

## IMPACT OF OXYTETRACYCLINE AND PROSTAGLANDIN F2 $\alpha$ DURING PUERPERIUM PERIOD ON UTERINE RECOVERY AND POST-PARTURIENT REPRODUCTIVE CHARACTERISTICS IN BALADI COWS

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### SUMMARY

This study aims to determine the influence of oxytetracycline and prostaglandin F2 $\alpha$  during the puerperium period, on uterine recovery and post-parturient reproductive characteristics in Baladi cows. Twenty Baladi cows were used immediately after birth and were divided into two groups of 10 cows per group. The first group (n= 10 cows) was treated with 20 ml intrauterine infusion of oxytetracycline hydrochloride solution for three consecutive days during the puerperium period and 5ml intramuscular prostaglandin F2 $\alpha$  injection once after three hours from calving, while the second group (n= 10 cows) was used as a control group. The present findings demonstrated the interval from parturition to uterine involution in Baladi cows was significantly ( $P < 0.05$ ) lower, ( $28.4 \pm 4.5$ , days) in treated cows compared to  $45.7 \pm 3.5$ , days in control group cows. However, the period from calving to the resumption of estrus activity postpartum was significantly ( $P < 0.05$ ) below,  $45.2 \pm 9.1$ , days in treated cows compared to  $68.2 \pm 6.2$ , days in control cows. Meanwhile, the time from calving to conceived was significantly ( $P < 0.05$ ) less ( $96.5 \pm 12.3$ , days) in treated cows than ( $155.3 \pm 15.2$ , days) in controlled cows. In addition, the conception rate from first mating was significantly ( $P < 0.05$ ) higher, 60% in treated cows compared to 30% in control cows. In conclusion, the current study demonstrated improvement in post-partum reproductive performance in cows which treated with oxytetracycline and prostaglandin F2 $\alpha$  during the puerperium period. So, the study recommends that small breeders should treat their cows during the puerperium period.

**Keywords:** Oxytetracycline, prostaglandin F2 $\alpha$ , uterine recovery, reproductive characteristics, Baladi cows

### INTRODUCTION

The puerperium period in cows is one of one of the most harmful periods in the life of the animal, as cows are exposed to infection by some pathogenic microbes inside the uterus that affect their reproductive performance after calving. Most the cow breeders under the traditional and, bind, stalls system, especially in Upper Egypt, villages, would intervene to help their cows during parturition, thus exposing the cows to microbial pollution infection. Management factors and complications at parturition such as calving assistance can increase the incidence of uterine disease and have been identified as risk factors for clinical and subclinical endometritis (Wagener *et al.*, 2014). The calving environment, dystocia, retention of the placenta, twins, and diet are considered the plausible risk factors for uterine infection (Sheldon *et al.*, 2008). We must understand that there is an interactive relationship between the environment and uterine infection, immunity, and reproduction so that we can make strategies to counteract the fertility decline in cattle (Sheldon *et al.*, 2008). Bacterial contamination of the uterine lumen is common in cattle during calving which leads to infection and uterine disease (Sheldon *et al.*, 2008). One of the costliest issues facing the dairy

industry is a uterine disease. Eicosanoids have the potential to directly affect uterine immunity, and exogenous PGF2 $\alpha$  is possibly an effective treatment for uterine diseases (Lewis and Wulster-Radcliffe, 2006). Infertility conjugated with the uterine diseases causes harm to the endometrium and disruption of ovarian activity. Bacteria causes fluctuation in endometrial prostaglandin secretion and perturb ovarian follicle growth and function (Sheldon *et al.*, 2008). Subclinical endometritis declines conception rates (Kasimanickam *et al.*, 2004 and Gilbert *et al.*, 2005). The primary goal of postpartum reproductive health in cows is the full involution of the uterus, the defense against infection, and the resumption of normal estrous cycle activity (LeBlanc *et al.*, 2002 and Gautam *et al.*, 2009). The uterine size declines during the puerperal cycle as the endometrium regenerates, a bacterial infection is removed and ovarian cyclicity in a phase known as uterine involution resumes, a condition for effective reproduction afterward (Heppelmann *et al.*, 2013). A uterine bacterial infection occurs shortly after calving in many cows (Sheldon *et al.*, 2009a and Molina-Coto and Lucy, 2018). Prunner *et al.* (2014) showed that the rate of uterine bacterial growth increased during the 15 days post- partum. Sheldon *et al.* (2006) and Földi *et al.* (2006) observed that uterine

infections at or after calving are considered common, with 80-100% of animals possessing uterine lumen bacteria in the first 2 weeks, after birth. Subclinical endometritis is characterized as endometrial inflammation without systemic symptoms (Madoz *et al.*, 2014 and Mariño *et al.*, 2017). Subclinical endometritis is characterized as endometrial inflammation with a lack of purulent vaginal discharge, (Sheldon *et al.*, 2019 and Tobolski *et al.*, 2021). Subclinical endometritis is a uterine disease with no clinical symptoms that cannot be reliably identified at a farm site (Ricci *et al.*, 2015). Cows with uterine inflammation have poor reproductive efficiency, resulting in lower conception rates, more open days, and more losses in pregnancy (Galvão *et al.*, 2009 and Vieira-Neto *et al.*, 2014). Changes in the immune and endocrine systems are associated with increased sensitivity of cows to infections during the periparturient period (Cai *et al.*, 1994). Pothmann *et al.* (2015) found that more than 90% of the subclinical endometritis diagnosed have been found in multiparous cows. Alterations of a prostaglandin E2 and F2 $\alpha$  synthesis pattern were associated with infected cows with subclinical endometritis (Gabler *et al.*, 2009 and Baranski *et al.*, 2013). Estradiol and progesterone impair the production of PGE and PGF in response to lipopolysaccharides (LPS), indicating the role of steroid hormones in interaction with bacterial contamination (Herath *et al.*, 2006). The production of dairy cows is adversely affected by clinical, and subclinical endometritis, and economic losses are attributed to delays in resumption of ovarian activity, increased number of services per conception, and reduced milk yield (LeBlanc, 2008 and Cheong *et al.*, 2011). The percentage of incidence rate of subclinical endometritis in normal parturition was 36.47% compared with 85.5% in abnormal parturition (Moges, 2015). Reduced activity of the dominant ovarian follicle was correlated with bacterial infection of the endometrium (Sheldon *et al.*, 2002 and Williams *et al.*, 2007). One of the best protocols for the treatment of postpartum endometritis in dairy cows is an intrauterine antibiotic infusion (Drillich *et al.*, 2005). Intrauterine administration is helpful, especially in cows' treatment and prophylaxis of postpartum endometritis (Malinowsk *et al.*, 2004).

Kasimanickam *et al.* (2005) and Denis-Robichaud and Dubuc (2015) reported the importance of using antimicrobials and prostaglandin F2 $\alpha$  in treatments of dairy cows with subclinical endometritis. Oxytetracycline is one of the broad-spectrum antibiotics used to treat postpartum endometritis in dairy cows (Sheldon *et al.*, 2004). Noakes and England (2009) reported that oxytetracycline administration can be used as a prophylactic intrauterine antibiotic post-assisted parturition. For the treatment and prevention of endometritis, two major methods are commonly used: the use of antibiotics (intrauterine or systemic) or prostaglandins (PGF2 $\alpha$ ) (Lefebvre and Stock, 2012). PGF2 $\alpha$  seems to be beneficial for clinical endometritis therapy (Salasel and Mokhtary, 2011). Intrauterine treatment with chlortetracycline was better than no treatment in dairy cows (Goshen and Shpigel, 2006). This study aims to determine the influence of oxytetracycline and prostaglandin F2 $\alpha$  during the puerperium period in Baladi cows, which need simple assistance in parturition on uterine recovery and post-parturient reproductive characteristics.

## MATERIALS AND METHODS

### *Farm and environment conditions:*

The study was performed on a traditional farm in the Kom Ombou region (32° ,31' 23" east and 22° , 28' 09" north), in the Aswan governorate. In traditional farm conditions, the cows were raised and housed in semi-shaded sheds and tied. Table (1) illustrates ambient temperature (°C), relative humidity (RH %), and temperature humidity index (THI) during the study. Table (2) clarifies the classification of zones based on THI values in cattle with THI model proposed by (Samal, 2013). The study extended from November to April. Estimated temperature humidity index (THI) according to the formula suggested by Mader *et al.* (2006):

$$\text{THI} = (0.8 \times T_{\text{max}} - \text{db}) + [(RH/100) \times (T_{\text{max}} - 14.4)] + 46.4$$

$$\text{Temperature-humidity index (THI)} = 0.8 \times \text{ambient temperature} + [(\% \text{ relative humidity} / 100) \times (\text{ambient temperature} - 14.4)] + 46.4$$

**Table 1. Ambient temperature (°C), relative humidity (RH %), and temperature humidity index (THI) during the experimental period**

Months of calving	Average Ambient Temperature (° C)		Average Relative humidity (RH %)	THI
	Min.	Max.		
November	20.4	30.2	19	73.56
December	16.1	29.5	20	73.02
January	13.2	20.5	23	64.20
February	14.3	23.4	22	67.10
March	19.3	31.3	19	74.65
April	21.4	35.0	17	77.90

**Table 2. Classification of zones based on THI values in cattle with THI model according to (Samal, 2013)**

THI	Stress level	Response of cattle
<72	None	Non-noticeable
72-79	Mild	Dairy cows will adjust by seeking shade, increasing respiration rate and dilation of the blood vessels. The effect on milk production will be minimal.
80-89	Moderate	Both salivaproduction and respiration rate will increase. Feed intake may be depressed and water consumption will increase. There will be an increase in bodytemperature. Milk production and reproduction will be decreased.
90-98	Severe	Cows will become very much uncomfortable due to high body temperature, rapid respiration (panting) and excessive saliva production. Milk production and reproduction will be markedly decreased.
>98	Danger	Potential cow death can occur.

**Trial animals and feeding:**

Twenty Baladi cows were included in the current study. The cow parity ranged from 3<sup>rd</sup> to 6<sup>th</sup> and the live body weight varied from 330 to 350 kg at calving. During the experiment, bran, wheat hay and concentrate feed mixture (16% protein) alongside Barseem Higazee (*Alfa- alfa*) as a green fodder was given to animals. Both cows were kept in the same environmental and administrative conditions according to a work routine.

**Designing the trial:**

Cows number was divided into two equal groups (n= 10 cows per group). The first group was treated with oxytetracycline and prostaglandin F2 $\alpha$ , while the second group was served as a control. As recommended by the producer, the cows were treated with a 20ml intrauterine infusion of oxytetracycline sterile solution (Pan-Terramycin oxytetracycline hydrochloride solution 3g. *Pfizer*, Egypt) for three consecutive days during the puerperium period and 5ml equivalent 25 mg Dinoprost Tromethamine (Lutalyse<sup>TM</sup>, *Zoetis*, 5mg/ml) intramuscular prostaglandin F2 $\alpha$  injection once after three hours from calving.

**Postpartum reproductive parameters evaluation:**

The uterine condition score (UCS) was measured and categorized as proposed by (Okawa *et al.*, 2017): **UCS1** = the uterus was completely palpable, with uterine horn symmetry and evidence of typical uterine conditions.

**UCS2** = the uterus was completely noticeable, but with uterine horn asymmetry and incomplete involution.

**UCS3** = the uterus was not completely palpable and was located outside the pelvic cavity

**Uterine involution:** When both uterine horns return to their normal position and sit in the pelvic region at the same or almost equal non-gravid scale, their regular tone and quality are called full according to the uterine involution in accordance with Elmetwally *et al.* (2016) and Gohar *et al.* (2018).

**Assisted calving:** Those cows that need little help just pull the front legs during the delivery of the fetus.

**Conception rate:** The percentage of cows that are pregnant from the first postpartum mating, and calculated as:

$$\frac{\text{Number pregnant cows} \times 100}{\text{Number served cows}}$$

**Identification of estrus and the diagnosis of pregnancy:**

Daily regular visual monitoring of cows was performed. Cows were considered in the estrus period once one of the estrus symptoms was exhibited like, mucus discharge and standing behavior. Post-sixty days (without any estrus symptoms) after service, the pregnancy was diagnosed by rectal palpation method.

**Analysis of hormones:**

Blood samples (10 ml) were collected from cows at estrus, 7<sup>th</sup>, 15<sup>th</sup> and 21<sup>th</sup> days post-service from the jugular vein in heparinized tubes. For plasma processing, samples were centrifuged for 20 minutes at 3000 rpm, plasma was separated, and stored at -18 °C until assay time. The Immunotech (France) radioimmunoassay package was used to test the hormones progesterone (P4) and estradiol-17 $\beta$  (E2). The susceptibility values of progesterone and estradiol-17 $\beta$  were 0.03ng/ml and 4.0pg/ml, respectively, according to the manufacturer's information. For progesterone (P4) and estradiol-17 $\beta$  (E2), the intra-assay variance coefficient was 6.4% and 12.1%, respectively.

**Statistical analysis:**

One factor (treatment effect) on uterine involution and postpartum reproductive characteristics was included in the statistical design. Chi Square was done to test the significance of percentage values. The statistical analysis was carried out using software (SAS, 2002). The following statistical model was used:

$$Y_{ij} = \mu + T_i + e_{ij}$$

**Where:**

$Y_{ij}$  = the observation trait,

$\mu$  = overall mean,

$T_i$  = the fixed effect of  $i^{\text{th}}$  treatment ( $i=1,2$  where 1=treated and 2=untreated)

$e_{ij}$  = experimental error

The Multiple Range Test of Duncan (Duncan, 1955) was used to verify the importance of the variations between means.

## RESULTS AND DISCUSSION

### *Effect of treatment with oxytetracycline and prostaglandin F2 $\alpha$ during the puerperium period on uterine involution in Baladi cows:*

Table (3) shows that the period from parturition to uterine involution in Baladi cows was significantly ( $P < 0.05$ ) lower,  $28.4 \pm 4.5$  days in treated cows compared to  $45.7 \pm 3.5$  days in the control group cows. The return of the uterus to its normal non-pregnant size and postpartum role is called uterine involution, which relies on the rate of myometrial contractions, bacterial infection clearance, and endometrium histological regeneration (Elmetwally *et al.*, 2016 and Elmetwally and Bollwein, 2017). During the normal uterine involution process after parturition, a variety of aerobic and anaerobic bacteria grow in the uterine lumen (Sheldon *et al.*, 2008). Epithelial regeneration occurs approximately 25 days after parturition, while full histological regression occurs approximately 6-8 weeks postpartum (Sheldon *et al.*, 2008). The time taken for complete uterine involution was recorded to range from 26 to 52 days in dairy cattle (Noakes *et al.* 2001). The present findings agreed with those reported by Swelum (2013) who proposed that the intrauterine treatment of dairy cows and camels with oxytetracycline in the puerperium period contributes to uterine tissue regeneration. Sheldon *et al.* (2004) stated that oxytetracycline is a broad-spectrum antibiotic used to reduce developing uterine bacteria. Beagley *et al.* (2010) found that intrauterine antibiotics in cattle have an adverse effect on local bacterial development. Malinowsk *et al.* (2004) reported that intrauterine therapy has been found effective in the prevention and prophylaxis of postpartum uterine diseases in cows. In the current research, the beneficial impact of PGF2 $\alpha$  therapy on the shortened time from calving to uterine involution was shown to indicate these results in line with those reported by Tobolski *et al.* (2021). Procedures involving uterine involution involve contractions and peristalsis, so conditions that lower blood calcium content or uterine production of PGF2 $\alpha$  can decrease uterine involution and prolong intrauterine infection (Roberts, 1986). There is a positive association between the concentration of PGF2 $\alpha$  in puerperal circulation and the uterine horn diameter (Sheldon *et al.*, 2003). Hanzen *et al.* (2003) reported that repeated administration of PGF2 $\alpha$ , 3-13 days after calving accelerates uterine involution by facilitating the removal of the contents of the uterus. To help the uterus overcome infections, exogenous PGF2 $\alpha$  can improve immune functions or boost uterine motility (Hirsbrunner *et al.*, 2003). Elsheikh and Ahmed (2005) observed that PGF2 $\alpha$  injection within the first week resulted in rapid involution of the uterus in dairy cows. Melendez *et al.* (2004) reported that at 8 d postpartum, two doses of PGF2 $\alpha$  8 h apart in

primiparous Holstein cows diminished the diameter of the uterine horns. Masoumi *et al.* (2018) observed that 25mg PGF2 $\alpha$  injection led to uterotonic effects, which may aid accelerate uterine involution in puerperal dairy cows. PGF2 $\alpha$  is commonly used during early postpartum to facilitate uterine involution in dairy cows (Salasal and Mokhtari, 2011 and Jeremejeva *et al.*, 2012). A certain amount of PGF2 $\alpha$  is assumed to be a prerequisite for the uterine involution process, primarily to induce uterine smooth muscle shrinkage to enhance lochia discharge and uterine morphological and functional recovery (Williams, 2013). Ingawale and Bakshi (2016) suggested that injection of PGF2 $\alpha$  on day 14 post-calving led to lowering the time needed for involution of the uterus from 31.5 days to 27.4 days in control and treated buffaloes groups respectively. During 30 days postpartum, dairy cows that received an injection of PGF2 $\alpha$  on the day of calving, nearly 60% of cows had their uterus involution, compared to 30% of control dairy cows (Zidane *et al.*, 2011). In cows with subclinical endometritis, PGF concentrations are lower than PGE in the fourth week postpartum, and the ratio of PGE to PGF production may be one of the causes of delayed involution or endometrial regeneration (Baranski *et al.* 2013).

### *Effect of treatment with oxytetracycline and prostaglandin F2 $\alpha$ during the puerperium period on resuming estrus cyclicity in Baladi cows:*

Table (3) illustrates that the time from parturition to 1<sup>st</sup> postpartum estrus was significantly ( $P < 0.05$ ) below  $45.2 \pm 9.1$ , days in treated cows compared to  $68.2 \pm 6.2$ , days in control cows. The current results agreed with those reported by Schofield *et al.* (1999) who found that treatment of dairy cows with prostaglandin F2 $\alpha$ , 21 days after calving shortened the first estrus period by around 10 days. Etherington *et al.* (1985) and Young *et al.* (1986) suggested that the use of PGF2 $\alpha$  between 14 and 28 days postpartum resulted in reduced the period to the postpartum first estrus in dairy cows. Ingawale and Bakshi (2016) stated that on day 14 postpartum, PGF2 $\alpha$  injection resulted in a short interval from calving to the first postpartum estrus of 47.6 days relative to 67.1 days in control buffaloes. Intrauterine treatment with oxytetracycline twice weekly for 2 weeks prevented the negative effects of uterine disease on fertility in multiparous dairy cows (Goshen and Shpigel, 2006). Intrauterine therapy is a helpful medication, especially for the treatment and prophylaxis of postpartum uterine diseases in cows (Malinowsk *et al.* 2004). Beagley *et al.* (2010) reported that intrauterine antibiotics have a detrimental and effective impact on local bacterial growth in cattle. Usage of uterine oxytetracycline infusion provided better reproductive performance than the intramuscular method in the first 21<sup>st</sup> postpartum in cows diagnosed with uterine diseases (Armengol and Fraile, 2015). Intrauterine oxytetracycline can cause inflammatory responses and uterine defense reactions and stimulate uterine

leukocyte cells. It can also contribute to uterine tissue regeneration (Noakes and England (2009) and Swelum, 2013). The interval between parturition and the incidence of first ovulation was positively associated with the time needed to complete uterine involution (Madej *et al.*, 1984). Gundling *et al.* (2012) found that treatment with PGF2 $\alpha$  in cattle shows a positive effect on uterine involution. Uterine inflammation prevents the release of PGF2 $\alpha$  by the endometrium and extends the luteal phase of the estrous cycle (Pepper and Dobson, 1987 and Bondurant, 1999). A single administration of PGF2 $\alpha$  accelerates uterine involution and hastens a return to fertile estrous cyclicity in the early post-partum period (Lindell and Kindahl, 1983 and Kindahl *et al.*, 1984). Archbald *et al.* (1993) suggested that during the early postpartum period, the use of PGF2 $\alpha$  led to increasing fertility in dairy cattle. Cows with subclinical endometritis recorded a delayed return to postpartum calving ovarian activity (Salehi *et al.*, 2017). In healthy cows, the number of ovarian follicles has been found to be higher and less incidence of cystic follicles than in cows with uterine disease (Maquivaret *et al.*, 2015). Anovulation is associated in Holstein Friesian cows with subclinical endometritis (Tsousiset *et al.* (2009). Galvao *et al.* (2010) suggested that cows that started to cycle by 21 days postpartum had fewer incidences of subclinical endometritis postpartum and a greater pregnancy rate than an anovulatory cow. Dubucet *et al.* (2012) observed that cows with subclinical endometritis had a delayed restart of ovarian activity postpartum. Opsomer *et al.* (2000) stated that the first postpartum ovulation is deferred in cows with uterine infections. Kudlac (1991) increased the duration of uterine involution resulting in an extended period of resumption of ovarian activity in the postpartum period in cows. Infected cows with subclinical endometritis early postpartum were less likely to ovulate than healthy cows (Burke *et al.*, 2010). Bacteria modulate the secretion of endometrial prostaglandin and disrupt the development and activity of ovarian follicles (Sheldon *et al.*, 2008). Uterine disease is associated with an increased incidence of anestrus and ovarian cystic (Peter, 2004). McDougall *et al.* (2007) and Senosy *et al.* (2009) showed a delayed resumption of dairy cattle to normal postpartum cycles in cows with uterine inflammation.

**Effect of treatment with oxytetracycline and prostaglandin F2 $\alpha$  during the puerperium period on days open in Baladi cows:**

Table (3) indicates that the interval from calving to conceived (Days open) was significantly ( $P < 0.05$ ) less,  $96.5 \pm 12.3$ , days in treated cows compared with  $155.3 \pm 15.2$ , days in controlled cows. The present findings align with those reported by Kasimanickam *et al.* (2005), who observed that in dairy cows treated

with a single PGF2 $\alpha$  and antibiotics dose, the period from calving to conception was less than 101, 103 days compared to 119 days in control cows, respectively. Similar findings reported by Riscoet *et al.* (1994) showed that routine postpartum application of PGF2 $\alpha$  decreases the time from calving to pregnancy in dairy cows. Goshen and Shpigel (2006) suggested that usage of intrauterine antibiotics in normal, treated, and untreated dairy cows with clinical metritis resulted in 140.5, 136.2, and 165.5 days of open days, respectively. McClary *et al.* (1989) treatment of dairy cows with PGF2 $\alpha$  during early postpartum resulted in a decline in days open 98.6 days compared to 118.8, days for untreated cows. There were fewer days open for dairy cows treated with prostaglandin F2 $\alpha$  (Folman *et al.*, 1990). The dairy cows treated with PGF2 $\alpha$  on day 8 postpartum recorded lower days open (White and Dobson 1990). Lopez-Gatius (2003) observed a drop in days open after administration of PGF2 $\alpha$  during the early postpartum phase relative to the control group in dairy cattle. Cows with uterine disease (endometritis) recorded a longer interval (151 days) from calving to conception than unaffected dairy cows (119 days) (LeBlanc *et al.*, 2002). Galvao *et al.* (2009) showed that PGF2 $\alpha$  treatment in dairy cows with subclinical endometritis declines the time from parturition to conception. Bicalhoet *et al.* (2016) reported that cows with subclinical endometritis had longer 42 days open compared to healthy cows. Kasimanickam *et al.* (2004) stated that in cows with subclinical endometritis the time from calving to pregnancy was longer 141 days compared to 112 days in healthy cows. Similar findings were reported by Gilbert *et al.* (2005) who found that in cows with subclinical endometritis the days open was longer 206 days compared to 118 days in healthy cows. Madoz *et al.* (2013) observed that cows with subclinical endometritis had an increase in the interval from parturition to conception compared with normal cows 133 and 93, days respectively. Galvao *et al.* (2009) reported that treatment with PGF2 $\alpha$  in dairy cows with subclinical endometritis led to a decrease in the time from calving to pregnancy. Ricci *et al.* (2015) proposed that there was a 40-day delay to conception in beef cows with subclinical endometritis relative to normal cows. Vieira-Neto *et al.* (2014) proposed that cows with subclinical endometritis recorded a longer number of days open compared to healthy cows. Uterine disease results in an increase in the time from calving to pregnancy in multiparous cows (Toni *et al.*, 2015). The time from calving to pregnancy (DO) extended in cows with postpartum uterine disorders such as subclinical endometritis (Barański *et al.*, 2012). Barrio *et al.* (2015) found that the time from calving to conception (DO) was longer 154 days in cows suffering from subclinical endometritis compared with 119 days in healthy cows.

**Table 3. Effect of treatment with oxytetracycline and prostaglandinF2 $\alpha$  during puerperium period on uterine involution and post-parturient reproductive aspects in Baladi cows**

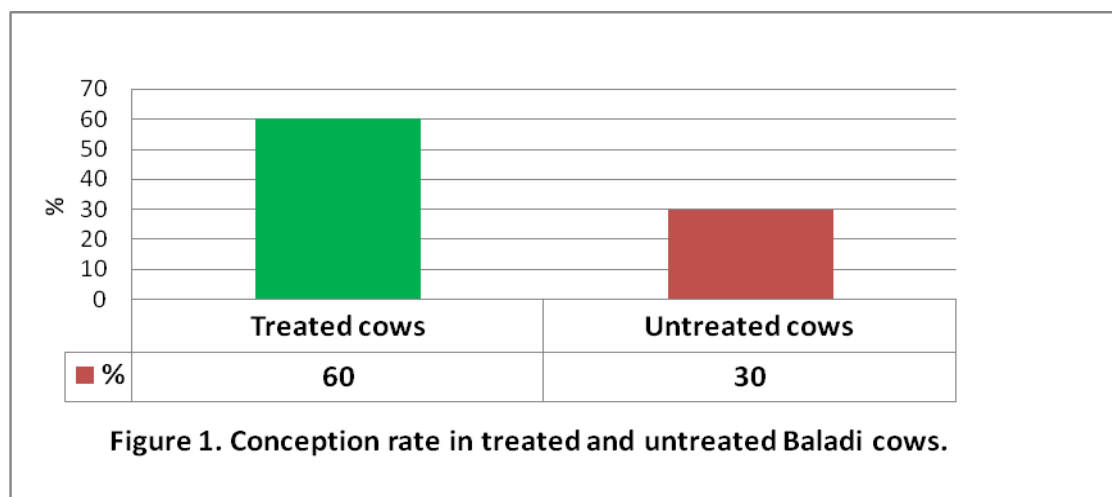
Items	Treated cows (10 cows)	Untreated cows (10 cows)
Uterine involution period (days)	28.4 <sup>a</sup> $\pm$ 4.5	45.7 <sup>b</sup> $\pm$ 3.5
The interval from parturition to 1 <sup>st</sup> postpartum estrus (days)	45.2 <sup>a</sup> $\pm$ 9.1	68.2 <sup>b</sup> $\pm$ 6.2
The interval from parturition to conceived (days open)	96.5 <sup>a</sup> $\pm$ 12.3	155.3 <sup>b</sup> $\pm$ 15.2

a, b: values within the same row having different superscripts are significantly different at P < 0.05.

**Effect of treatment with oxytetracycline and prostaglandinF2 $\alpha$  during the puerperium period on conception rate in Baladi cows:**

Figure (1) shows that the conception rate from the first service was significantly (P < 0.05) higher, 60% in treated cows compared with 30% in control cows. One of the safest and most effective protocols for the treatment of postpartum endometritis in dairy cows is an intrauterine infusion of antibiotics (Drillich *et al.*, 2005). The present findings correspond with those stated by Armengol and Fraile (2015) reported that intrauterine infusion of oxytetracycline produce improve reproductive performance in cows during the first 21 days postpartum and increases conception rate from the first service. Ahmadi *et al.* (2005) found that the pregnancy rate of oxytetracycline-treated cows was 66.7%, compared with 33% of cows receiving only PGF2 $\alpha$ . McDougall (2002) stated that intrauterine antibiotic therapy has increased the reproductive efficiency of dairy cattle. Sheldon and Noakes (1998) reported that the pregnancy rate from the first service was 48.7% when treating the cows with tetracycline intrauterine infusion but was 52.5% when PGF2 $\alpha$  was used. Goshen and Shpigel (2006) in normal, treated, and untreated clinical metritis (CM) cows after intrauterine antibiotics, conception rates after the first insemination were 38.3%, 42.5%, and 18%, respectively. A lower conception rate from the first service was recorded in dairy cows with uterine infection (endometritis) (29.8%) than in unaffected (37.9%) (LeBlanc *et al.*, 2002). A single dose of antibiotics or PGF2 $\alpha$  increases the reproductive efficiency of dairy cows with subclinical endometritis (Kasimanickam *et al.* 2005). Ribeiro *et al.* (2015) recorded that the occurrence of disease in dairy cows is 42%, from calving to service and these diseases are responsible for the decline in fertilization and conceptus development. Bicalho *et al.* (2016) found that pregnancy rates were 27% lower in cows with subclinical endometritis than in healthy cows. Barlund *et al.* (2008) reported that cows with subclinical endometritis had a significantly lower first-service conception rate than healthy cows. Embryonic viability is likely to be impaired in a contaminated uterus owing to a decline in uterine milk quantity and the harmful effects of bacterial compounds (McDougall, 2001). The postpartum uterine disease may affect sperm transfer, embryonic attachment failure, and poor placental development (Sheldon *et al.*, 2009a). Early postpartum subclinical endometritis in dairy cows reduces the pregnancy rate by 29%, relative to 45%, in normal cows (Madoz

*et al.* 2013). Vieira-Neto *et al.* (2014) suggested that cows with subclinical endometritis have a lower conception rate compared to healthy cows. Salasel *et al.* (2010) and Janowski *et al.* (2013) reported that 50% of repeat breeder dairy cows suffer from subclinical endometritis. Kasimanickam *et al.* (2004) suggested that during the postpartum period, the first service pregnancy rate in dairy cows with subclinical endometritis was 18% compared to 32% in healthy cows. Gilbert *et al.* (2005) showed that the pregnancy rate from the first service was 11% in cows with the uterine disease compared to 36% for healthy cows. Treatment of dairy cows in early postpartum with two doses PGF2 $\alpha$  8 h apart led to an increased first service conception rate (47.1%) in treated cows compared to (27.6%) in the control group (Salasel and Mokhtari, 2011). After the first artificial insemination, the pregnancy rate was zero percent in control cows, but 25.0% in dairy cows who administered PGF2 $\alpha$  (Okawa *et al.*, 2021). Melendez *et al.* (2004) demonstrated that when Holstein cows were administered two doses of PGF2 $\alpha$  8 h apart at 8 d postpartum, the treatment led to an improved pregnancy rate at first service by 17%. Jeremejeva *et al.* (2012) showed that injections of prostaglandin F2 $\alpha$  plus anti-inflammatory drug at periods of 8 h after 8 days postpartum led to a rise in the pregnancy rate by 50% in treated cows compared to 37% in the control group in dairy cows after the first services. Herath *et al.* (2009) observed that in cows with *E. coli* infection evidence for raising production of PGE relative to PGF2 $\alpha$ . Single PGF2 $\alpha$  administration 14 to 28 days post-partum resulted in a 68% increase in first-service conception rate compared to 43% in control cows (Young *et al.* 1984). McClary *et al.* (1989) reported that treatment of the dairy cow in early postpartum with prostaglandin F2 $\alpha$  led to an improvement of first service pregnancy rates (41.3%) in the treated cows and (35.7%) in the control group). PGF2 $\alpha$  has a local influence on the hypothalamic-pituitary axis and an elevated frequency of LH pulses (Peters *et al.*, 1989). Guilbault *et al.* (1987) stated that higher concentrations of PGF2 $\alpha$  early in the postpartum period are associated with the early resumption of ovarian activity. Ingawale and Bakshi (2016) suggested that PGF2 $\alpha$  injection resulted in an improvement in the rate of first-service pregnancy (33.33%) in treated buffaloes on day 14 postpartum, compared to (16%) in untreated buffaloes. Galvao *et al.* (2009) stated that PGF2 $\alpha$  treatment in cows with subclinical endometritis improves the first-service conception rate.



#### **Concentrations of progesterone (ng/ml) and estradiol-17 $\beta$ (pg/ml) during the estrous cycle in treated and untreated Baladi cows**

As shown in table (4), concentrations of progesterone and estradiol-17 $\beta$  at estrus were significantly ( $P < 0.05$ ) higher in pregnant cows than in non-pregnant cows. Atypical progesterone profiles that indicate delayed ovulation, cystic ovarian disease, or prolonged luteal phases are frequently caused by uterine diseases, such as retained placenta and uterine infection (Opsomer *et al.*, 2000; Royal *et al.*, 2000). *E. coli* or LPS led to fluctuations in the secretion of these hormones PGF2 $\alpha$  and PGE2 (Herath *et al.*, 2006). The current results agree with those reported by Waldman *et al.* (2001) who found that there was a strong inverse association between the likelihood of non-return and the concentration of progesterone in cows at mating time. Conceived cows had a higher frequency of d 10 post-service progesterone concentration compared to non-conceived cows (Busch *et al.*, 2008). Table (4) shows that 21-day post-service progesterone concentrations were higher in treated cows than in untreated cows, perhaps responsible for and/or promoting higher pregnancy rates in treated cows than in untreated cows. The results obtained agree with those stated by Lemley *et al.* (2010) who recorded that the rise in progesterone after mating was associated with improved retention in pregnancy and growth in embryonic development. Rivera *et al.* (2011) stated that less development and quality of cow embryos are attributed to lower levels of progesterone in lactating dairy cows during follicle formation. Cerri *et al.* (2011) found that higher progesterone concentrations before and after service were associated with increased fertility. Progesterone affects ovarian and uterine functions during conception by direct or indirect methods and also in the early stages of embryo development. During follicular growth, a drop in plasma progesterone levels is associated with lower fertility rates and impedes embryo survival during early pregnancy periods (Inskip, 2004 and Pursley and Martins, 2011). A high level of

progesterone affects pregnancy by causing synchrony between the uterus and embryos. However, a low uterine system level of progesterone does not induce important changes in dairy cows to host and retain embryos (Kenyon *et al.*, 2013 and Randi *et al.*, 2016). The present findings showed, that during the estrous cycle, progesterone concentrations reached a lower level at estrus but, in estradiol, they had higher concentrations of these fluctuations or modifications which had a positive effect on conception. Progesterone is immunosuppressive, while estradiol has been used to treat uterine disease and can support immunity (Lewis, 2003). In cows with subclinical endometritis, estradiol concentrations were lower compared to healthy cows 21 days postpartum (Green *et al.* 2011). Kasimanickam *et al.* (2005) suggested an increase in the uterine defenses when progesterone concentrations were low in dairy cows. Cows with uterine diseases are less likely to ovulate the first primary follicle than normal cows (8% vs. 40%) and are more likely to have abnormal progesterone concentrations (58% vs. 39%) (Sheldon *et al.*, 2008). Dairy cows with uterine infections have slower development of the first postpartum dominant follicle from 7 to 16 days after calving, have less plasma estradiol concentrations, and are less susceptible to ovulation (Sheldon *et al.*, 2002). Williams *et al.* (2007) found decreased follicle development and estradiol secretion in cows with uterine infections besides a decline in progesterone concentrations after the first post-calving corpus luteum formation. Sheldon *et al.* (2009b) showed that a drop in follicular size and estradiol concentrations is caused by uterine disease. In cows with greater uterine pathogen load, the diameter of the corpus luteum was smaller and progesterone concentrations declined (Williams, 2013). Changes in liver transcription for genes linked to steroid hormone production and inflammation were correlated with subclinical endometritis in dairy cows. These modifications resulted in impairments in fertility (Akbar *et al.*, 2014).

**Table 4. Concentrations of progesterone (ng/ml) at estrus, 7<sup>th</sup>, 15<sup>th</sup> and 21<sup>th</sup> days post-service and estradiol-17 $\beta$  (pg/ml) in treated and untreated Baladi cows**

Items	Treated cows (10 cows)		Untreated cows (10 cows)	
	Pregnant	Non-pregnant	Pregnant	Non-pregnant
<b>Progesterone (ng/ml)</b>				
At estrus	0.38 <sup>a</sup> ±0.09	0.22 <sup>b</sup> ±0.04	0.24 <sup>a</sup> ±0.02	0.18 <sup>b</sup> ±0.04
7 <sup>th</sup> days post-service	3.22 <sup>a</sup> ±0.03	2.21 <sup>b</sup> ±0.01	2.94 <sup>a</sup> ±0.02	2.11 <sup>b</sup> ±0.03
15 <sup>th</sup> days post-service	5.81 <sup>a</sup> ±0.06	3.32 <sup>b</sup> ±0.04	4.34 <sup>a</sup> ±0.06	2.32 <sup>b</sup> ±0.02
21 <sup>th</sup> days post-service	8.23 <sup>a</sup> ±0.12	0.20 <sup>b</sup> ±0.01	5.45 <sup>a</sup> ±0.12	0.23 <sup>b</sup> ±0.01
<b>Estradiol-17<math>\beta</math> (pg/ml)</b>				
At estrus	32.3 <sup>a</sup> ±0.32	18.3 <sup>b</sup> ±0.22	24.2 <sup>a</sup> ±0.31	17.2 <sup>b</sup> ±0.32

a, b: values within the same row having different superscripts are significantly different at P < 0.05.

1-Conception rate calculated from the first service.

## CONCLUSION

The current study demonstrated improvement in post-partum reproductive performance in cows which treated with oxytetracycline and prostaglandinF2 $\alpha$  during the puerperium period. So, the study recommends that small breeders should treat their cows during the puerperium period.

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### تأثير الأوكسي تتراسيكلين والبروستاجلاندين F2 $\alpha$ خلال فترة النفاس على عودة الرحم والخصائص التناسلية بعد الولادة في الأبقار البلدية

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تهدف هذه الدراسة الى تقدير تأثير الأوكسي تتراسيكلين والبروستاجلاندين F2 $\alpha$  خلال فترة النفاس على تعافي الرحم والخصائص التناسلية بعد الولادة في الأبقار البلدية. تم استخدام عشرين بقرة بلدية بعد الولادة مباشرة وتم تقسيمها إلى مجموعتين من 10 أبقار لكل مجموعة. المجموعة الأولى (ن = 10 أبقار) عوملت بـ 20 مل من محلول الأوكسي تتراسيكلين هيدروكلوريد بالتسريب داخل الرحم لمدة ثلاثة أيام متتالية خلال فترة النفاس و 5 مل حقنة في العضل بـروستاجلاندين F2 $\alpha$  مرة واحدة بعد ثلاث ساعات من الولادة، بينما المجموعة الثانية (ن = 10 أبقار) كانت ضابطة. أظهرت النتائج الحالية أن الفترة من الولادة إلى ارتداد الرحم في الأبقار البلدية كانت أقل معنويًا (P < 0.05) (28.4 ± 4.5 يوم) في الأبقار المعاملة مقارنة بـ (3.5 ± 45.7 يوم) في أبقار المجموعة الضابطة. كانت الفترة من الولادة إلى استئناف النشاط الشبقى بعد الولادة أقل معنويًا (P < 0.05)، (9.1 ± 45.2 يوم) في الأبقار المعاملة مقارنة بـ (6.2 ± 68.2 يوما) في أبقار المجموعة الضابطة. بينما كان الوقت من الولادة حتى الحمل أقل معنويًا (12.3 ± 96.5 يوم) (P < 0.05) في الأبقار المعاملة من (15.2 ± 155.3 يوم) في مجموعة الأبقار الضابطة. بالإضافة إلى ذلك، كان معدل الحمل من التلقيح الأول أعلى معنويًا (P < 0.05) 60٪ في الأبقار المعاملة مقارنة بـ 30٪ في مجموعة الأبقار الضابطة. في الختام، أظهرت الدراسة الحالية تحسناً في الأداء التناسلي بعد الولادة في الأبقار التي عوملت بأوكسي تتراسيكلين والبروستاجلاندين F2 $\alpha$  خلال فترة النفاس. لذلك، توصي الدراسة بضرورة قيام المربين الصغار بمعاملة أبقارهم خلال فترة النفاس.