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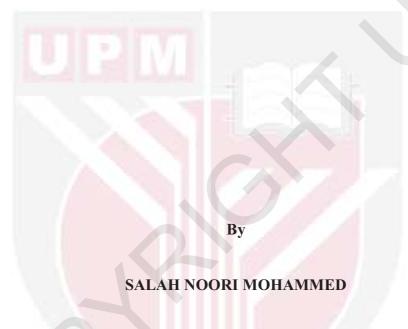
DIAGNOSIS OF SUBCLINICAL ENDOMETRITIS AND SUBSEQUENT REPRODUCTIVE STATUS IN POSTPARTUM CATTLE

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FPV 2018 27



# DIAGNOSIS OF SUBCLINICAL ENDOMETRITIS AND SUBSEQUENT REPRODUCTIVE STATUS IN POSTPARTUM CATTLE



Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

May 2018

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# DEDICATION

# THIS THESIS IS DEDICATED TO MY FATHER AND IN MEMORY OF MY LATE MOTHER AND TO MY FAMILY WITH LOVE AND RESPECT



Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirements for the degree of Doctor of Philosophy

## DIAGNOSIS OF SUBCLINICAL ENDOMETRITIS AND SUBSEQUENT REPRODUCTIVE STATUS IN POSTPARTUM CATTLE

By

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May 2018

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Endometritis is one of the most common diseases that affect reproductive performance in dairy and beef cows (Sheldon *et al.*, 2006). There is lack of studies about occurrence of subclinical endometritis and its diagnosis using cytological methods in Malaysia. Moreover, failure of response to antibiotics by pathogenic bacteria in uterine infections possibly due to drug resistance warranted the need to conduct this study.

The aims of this study were: 1) to evaluate three different methods of collection of endometrial cytological samples, 2) to determine the agreement among bacteriological findings, vaginal discharges, and endometrial cytology for endometritis detection in postpartum beef cows, 3) to determine the occurrence of subclinical endometritis (SCE) in postpartum beef cows, to compare the ovarian activity between SCE and healthy cows , 4) to assess the interaction between SCE cows and selected cytokines, acute phase proteins (APPs) and 5) to evaluate the agreement between endometrial cytology and ultrasound examination for diagnosis of SCE in postpartum beef cows. All parametric data after testing by the Shapiro–Wilk test were analyzed using t-test, one-way ANOVA as well as Tukey and Duncan post hoc tests at a probability threshold, P < 0.05. For non-parametric data, Kruskal-Wallis and Mann-Whitney tests were performed; all by using SPSS software.

Three different methods to collect cytological endometrial samples cotton swab (CS), cytobrush (CB) and low volume flush (LVF) were used to determine the mean of polymorphonuclear leukocytes (PMN) under high power field (HPF) microscopy (400x). Forty beef cows aged 3 to 7 years were subjected for cytological sampling at week three and four postpartum using the above methods. The mean number of

PMN from CB alone was significantly higher  $(11.3 \pm 0.53 \text{ cells HPF}^{-1})$  than CS  $(7 \pm 0.37 \text{ cells HPF}^{-1})$  and LVF  $(6 \pm 0.35 \text{ cells HPF}^{-1})$  methods. Smears from CB had more endometrial cells and PMN (58.55  $\pm$  1.41 cells HPF<sup>-1</sup>), which were significantly higher (P < 0.05) than CS and LVF methods. Both CB and CS methods yielded significantly more intact PMN and endometrial cells (62.4 % and 61.9 %) than LVF (52.4 %). In conclusion, CB was found to be better and effective technique compared with the other cytological methods.

For objective 2, a total of 82 postpartum beef cows at 20–30 days post-calving, were used in this study. All the cows were examined by transrectal palpation and vaginal secretions collection. Endometrial swab samples for cytology and bacteriology were collected using CB. A four-grade system (0 = clear mucus, 1 = mucus containing flecks of pus, 2 = discharge including < 50% pus, and 3 = involving > 50% pus) was used to categorize vaginal secretions of these cows. Of the total 82 cows studied, 11% (9/82) had grade 1-3 vaginal secretions and indicated to have clinical endometritis (CE), whereas nine of the 73 clinically healthy cows (12.32%) were diagnosed with subclinical endometritis (SCE  $\geq$  8 % PMN). *Escherichia coli* was the most common bacteria isolated from SCE (42%), and CE cows (38%), which were significantly higher (P<0.05) than healthy cows (14.6%). The antimicrobial sensitivity test assessed based on the inhibition effects on in vitro bacterial growth showed that most of the isolated bacteria were sensitive to enrofloxacin and tetracycline.

To compare ovarian activity between cows with SCE and healthy cows, and also to determine the interaction between SCE and selected proinflammatory cytokines (IL-6 and IL-8), and acute phase proteins (APPs) like haptoglobin (Hp). A total of 96 postpartum beef and 52 Friesian Sahiwal dairy cows were used. All postpartum cows were checked by transrectal palpation weekly beginning from week 3 until week 16 to evaluate uterine involution, and resumption of ovarian activity by detecting growing follicles on both ovaries. Endometrial samples were collected using CB technique between day 22 and day 28 after calving to identify cows with SCE. The occurrence of SCE was higher 15.3% (8/52) in a dairy group than the beef group 12.5% (12/96) at week 4 postpartum. Twelve beef and 8 dairy healthy cows were randomly selected as control to compare with cows diagnosed with SCE. Blood samples were collected from SCE and healthy cows from week 3 until week 7 to check the level of serum progesterone, IL-6, IL-8 and Hp. Results showed prolonged postpartum anestrus in postpartum beef cows mainly associated with cessation of ovarian activity, leading to increased days open. Progesterone concentration was less than 1 ng/mL in both SCE and healthy beef cows. In dairy cows, the resumption of ovarian activity was faster in healthy cows ( $20.5 \pm 0.9$  days) than SCE ( $37.1 \pm 0.7$ days) postpartum and the interval from calving to first ovulation was significantly shorter in healthy cows (29.4  $\pm$  0.7 days) than cows with SCE (47.5  $\pm$  0.9 days). Results revealed elevated levels of proinflammatory cytokines (IL-6 and IL-8) in cows with SCE (P < 0.05) compared with healthy cows during week 4 -7 postpartum in both beef and dairy groups. The level of Hp in beef and dairy group was higher (P < 0.05) in cows with SCE than healthy cows during most of the weeks of 4 -7 postpartum periods.

Lastly, using ultrasonography as a diagnostic tool to diagnosis endometritis compared with endometrial cytology method was evaluated in 53 postpartum beef cows. The study was conducted between day 20 and day 35 postpartum (at week 4 and 5) postpartum using ultrasound and CB endometrial examination methods to diagnose endometritis. Results showed that the ultrasound method is a useful and practical tool to diagnose endometritis, especially when it is combined with evaluation of intrauterine fluid accumulation and the cervical diameter ( $\geq 5$  cm).

Overall, the study revealed that prevalence of SCE in cows was low and cytobrush method was found to be superior and effective technique to obtain endometrial cytological samples. *E. coli was* the major risk factor found associated with SCE in beef cows. The antimicrobial sensitivity test showed that most of the bacteria isolated were sensitive to enrofloxacin and tetracycline. The levels of IL-6, IL-8, Hp can use as diagnostic markers for SCE as long as these cows are without clinical diseases and not exposed to stress factors. The ovarian activity was faster significantly in healthy dairy cows than endometritis cows. Prolonged postpartum anestrus was the common cause to increased calving-to-conception interval and impaired beef reproductive performance.

Abstrak tesis yang disampaikan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

## DIAGNOSIS SUBKLINIKAL ENDOMETRITIS DAN STATUS REPRODUKTIF SELANJUTNYA DALAM LEMBU PASCA BERSALIN

Oleh

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Endometritis adalah salah satu penyakit paling biasa yang mempengaruhi prestasi pembiakan dalam lembu tenusu dan lembu pedaging (Sheldon et al., 2006). Terdapat kekurangan kajian tentang kejadian endometritis subklinikal dan penggunaan kaedah sitologi untuk mendiagnosisnya di Malaysia. Selain itu, kegagalan tindak balas terhadap antibiotik oleh bakteria patogen dalam jangkitan rahim mungkin disebabkan oleh rintangan dadah yang menjamin keperluan untuk menjalankan kajian ini.

Tujuan kajian ini adalah: 1) untuk menilai tiga kaedah pengumpulan sampel sitologi endometrium, 2) untuk menentukan kesepakatan antara penemuan bakteriologi, lelehan vagina, dan sitologi endometrium untuk pengesanan endometritis dalam lembu pedaging postpartum, 3) untuk menentukan kejadian endometritis subklinikal dalam lembu pedaging postpartum, membanding aktiviti ovari dan keseimbangan tenaga antara endometritis subklinikal (SCE) dan lembu yang sihat semasa tempoh selepas bersalin, 4) untuk menilai interaksi antara lembu SCE dan sitokin terpilih, protein fasa akut (APP) dan 5) untuk menilai persetujuan antara sitologi endometrium dan pemeriksaan ultrasound untuk diagnosis SCE dalam lembu pedaging postpartum.

C

Tiga kaedah yang berbeza untuk mengumpul sampel endometrium sitologi (swab kapas, CS, cytobrush, CB dan flush volume rendah, LVF) digunakan untuk menentukan purata polimorfonuklear leukosit (PMN) di bawah mikroskop medan kuasa tinggi (HPF) (400x). Empat puluh ekor lembu pedaging berumur 3 hingga 7 tahun tertakluk kepada sampel sitologikal pada minggu ke tiga dan empat selepas bersalin menggunakan kaedah di atas. Jumlah purata PMN dari CB sahaja jauh lebih

tinggi (11.3  $\pm$  0.53 sel HPF<sup>-1</sup>) daripada kaedah CS (7  $\pm$  0.37 sel HPF<sup>-1</sup>) dan LVF (6  $\pm$  0.35 sel HPF<sup>-1</sup>). Smear dari CB mempunyai lebih banyak sel endometrium dan PMN (58.55  $\pm$  1.41 sel HPF<sup>-1</sup>), yang jauh lebih tinggi (P < 0.05) daripada kaedah CS dan LVF. Kedua-dua kaedah CB dan CS menghasilkan PMN dan sel endometrium yang lebih utuh (62.4% dan 61.9%) daripada LVF (52.4%). Sebagai kesimpulan, CB didapati lebih baik dan berkesan berbanding dengan kaedah sitologi yang lain.

Untuk objektif 2, sebanyak 82 ekor lembu pedaging postpartum pada 20-30 hari pascaberanak, telah digunakan dalam kajian ini. Semua lembu diperiksa oleh palpasi transrectal, dan koleksi rembesan faraj. Sampel swab endometrial untuk sitologi dan bakteriologi telah dikumpul menggunakan CB. Sistem empat gred (0 = lendir jelas, 1 = lendir yang mengandungi tompok-tompok nanah, 2 = lelehan termasuk <50% nanah, dan 3 = melibatkan > 50% nanah) digunakan untuk mengkategorikan rembesan faraj lembu-lembu ini. Daripada jumlah 82 ekor lembu yang dikaji, 11% (9/82) mempunyai rembesen faraj gred 1-3 dan menunjukkan mempunyai endometritis klinikal (CE), sedangkan sembilan daripada 73 lembu yang sihat secara klinikal (12.32%) didiagnosis dengan endometritis subklinikal (SCE ,  $\geq$  8% PMN). *Escherichia coli* adalah bakteria yang paling biasa diasingkan dari SCE (42%) dan lembu CE (38%), yang jauh lebih tinggi (P < 0.05) daripada lembu yang sihat (14.6%). Ujian kesensitifan antimikrobial yang dinilai berdasarkan kesan perencatan pertumbuhan bakteria in vitro menunjukkan kebanyakan bakteria yang diasingkan sensitif terhadap enrofloxacin dan tetracycline.

Untuk membandingkan aktiviti ovari antara lembu yang menghidapi SCE dan lembu yang sihat, dan juga untuk menentukan interaksi antara SCE dan sitokin terpilih, protein fasa akut (APP). A sejumlah 96 daging lembu pasca lahir dan 52 lembu tenusu Friesian Sahiwal telah digunakan. Semua lembu postpartum diperiksa mingguan secara palpasi transrektum bermula dari minggu 3 hingga minggu ke-16 untuk menilai involusi rahim, simetri tanduk rahim dan penyambungan semula aktiviti ovari dengan mengesan folikel-folikel yang membesar pada kedua-dua ovari. Sampel endometrial dikumpulkan menggunakan teknik CB antara hari ke-22 dan hari ke-28 selepas anak lembu dilahirkan untuk mengenal pasti lembu dengan SCE. Kejadian SCE adalah lebih tinggi 15.3% (8/52) dalam kumpulan lembu tenusu daripada kumpulan lembu pedaging 12.5% (12/96) pada minggu 4 postpartum. Dua belas lembu pedaging dan 8 lembu tenusu yang sihat dipilih secara rawak sebagai kawalan untuk membandingkan dengan lembu yang didiagnosis dengan SCE. Sampel darah dikumpulkan dari SCE dan lembu yang sihat dari minggu 3 hingga minggu 7 untuk memeriksa tahap serum progesteron, IL-6, IL-8 dan haptoglobin (Hp). Hasil menunjukkan anestrus postpartum yang berpanjangan dalam lembu pedaging postpartum berkaitan rapat dengan pemberhentian aktiviti ovari, yang menyebabkan peningkatan hari terbuka. Kepekatan progesteron adalah kurang daripada 1 ng/ml dalam kedua-dua endometritis dan lembu sapi yang sihat. Walau bagaimanapun, kepekatan IGF-1 serum lebih tinggi dalam lembu yang sihat berbanding dengan lembu pedaging SCE walaupun tidak penting. Dalam lembu tenusu, pemulihan aktiviti ovari adalah lebih cepat pada lembu yang sihat  $(20.5 \pm 0.9)$ hari) daripada SCE  $(37.1 \pm 0.7 \text{ hari})$  postpartum dan tempoh diantara masa beranak

dan ovulasi pertama jauh lebih pendek pada lembu yang sihat  $(29.4 \pm 0.7 \text{ hari})$ daripada lembu dengan SCE  $(47.5 \pm 0.9 \text{ hari})$ . Keputusan menunjukkan tahap sitokin proinflamasi yang meningkat (IL-6 dan IL-8) dalam lembu dengan SCE (P <0.05) berbanding dengan lembu yang sihat pada minggu ke-4 hingga ke-7 postpartum dalam kedua-dua kumpulan lembu pedaging dan tenusu. Tahap Hp dalam kumpulan lembu pedaging dan tenusu adalah lebih tinggi (P < 0.05) dalam lembu dengan SCE daripada lembu yang sihat pada kebanyakan minggu 4 -7 tempoh postpartum.

Akhir sekali, menggunakan ultrasonografi sebagai alat diagnostik untuk mendiagnosis SCE berbanding kaedah sitologi endometrial telah dinilai pada 53 ekor lembu postpartum. Kajian ini dijalankan antara hari postpartum ke-20 dan ke-35 (pada minggu ke-4 dan 5) postpartum menggunakan kaedah pemeriksaan ultrabunyi dan pemeriksaan endometrium CB untuk mendiagnosis SCE. Keputusan menunjukkan bahawa kaedah ultrabunyi adalah kaedah yang berguna dan praktikal untuk mendiagnosis endometritis pada minggu ke-4 dan 5 postpartum, terutama sekali apabila digunakan bersama pernilaian pengumpulan cairan intrauterin dan diameter serviks (≥5 cm).

Secara keseluruhan, kajian menunjukkan bahawa kelaziman SCE dalam lembu pedaging adalah rendah dan kaedah cytobrush didapati merupakan teknik yang unggul dan berkesan untuk mendapatkan sampel sitologi endometrium. *E. coli* merupakan faktor risiko utama yang dikaitkan dengan SCE dalam lembu pedaging. Ujian kepekaan antimikrobial menunjukkan bahawa kebanyakan bakteria yang diasingkan sensitif terhadap enrofloxacin dan tetracycline. Tahap IL-6, IL-8, dan Hp adalah lebih tinggi dalam lembu dengan SCE berbanding dengan lembu yang sihat, menunjukkan potensi mereka sebagai penanda diagnostik untuk SCE. Aktiviti ovari adalah lebih cepat dalam lembu tenusu yang sihat daripada lembu pedaging yang sihat dan lembu endometritis. Anestrus postpartum yang berpanjangan adalah punca paling biasa meningkatkan kadar beranak kepada tempoh penghamilan dan prestasi pembiakan lembu pedaging.

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I certify that a Thesis Examination Committee has met on 16 May 2018 to conduct the final examination of Salah Noori Mohammed on his thesis entitled "Diagnosis of Subclinical Endometritis and Subsequent Reproductive Status in Postpartum Cattle" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

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Date: 28 June 2018

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# LIST OF ABBREVIATIONS

	AI	Artificial insemination
	BA	Blood agar
	BCS	Body condition score
	BHBA	β-Hydroxybutyric acid
	CB	Cytobrush
	CE	Clinical endometritis
	CI	Calving interval
	CL	Corpus luteum
	CS	Cotton swab
	CTE	Cytological endometritis
	DF	Dominant follicle
	FSH	Follicle stimulate hormone
	GnRH	Gonadotrophin releasing hormone
	E coli	Escherichia coli
	ELISA	Enzyme-Linked Immunosorbent Assay
	Нр	Haptoglobin
	HPF	High-power field
	КК	Kedah-Kelantan
	IL-6	Interleukin-6
	IL-8	Interleukin-8
	LH	Luteinizing hormone
	LP	Luteal phase
	LPS	Lipopolysaccharide
	LVF	Low volume fluid
	MCA	MacConkey Agar
	NEB	Negative energy balance
	NaCl	sodium chloride
	NEFA	Nonesterified fatty acid
	P4	Progesterone
	PMN	Polymorphynuclus
	PGF2a	Prostaglandin F2 alaph

RIA	Radioimmunoassay
rpm	Revolution per minute
SAA	Serum amyloid A
SCE	Subclinical endometritis
SPSS	Statistical package for social science
UPM	Universiti Putra Malaysia
US	Ultrasonography



#### **CHAPTER 1**

#### **INTRODUCTION**

Reproduction is considered as one of the most important features of cattle production. Studies have shown that many cows do not achieve peak reproductive performance and thus, result in a significant economic loss (Thatcher *et al.*, 1996; LeBlanc *et al.*, 2002; Galvao *et al.*, 2010a). Approximately, 75% of postpartum disorders in cattle happen during the first 30 days after parturition (LeBlanc *et al.*, 2006). There are many disorders and diseases like dystocia and uterine infection related to the postpartum period (McDougall, 2001; Sheldon *et al.*, 2009), impairment of postpartum immune activity (Hammon *et al.*, 2006), hormonal and metabolic alterations (Bauman and Currie, 1980; Yimer *et al.*, 2010), energy balance (Drackley, 1999).

The uterus after calving is exposed to several types of microbial contamination and this causes many postpartum uterine diseases (Sheldon et al., 2006; Evans and Walsh, 2011). Metritis is an acute inflammatory reaction mostly due to bacterial infection of the uterus during the first few weeks after parturition. On the other hand, endometritis is a chronic condition of the cows due to incomplete clearance of the bacterial contaminants or due to persistent bacterial pathogens in the uterus (Sheldon et al., 2004). Clinically, it is manifested by a substantial increase in the number of polymorphonuclear leukocytes (PMN) in the uterus (Barlund et al, 2008) and has been classified into clinical and subclinical types (Sheldon et al., 2006). Clinical endometritis (CE) is associated with purulent or mucopurulent uterine discharge, 21 to 26 days postpartum. While the presence of more than 18% of polymorphonuclear (PMN) cells in uterine cytology samples collected 21–33 days postpartum or more than 10% PMNs in samples taken at days 34-47 is seen in cases of subclinical endometritis (SCE) (Kasimanickam et al., 2004). The incidence of CE and SCE is high and has been reported by many authors (Gilbert et al., 2005; Dubuc et al., 2010; Plöntzke et al., 2010; McDougall et al., 2011). For instance, more than 40% of cows were reported to have various degrees of uterine disease one-week post-calving. The incidence of reported cases, however, varied between 36-50% in cow farms surveys (Zwald et al., 2004). Additionally, about 20% of cows were reported to have suffered from systemic signs of metritis (Benzaquen et al., 2007) and more than 15% of cows that suffered from metritis developed clinical endometritis while about 30% converted to subclinical endometritis after three weeks post calving (Gilbert et al., 2005; Sheldon et al., 2006). In more than 90% of cows, several species of microorganisms can be isolated few weeks after parturition (Földi et al., 2006). However, the majority of the cows can clear these bacteria spontaneously (LeBlanc et al., 2002). Initial contamination of the uterus in the beginning of the postpartum period with Escherichia coli paves the way for subsequent infection with other bacteria or viruses (Donofrio et al., 2008). However, cases of acute endometrial lesions are basically caused by Arcanobacterium pyogenes (Sheldon et al., 2009) which is the most common prevalent microbial in the late postpartum period



(Williams et al., 2005) and cohabits synergistically with other anaerobe bacteria, like Fusobacterium necrophorum (Földi et al., 2006). Most pathogenic bacteria isolated from postpartum cows with uterine diseases are Escherichia coli, Prevotella sp. (Sheldon et al., 2006). Also, many studies isolated Streptococcus sp., Staphylococcus sp., or non-coliform aerobic gram-negative rods (Kaczmarowski et al., 2004; Jadon et al., 2005). To choose a suitable and effective antimicrobial drug to treat postpartum uterine diseases, it is very important to know the sensitivity of the pathogen to antibiotics. Infiltration of endometrium by microorganisms induced inflammatory responses characterized by the secretion of proinflammatory factors such as cytokines and chemokines. This lead to the influx of neutrophils and culminated with bacterial clearance (Hussain, 1989). The endometrium is considered as the first line of immune defense against invading microorganisms, the endometrium is fortified by innate immune capabilities such as Toll-like Receptors (TLRs1 to 10). The endometrium is activated to elicit a number of proinflammatory immune factors such as interleukin 1, 4 and 6 (IL-1, IL-4, and IL-6) which helps to attract and mobilize more neutrophils and monocytes to the endometrium (Davies et al., 2008). Thus, assessing these cytokines, chemokines, and acue phase proteins in the blood could relate to the endometrial clinical condition of these animals in our study

Predisposing factors like the physiological status of the cow and accompanied by energy deficiency increases the susceptibility of the dairy cows to microbial and metabolic diseases like endometritis, ketosis, milk fever, displaced abomasum and retained placenta (Duffield, 2000). A complicated relationship is present among factors that affect uterine health and postpartum cows (Kinsel, 1996). Energy balance, particularly negative energy balance, has an immediate effect on reproductive performance in bovine (Grummer et al., 2010; Cardoso et al., 2013). Hammon et al. (2006) reported that uterine infection is accompanied with negative energy balance that begins prior to parturition and continues through to the early stage of lactation and reported that cows with acute negative energy balance had reduced neutrophil function. Studies have shown that cows with uterine infection manifest a greater degree of negative energy balance represented by increasing nonesterified fatty acids (NEFA) and beta-hydroxybutyrate (BHBA) (Hammon et al., 2006) Ovarian activity is known to play a crucial role in changing the reproductive performance of a cow, first resulting in pregnancy and then calving. Early onset of ovarian activity immediately following calving is important for the onset of timely conception. Uterine diseases at early postpartum period inhibit ovarian granulosa cell activity as well as the growth of dominant follicles (Williams et al., 2007) and this causes a suppression in synthesis and release of estradiol resulting in change in follicle lifespan and ovulation (Herath et al., 2007).

Newer techniques like uterine cytology have also been used to improve and obtain an accurate diagnosis of endometritis cases in apparently healthy cows. Both cytobrush and the small volume uterine lavage technique can be used to get endometrial cells samples from the uterus (Lincke *et al.*, 2007). Cytobrush cytology is considered as the gold standard when compared to other methods (Drillich *et al.*, 2004). The percentages of PMN in the total number of endometrial cells in the uterine sample provide sufficient evidence for subclinical endometritis. Threshold point percentage for the proportion of PMN varied from 5 to 18% (Galvao *et al.*, 2009). Ultrasonography is another technique used to reveal the level of accumulation of intrauterine fluid associated with endometritis (Kasimanickam *et al.*, 2004). It also provides useful information that facilitates the immediate detection of endometritis. The application of ultrasonography techniques has shown that accumulation of intrauterine fluid is associated with delayed intrauterine involution and increased bacterial growth (Mateus *et al.*, 2002).

#### **Problem statement**

At present, there is a lack of study about the occurrence of SCE in beef and dairy cows in Selangor state, Malaysia. The treatment failure of uterine infection (possibly due to resistance to antibiotics), and lack of quick and standard diagnostic methods for SCE that depends on PMNs, warranted the need to conduct this study.

#### Justification

As mentioned above, in Malaysia, there is a paucity of information on SCE in postpartum cows, associated bacterial contaminants and their spectra of sensitivity to antibiotics, diagnosis, as well as effects of SCE on reproductive performance. There is lack of studies about uterine infections like clinical and subclinical endometritis in Serdang, especially in TPU and resumption of ovarian activity during the postpartum period. Our study also focused on investigating the potential risk factors that could affect the occurrence of endometritis and reproductive statuses such as dystocia, parity, body condition score as well as isolation of pathogenic uterine bacteria after 4 weeks postpartum. To choose a suitable and effective antimicrobial drug to treat endometritis cows, it is very important to know the sensitivity of the bacteria to antibiotics. Also, the study tried to look for the interaction between serum proinflammatory cytokines and acute phase proteins and SCE in postpartum cows and the possibility to use them as biomarkers for endometritis in cattle without any clinical signs of other clinical diseases. Our population target of current study involved all calving cows in TPU and some farms in the vicinity.

## **Research objectives**

The main objectives of this study were:

- 1. To evaluate three different cytological methods to obtain endometrial samples.
- 2. To correlate the bacteriological findings with vaginal discharges, and endometrial cytology for endometritis detection in postpartum beef cows.
- 3. To compare the postpartum ovarian activity and energy balance between SCE and healthy cows
- 4. To measure the interactions between SCE and selected cytokines, and acute phase proteins (APPs)
- 5. To compare between the use of ultrasonography (US) and endometrial cytology (EC) to diagnosis endometritis in postpartum beef cows.

## **Research hypotheses**

The major research hypotheses can be outlined as follows:

Ho: There is no significant difference among three different endometrial cytological sampling methods and ovarian resumption between SCE and healthy postpartum cows

Ha: There is a significant difference among three different endometrial cytological sampling methods, and the correlation among endometrial cytology (PMN %), vaginal discharges and bacterial findings from postpartum cows. Also, the study proposes significant differences between SCE and healthy cows in ovarian resumption, energy balance, and interaction with selected cytokines and acute phase proteins.

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