011). 100% response was obtained with treatment using cabergoline and bromocriptine but the number of days of treatment may need to be adjusted based on the individual animal.

In this study, animals in group 3 were advised managemental changes like withdrawal of food and water during night hours (8pm to 8am) for 14-20 days and application of Elizabethan collar. The average duration of recovery was recorded to be 15± 0.77 days compared to an average of 23.4 ± 1.25 days when no treatment was practised (Table 8). Managemental changes also produced a statistically significant effect than the control group but effect was less than the use of dopamine agonists. In early times, conservative therapy included bathing and emptying of the mammary glands and administration of tranquilizers and diuretics (Mialot and Bohnert, 1980). Licking, milking and hot or cold application on mammary glands were later found to be stimulants for lactation and were advised to be avoided. Mialot *et al.* (1984) and Feldman and Nelson (1996) have recommended withdrawal of water for 5-7 nights to bring down clinical signs of pseudopregnancy by forcing fluid conservation and thereby reducing lactation. This method was used in the current study and it produced good response in the animals under treatment. Gobello *et al.* (2001a) have suggested the discouraging of maternal behaviour and use of Elizabethan collars to prevent self-nursing effectively and in reducing the

clinical signs of pseudopregnancy. This method is also reported to have significant advantage as self-nursing itself can act as stimulus for lactation. So when the signs are relatively mild and veterinary aid is difficult such managemental changes can be effectively used to reduce the clinical signs caused by pseudopregnancy.

It is concluded that even though pseudopregnancy is a self- limiting condition, the use of dopamine agonists like cabergoline or bromocriptine is safe and effective in complete remission of clinical signs of pseudopregnancy within a short duration of time. In the absence of veterinary aid or in mild cases, managemental changes can also be followed to reduce the behavioural changes associated with pseudopregnancy.

SUMMARY

VII. SUMMARY

The present study was conducted in the non-pregnant dogs with clinical signs of pseudopregnancy. It was aimed at determining the prevalence of pseudopregnancy among the non-pregnant dogs and ascertaining the influence of various risk factors like breed, age, parity and previous history of pseudopregnancy on the prevalence of overt pseudopregnancy. The study was carried out also to record the various clinical signs exhibited by pseudopregnant dogs and to evaluate the efficacy of cabergoline, bromocriptine and managemental changes in treating pseudopregnancy.

The overall prevalence of pseudopregnancy in the current study was 35.41% among the non-pregnant dogs presented to the Department of Veterinary Gynaecology and Obstetrics, Veterinary College, Hebbal, Bengaluru. Overt pseudopregnancy was recorded in 51 females of 15 different breeds of dogs with the highest prevalence in medium sized dog breeds and the lowest in small dog breeds. Further, highest prevalence was recorded in dogs below 2 years of age and lowest in adult dogs of 5-8 years age group and above eight years of age. Among the dogs with overt pseudopregnancy majority were nulliparous animals and prevalence was lowest in pluriparous animals. Statistical analysis showed that the age and parity had a significant effect on exhibition of clinical signs of pseudopregnancy. The present study data showed that the breed did not have any significant effect on expression of pseudopregnancy. The percent of recurrence of pseudopregnancy was recorded as 9.8% in the current study.

The female dogs with pseudopregnancy in the current study was presented on an average 63.70 ± 2.25 days from last estrus with majority of dogs being above 60 days from last estrus. The average serum progesterone concentration in these pseudopregnant dogs was 0.95 ± 0.015 ng/ml. Both the average number of days from last estrus and serum progesterone concentration showed that majority of the dogs that exhibited pseudopregnancy in the current study was in anestrus phase of estrous cycle rather than the late luteal phase.

The dogs in pseudopregnancy show different clinical signs with physical changes including mammary development with evident secretions being the most common sign. Physical changes also included weight gain, abdominal distension and vaginal discharges. The least evident physical sign was abdominal contractions mimicking whelping in pseudopregnant dogs. Along with physical signs the other common sign is maternal behaviour like nesting and caring for inanimate objects. Adoption of orphaned puppies was not observed in any of the dogs studied. Among the behavioural changes licking of abdomen was observed in majority of dogs whereas, aggressiveness towards the owners was the least prominent sign. Decreased activity, restlessness, inappetance, whining, anxiousness and hyperexitability are other behavioural signs observed. Clinical signs associated with pseudopregnancy were not common and exhibited by less than 50% of the pseudopregnant dogs. Complications like mastitis were not common and observed only in 3.92% if the dogs with pseudopregnancy. The type of clinical signs exhibited and the intensity of each sign vary widely with individuals. This could be due to variation in the expression of peripheral prolactin receptors and the sensitivity of prolactin receptors in the target organs.

Pseudopregnancy is a self-limiting physiological syndrome but when clinical signs exacerbate, it demands medical attention. Use of dopamine agonists was found to be more effective than conventional conservative treatments. Cabergoline was more effective than bromocriptine in the number of days needed for complete recovery of the clinical signs. The side effects were also milder with cabergoline at the dose rate of 5 µg/ Kg BW than bromocriptine at the dose rate of 10 µg/ Kg BW. Effectiveness of cabergoline was more than bromocriptine, so cabergoline need be given only once daily whereas, bromocriptine be given twice daily. Managemental changes or conservative treatments were also effective in treating pseudopregnancy with an average 15 ± 0.77 days for complete remission of clinical signs.

From the present study, it can be concluded that pseudopregnancy is a physiological syndrome where female non-pregnant dogs mimic the signs of post-partum phase (anestrus) or the stage of lactation. Prevalence of the condition will vary widely with geographical location and the study group. Age and parity of the dogs have a significant effect on exhibition of overt signs of pseudopregnancy. Breed of the dog may affect the exhibition of overt clinical signs owing to an inherent genetic component in pre-disposed animals which cannot be ignored even though the present study did not show significant effect of breed on prevalence of pseudopregnancy. The intensity and type of clinical signs vary widely between individuals which could be due to difference in individual prolactin bioactivity. Though pseudopregnancy is a self-limiting disease, female dogs with exacerbated clinical signs demand treatment and dopamine agonists can be used to treat the condition without severe side effects. More studies on molecular difference in expression of prolactin receptor is needed to unveil the extent of genetic involvement and heredity in overt pseudopregnancy.

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VI. BIBLIOGRAPHY

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ABSTRACT

VIII. ABSTRACT

A study on the prevalence, predisposing factors, clinical signs associated with pseudopregnancy and efficiency of dopamine agonists and management practices to reduce the clinical manifestation of pseudopregnancy was conducted. The prevalence of pseudopregnancy was 35.41% with highest prevalence in medium breeds and lowest in small breeds. The prevalence was higher in young (less than 2 years) and nulliparous female dogs. Age and parity showed a statistically significant influence on the exhibition of pseudopregnancy. The signs were exhibited during the anestrus stage of estrous cycle in majority of dogs as indicated by the serum progesterone values less than 1 ng/ml. The average number of days from last estrus was 63±2.25 days. The clinical signs varied widely between individuals and mammary development with milk or milk like secretion was the most common sign (96.08%). Physical changes and maternal instincts were also recorded and clinical signs were seen in less than 50% of the dogs. The complications like mastitis or mammary dermatitis were rare (3.96%). Cabergoline at 5µg/Kg BW once daily took an average of 6.4±0.65 days for complete recovery and bromocriptine at 10µg/Kg BW twice daily took an average of 9.5±0.73 days. Managemental practices like food and water withdrawal during night hours and application of Elizabethan collars for an average of 15±0.77 days also had a significant effect in reducing clinical signs compared to control group. Even though pseudopregnancy is a self-limiting condition, when clinical signs are exacerbated, compared to bromocriptine, cabergoline was found to be safe and effective. Managemental interventions were found to be effective in absence of veterinary aid.

APPENDIX

XI APPENDIX 1

CLINICAL STUDIES ON PSEUDOPREGNANCY IN DOGS

Owners Name: Phone number:

SIGNALMENT:

Name of pet: Breed: Age: Parity:
Last day of estrus: Breeding history:

Previous history of pseudopregnancy: Yes/ No

SYMPTOMS

Behavioural signs		Yes	No
Anxiety			
Anorexia			
Aggressiveness			
Hyperexitability			
Restlessness			
Whining			
Decreased activity			
Licking of abdomen			
Clinical signs			
Vomiting			
Diarrhoea			
Polyuria			
Polydipsia			
Polyphagia			
Maternal behaviour			
Nesting			
Mothering toys/foot wears/other objects			
Adopting puppies			
Physical signs			
Abdominal distension			
Weight gain			
Mammary enlargement			
Milk secretion	Serous	Partly serous	Milk
Abdominal contractions			
Vaginal discharge			
Complications			
Mastitis			
Mammary dermatitis			