Tropical Animal Health and Production (2020) 52:3697–3706
https://doi.org/10.1007/s11250-020-02406-3

REGULAR ARTICLES

Serum biochemical profile in buffalo endometritis and impact of treatment with PGF2α and intrauterine gentamicin infusion on postpartum reproductive performance

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Received: 14 May 2020 / Accepted: 16 September 2020 / Published online: 28 September 2020

Abstract

Improving reproductive performance of repeat breeder buffalo cows due to clinical endometritis is crucial in overcoming infertility problems in buffalo cows. The aim of the present study was to use PGF2α and/or gentamicin 10% for treatment of endometritis and to determine biochemical parameters in serum that could be used to diagnose endometritis in buffalo cows. A total of 64 anestrous buffalo cows were assigned into one of five treatment groups: group one ($n = 9$) buffalo cows were physiological normal cows and served as a control group; group 2 buffalo cows had endometritis, but were not treated ($n = 10$); group 3 buffalo cows had endometritis and were treated with intrauterine delivery of 100 ml of a 10% gentamicin sulfate solution in three times within 1 week ($n = 15$); group 4 buffalo cows received two I.M. doses of PGF2α (2 ml Estrumate IM) at the time of corpus luteum dominance ($n = 15$) (treatment 4 does not make sense as you stated that the cows were in anestrus) on the ovary; group 5 buffalo cows received two IM doses of PGF2α at an 11 day interval and the 10% gentamicin solution as described for group 3. Serum samples were collected from control, pre-treated, and post-treated buffalo cows with endometritis to evaluate the diagnostic biochemical parameters. The days to first estrus (DFE), number of services per conception (S/C), days open (DO), and pregnancy rate (Preg) were the measures for determining reproductive performance for the buffalo cows. The buffalo cows treated by gentamicin and PGF2 exhibited their first estrus earlier than cows in the other four groups of cows. The number of days open for control cows was greater ($P < 0.05$) than for the other groups and the control cows, as were the number of services per conception ($P < 0.05$) and pregnancy rate (30%: $P < 0.05$). The receiver operating characteristic (ROC) curve was used to identify biochemical parameters in serum to predict endometritis. Creatine kinase (CK), aspartate aminotransferase (AST), and concentrations of total bilirubin and immunoglobulins in serum were greater ($P < 0.05$), while serum albumin values were lower ($P < 0.05$) in serum of buffalo cows with endometritis. From the ROC analyses, CK was the most predictable biomarker for endometritis with an area under the curve of 0.889, sensitivity of 80%, and specificity of 100% ($P < 0.001$). In conclusion, the use of gentamicin and PGF2 for treatment of endometritis improves the reproductive performance of buffalo cows, and concentrations of CK serve as an aid for diagnosing endometritis.

Keywords Buffalo · Egypt · Gentamicin · Prostaglandin · Days open · First estrus

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Introduction

Endometritis is a common reproductive disorder of buffalo cows and cattle. This problem affects milk yield and decreases reproductive efficiency. In cows, endometritis is defined as inflammation of the uterine endometrium for 21 days or more postpartum (Sheldon et al. 2009, Raliou et al. 2019). Endometritis may be either clinical or cytological endometritis according to the diagnostic criteria. Clinical endometritis is characterized by vaginal purulent or mucopurulent discharge and no systemic changes (LeBlanc et al. 2002, Sheldon et al.

2006, Bonsale et al. 2018, Arango-Sabogal et al. 2019). The diagnosis of cytological endometritis is based on the presence of a higher percentage of polymorphonuclear leukocytes (> 6%) on uterine cytology when compared with clinically healthy cows (Kaufmann et al. 2009, Machado et al., 2012a, b, Bogado Pascottini et al. 2017).

Clinical endometritis is highly prevalent in dairy cows with high milk yields and characterized by decreasing reproductive performance due to lower pregnancy rates, extended postpartum intervals to pregnancy, increased culling rates, and economic losses (Hay et al. 2019) (Helfrich et al. 2020) (Armengol and Fraile 2015) (Bartlett et al. 1995). The incidence of clinical endometritis ranges from 5.0 to 30% and affects about 20% of lactating dairy cows (Moraes et al. 2017) (Machado et al., 2012a, b). The causes of endometritis are multifactorial and more frequent during the peri-parturient period, (2 weeks pre-partum to 3 weeks post-partum). The incidence of uterine bacterial contamination post-partum increases and persists for 2 to 3 weeks. This is an inevitable and naturally occurring as the cervix dilates and the vestibule and vagina relaxes, resulting in the impairment of natural barriers and bacterial defenses after parturition (Pérez-Báez et al. 2019) (Cui et al. 2019) (Miranda-CasoLuengo et al. 2019) (Sheldon et al. 2019).

A number of risk factors play an important role in the prevalence of uterine diseases. These risk factors may be associated with damage to the uterus, metabolic stress, and/or deficits in hygiene (LeBlanc 2020) (Kelly et al. 2020) (Hay et al. 2019) (Giuliodori et al. 2017). The risk factors that are associated with uterine infection are those that likely lead to some trauma of the endometrium due to delivery of stillborn, twin, male and beef-sire calves, dystocia, cesarean section, and retention of the placenta (Gohar et al. 2018).

Other factors include endocrine disorders, deficiencies in selenium, vitamin E, vitamin A, and β-carotene, failure of the calf to suckle, hypocalcemia, and poor hygiene that predispose cows to uterine diseases during the early post-partum period (Borsberry and Dobson 1989, Spears 2000, Venjakob et al. 2018).

To overcome this problem, clinical endometritis in buffaloes was managed by the hormonal treatment either PGF2α (Lefebvre and Stock 2012) or PGF2α and oxytetracycline (Azawi et al. 2008, Gohar et al. 2018, Nehru et al. 2019), intrauterine infusion of ceftiofur (Nehru et al. 2019), intrauterine administration of mannose or bacteriophage (Machado et al., 2012a, b), intrauterine infusion of honey (M, 2019), and intrauterine infusion of oxytetracycline (Gohar et al. 2018).

In cows, the degree of endometritis is correlated with increases in creatine kinase (CK) and aspartate aminotransferase (AST) activities in serum (Sattler and Fürll 2004). There is also a positive relationship between uterine diseases and concentrations of albumin and blood urea nitrogen (BUN) (Walsh et al. 2007); (Raboisson et al. 2014, Ghanem et al. 2016). On other hand, Gahlot et al. 2018 (Gahlot et al. 2018) found that the concentrations of urea and bilirubin were altered in the uterine fluid of buffaloes with subclinical endometritis. The use of gentamicin for treatment of endometritis in buffaloes is not well documented. Therefore, the aim of the current study was to investigate changes in biochemical profiles in serum from buffalo cows with endometritis and evaluate the effects of treatment of cows with endometritis with PGF2α and/or intrauterine infusion of gentamicin on postpartum reproductive performance.

Material and methods

Animals and data collection

Animal experiments described in this article were conducted in accordance with the Guiding Principles for the Care and Use of Research Animals Veterinary Medicine Faculty, Mansoura University, Egypt (R. 35). Sixty-four buffalo cows, 3–7 years old and experiencing 1–5 parities were used in this study. The buffalo cows were in the village system of the Dakahlia Governorate from January 2016 until December 2018. The cows were fed a balanced ration consisting of ad libitum Berseem in winter and Darawa in summer and about 20 kg wheat straw and 5–8 kg concentrate mixture and milked two times daily. All animals were vaccinated and dewormed against the common infectious and parasitic diseases. Buffalo cows were admitted to our veterinary teaching clinic, Veterinary Medicine Faculty, Mansoura University, Egypt suffering from repeat breeder syndrome.

Estimation of serum biochemical parameters

The activity of CK and aspartate aminotransferase (AST) was measured by using Cobas Test Reagent, USA kits and Vitro Scientist, Germany kits, respectively. Total proteins and albumin were assayed using Stanbio Laboratory, USA kits. Concentrations of immunoglobulins were calculated by subtracting serum albumin from total protein. Serum urea and bilirubin kits were obtained from Diamond Company, Egypt. All assays were performed using a spectrophotometer (BM Co. Germany, 5010) according to the manufacturer's instructions.

Diagnosis of endometritis and animal grouping

The experimental animals experienced normal parturition, but had a history of 3–4 inseminations not resulting in pregnancy indicative of repeat breeder syndrome after natural service. The cows also exhibited watery and/or mucopurulent vaginal discharges. Ultrasound imaging was used for further diagnosis

of endometritis. The detection of intrauterine fluid using the SonoScape A5 ultrasound machine® (Shenzhen, Guangdong, China) is considered reliable for diagnosing endometritis (Kaya et al. 2016, Kelly et al. 2020).

The examination of buffaloes that came to our veterinary clinic was done when cows were in estrus. At that time, a 10 ml blood sample was obtained from the jugular vein. Blood samples were centrifuged at 3000 rpm for 20 min and the serum was stored at − 20 °C until analyzed for biochemical markers. Failure to conceive was diagnosed if the cow was not pregnant based on rectal examination and ultrasound imaging or if a subsequent breeding was required 17 to 24 days post-breeding. The buffalo cows were allocated into five groups and received one of the following treatments:

Group 1(control) cows with a normal parturition and physiologically normal uterus ($n = 9$);
Group 2 (endometritis control) cows with endometritis and did not receive any treatment ($n = 10$); group 3 cows received an intrauterine infusion of 10% gentamicin sulfate® 10% (Apigent, Amoun Pharmaceutical Co. El-Obour City, Cairo, Egypt) solution in 100 ml physiological saline every 3 days from the onset of estrus according to Kumar et al. (2019) ($n = 15$).
Group 4 cows received two intramuscular injections of 2 ml Estrumate® (500 mcg cloprostenol: Schering Plough, USA) 11 days apart in the presence of a corpus luteum ($n = 15$); and group 5 cows received intrauterine infusions of a 10% gentamicin sulfate solution as in group 3 and 2 injections of Estrumate at an 11 day interval ($n = 15$).

Buffalo cows were bred at the second estrus after evaluation of treatment outcomes based on rectal examination of the ovaries and uteri, the appearance of clear, translucent vaginal discharge, or no mucus 8–16 h after onset of estrus and normal reproductive organs based on ultrasound imaging. The dependent variables for reproductive performance were interval between treatment and first estrus, calving to conception (DO, the number of days between calving and conception), the number of services per conception (SC, defined as the number of services that a cow required to conceive) and pregnancy rate (Elmetwally et al. 2016, Elmetwally 2018). Pregnancy was diagnosed by rectal examination at 2 months post-breeding according to Gohar et al. 2018 (Gohar et al. 2018).

Statistical analysis

Normality of quantitative parameters (days to first estrus, days open, number of services per conception) was assessed using normal probability plots and the KolmogorovSmirnov test generated with the UNIVARIATE procedure of SAS according to Elmetwally et al. (Elmetwally et al. 2018, 2019). All data are reported as means ± SEM. Receiver operating characteristic (ROC) analysis was conducted using MedCalc software (version 16.4.3, Ostend, Belgium). Statistical analyses were done using SAS® (version 9.2, SAS Institute, Cary, NC, USA). For all analyses, $P \leq 0.05$ was defined as significant.

Results

Effects of treatment of cows with endometritis with the combination of gentamicin and PGF2α treatments compared with control cows on biochemical changes in serum

Results for biochemical parameters in serum are summarized in Table 1. CK activity was greater ($P < 0.05$) in cows with endometritis prior to treatment (92.80 ± 2.13 U/l: $P < 0.05$) as compared with values post-treatment (60.80 ± 3.76 U/l) and values for control cows (54.20 ± 3.12 U/l). AST activity in serum was greater ($P < 0.05$) for cows with endometritis prior to treatment (108.01 ± 2.21 U/l) compared with values post-treatment (90.20 ± 2.67 U/l) and when compared with values for control cows (65.20 ± 2.22 U/l). Concentrations of albumin in cows with endometritis were greater prior to treatment and decreased ($P \leq 0.05$) to (2.71 ± 0.17 g/dl) compared with post-treatment values (3.28 ± 0.05 g/dl) and values for control cows (3.31 ± 0.06 g/dl). Concentrations of immunoglobulins in serum were greater ($P \leq 0.05$) in cows with endometritis prior to treatment (4.09 ± 0.22 g/dl) in contrast to values post-treatment (3.36 ± 0.15 g/dl) and in control cows (3.21 ± 0.07 g/dl). However, total protein and concentrations of urea in serum of cows with endometritis were not affected by treatment and were not different from values for control cows ($P > 0.05$). Prior to treatment for endometritis, cows had

Table 1 Some selective serum biochemical parameters of normal, pre-treated, and post-treated endometritis-affected buffaloes

		Groups	
Parameters	Control	Pre-treated	Post-treated
CK (U/l)	54.20 ± 3.12^{b}	92.80 ± 2.13^{a}	60.80 ± 3.76^{b}
AST (U/l)	65.20 ± 2.22^{c}	108.01 ± 2.21^{a}	90.20 ± 2.67^{b}
Total protein (g/dl)	6.52 ± 0.09^{a}	6.80 ± 0.11^{a}	6.64 ± 0.12^{a}
Albumin (g/dl)	3.31 ± 0.06^{a}	2.71 ± 0.17^{b}	3.28 ± 0.05^{a}
Globulin (g/dl)	3.21 ± 0.07^{b}	4.09 ± 0.22^{a}	3.36 ± 0.15^{b}
Urea (mg/dl)	42.56 ± 1.65^{a}	48.06 ± 1.28^{a}	46.02 ± 1.49^{a}
Bilirubin (mg/dl)	0.61 ± 0.01^{b}	0.74 ± 0.02^{a}	0.62 ± 0.03^{b}

Data are expressed as mean ± standard error of the mean ($n = 5$)

Means in the same row with different superscripts are significantly different ($p < 0.05$)

CK, creatine kinase; *AST*, aspartate aminotransferase)

greater $P < 0.05$) concentrations of bilirubin (0.74 ± 0.02 mg/dl) compared with post-treatment values (0.62 ± 0.03 mg/dl) and values for control cows (0.61 ± 0.01 mg/dl).

ROC curve analysis

The area under curve (AUC) was greater for cows with endometritis for CK (Fig. 2A: AUC = 0.889, $P < 0.001$), urea (Fig. 2B: AUC = 0.811, $P = 0.005$), and total bilirubin (Fig. 2D: AUC = 0.783, $P = 0.032$), followed by albumin (Fig. 3A: AUC = 0.778, $P = 0.018$), total protein (Fig. 3B: AUC = 0.722, $P = 0.075$), globulin (Fig. 3C: AUC = 0.767, $P = 0.026$), and AST (Fig. 2C: AUC = 0.644, $P = 0.341$). The sensitivity (Se) %, specificity (Sp) %, and 95% confidence intervals (CI) were greater for CK (Se: 80%, Sp: 100%, CI: 0.791–0.985), total bilirubin (Se: 70%, Sp: 100%, CI: 0.538–0.936), albumin (Se: 60%, Sp: 100%, CI: 0.532–0.933), globulin (Se: 80%, Sp: 100%, CI: 00.520–0.927), and AST (Se: 60%, Sp: 100%, CI: 0.396–0.846), while urea (Se: 90%, Sp: 77.78%, CI: 0.568–0.951) and total protein (Se: 70%, Sp: 77.76%, CI: 0.473–0.899) had lower specificities % and 95% confidence intervals.

Overall, the AUC of 0.889 for CK (Se: 80%, Sp: 100%, CI: 0.791–0.985) indicates that it could serve as a valuable biomarker for differentiating endometritis-affected from healthy buffalo cows ($P < 0.001$). As well, the concentrations of total bilirubin, albumin, and globulin in serum, had high sensitivity and specificity percentages that may be used to support values for CK in the diagnosis of uterine tissue diseases including endometritis.

Effects of gentamicin and PGF2α treatments on postpartum reproductive performance in buffalo cows

a. Days to the first estrous

The buffalo cows treated with gentamicin and PGF2 exhibited fewer days to the first estrus (38.4 ± 1.35, $P < 0.05$) than for other treatment groups and control cows (gentamicin: 49.86 ± 1.19; PGF2: 51 ± 2.9, control: 51.55 ± 1.44 and endometritis control: 84.33 ± 1.65: Fig. 1A).

b. Days open

The number of days open for endometritis control buffaloes was greater (153.44 ± 2.98: $P < 0.05$) than for the other treatment groups (control: 77.22 ± 7.43; gentamicin: 126 ± 2.42; PGF2: 127.33 ± 2.9 and gentamicin + PGF2: 120.33 ± 2.69: Fig. 1B)

c. Services per conception

The buffalo cows in the control endometritis group required a greater number of services per conception (4.3 ± 0.31: $P < 0.05$) than control cows and cows in the other treatment groups (control: 2.22 ± 0.25; gentamicin: 2.06 ± 0.18; PGF2: 2.26 ± 0.23 and gentamicin + PGF2: 1.93 ± 0.20: Fig. 1C).

d. Pregnancy rate

The pregnancy rates were greater ($P < 0.05$) for buffalo cows following treatment with gentamicin only (73%) and gentamicin + PGF2 (80%) compared with control cows (66%) and cows receiving PGF2 alone (66%) (Fig. 1D). The lowest ($P < 0.05$) pregnancy rate was for buffalo cows with endometritis that were not treated (30%) (Figs. 2, 3).

Discussion

Endometritis is one of the most common reproductive disorders in buffalo cows and *Bos taurus* cows. Endometritis had a significant impact to decrease milk yield and reproductive efficiency including the interval between treatment and conception, days open, number of service per conception, pregnancy rate, culling rate, and economic losses (Rhoads et al. 2004, Sheldon et al. 2006).

Results of the current study showed that CK and AST are useful biomarkers for detection of endometritis; however, CK is much more sensitive than AST due to differences in the activities of these enzymes in uterine tissue (Sattler and Fürll 2004). Results of the present study are the first to reveal significant increases in CK and AST activities in serum of buffalo cows with endometritis that likely reflect the inflammatory status of the uterine endometrium (Azawi et al. 2008).

Albumin is considered a negative acute-phase protein with subnormal concentrations indicating impaired liver function due to increases in synthesis of acute-phase proteins (Bertoni et al. 2008). Results of the present study indicated significant changes in total protein in serum of cows with endometritis. Interestingly, concentrations of albumin decreased while concentrations of globulins increased in the serum of the buffalo cows with endometritis prior to treatment compared with values post-treatment and values for control cows. Similarly, lower concentrations of albumin and higher globulin levels were reported for serum from pasture-grazed cows with endometritis (Green et al. 2009, Burke et al. 2010, Raliou et al. 2019). The reduction in albumin may be a risk factor for fat infiltration of the liver as reported in cases of uterine diseases (Zerbe et al. 2000). The higher level of serum globulin may be attributed to the elevation in the serum acute-phase proteins such as amyloid A and haptoglobin in cows with subclinical uterine inflammation (Ahmadi et al. 2018). Moreover, greater concentrations of globulins in serum reflect increased activity

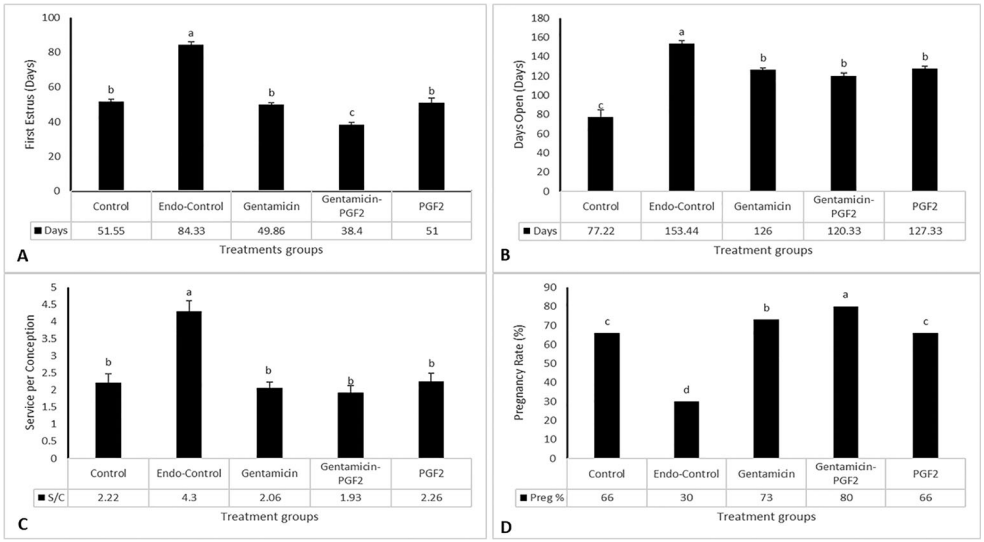

Fig. 1 Effect of different treatments on postpartum reproductive performance in buffalo cows with endometritis. A Days to the first estrus; B days open; C number of services per conception; D pregnancy rate. Significant effects are indicated by different superscript letters ($P < 0.05$). All quantitative data are presented as means and SEM

of immunocompetent cells in the uterus, primarily in the circumferential blood (Brodzki et al. 2018).

There are negative impacts of increased levels of bilirubin and urea in serum on the uterine environment and the prevalence of endometritis (Benedet et al. 2019, Gruber and Mansfeld 2019). In the present study, the concentrations of urea in serum changed significantly and bilirubin was elevated prior to treatment of buffalo cows prior to treatment as compared with values post-treatment and for control cows. A previous study reported insignificant difference in urea serum from cows with and without endometritis (Burke et al. 2010). Concentrations of total bilirubin concentration were reportedly greater in buffalo cows with subclinical endometritis (Gahlot et al. 2018, Bogado Pascottini et al. 2020, LeBlanc

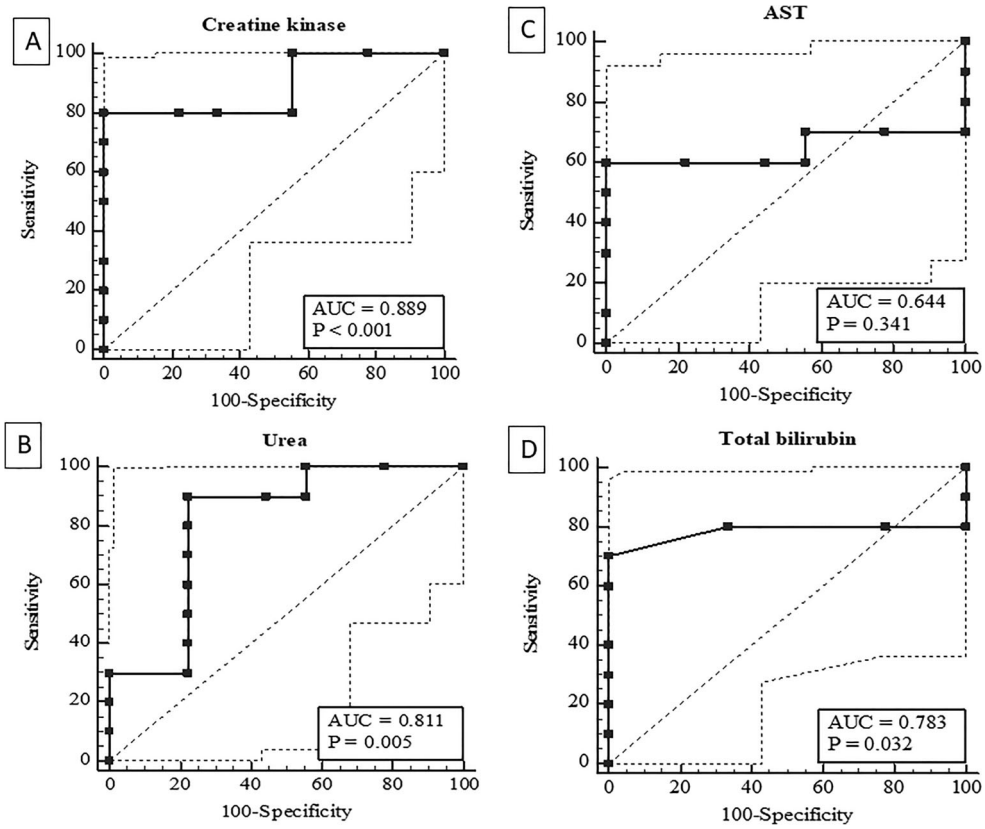

Fig. 2 The area under curve (AUC) for cows with endometritis for serum creatine kinase (CK: A), urea (B), aspartate aminotransferase (AST: B), and total bilirubin (D)

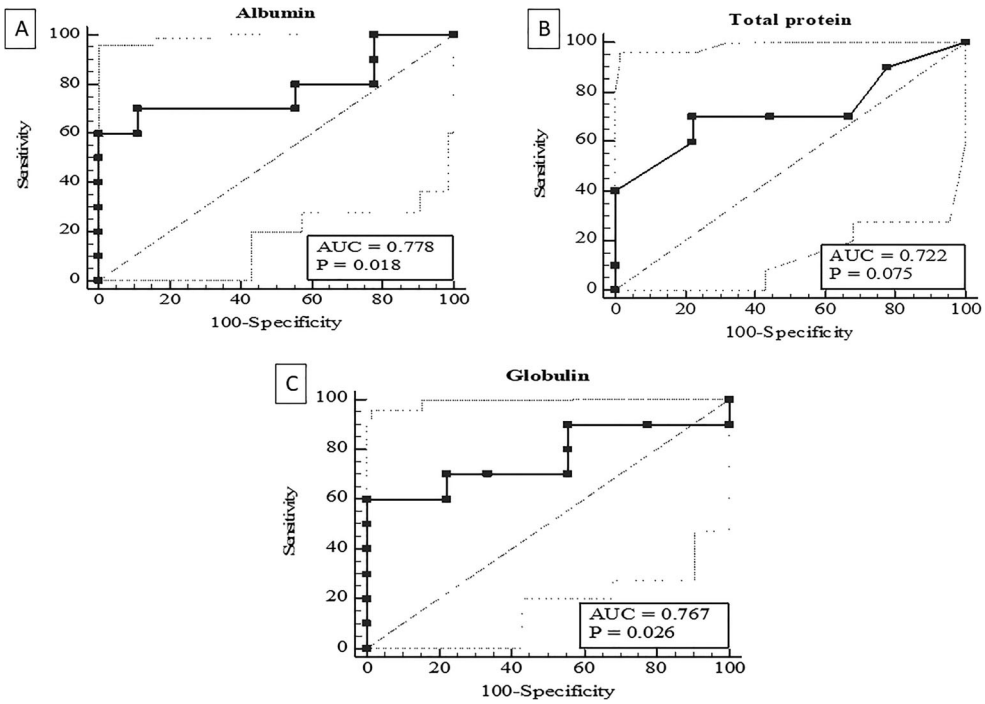

Fig. 3 The area under curve (AUC) for cows with endometritis for albumin (A), total protein (B), and globulin (C)

2020) and this may be related to alterations in liver function due to systemic toxins resulting from postpartum diseases that may result in hepatic failure (LeBlanc 2020).

In the current study, the metabolic parameters including CK, AST, total bilirubin, and globulin increased significantly while albumin decreased in buffalo cows with endometritis. The activity of CK may also increase in serum, skeletal muscle, and cardiac muscle in various diseases including diseases of the uterus (Sattler and Fürll 2004). Furthermore, CK, AST, and bilirubin increase in response to liver damage and Cholestasis (McSherry et al. 1984, Cebra et al. 1997). The decline in concentrations of albumin and increases in concentrations globulins was reported for cows suffering from metritis, mastitis, and other diseases (Overton et al. 2017).

Environmental variables and nutrition may also influence the biochemical parameters in serum of dairy cows. (Hanuš et al. 2018) revealed that values for calcium, AST, ALT, triglycerides, and cholesterol in serum of dairy cows differ among seasons especially during the first and third lactations (Hanuš et al. 2018).

In the current study, the Roc curve analysis was used for the first time to identify biochemical markers that are more specific and sensitive to endometritis in buffalo cows. The ROC analysis confirmed that CK (AUC: 0.889, Se: 80%, Sp: 100%, CI: 0.791–0.985) had greater sensitivity and specificity for predicting endometritis. Then, total bilirubin (AUC = 0.783, Se: 70%, Sp: 100%, CI: 0.538–0.936), albumin (AUC = 0.778, Se: 60%, Sp: 100%, CI: 0.532–0.933), and globulin (AUC = 0.767, Se: 80%, Sp: 100%, CI: 00.520–0.927) were less sensitive and specific. Although AST was significantly elevated in endometritis, the roc curve analysis showed it to be less sensitive (AUC = 0.644, Se: 60%, Sp: 100%, CI: 0.396–0.846). These variations may be correlated with variations in activities of these enzymes in the uterine tissue (Sattler and Fürll 2004).

In the current study, the buffalo cows treated with a combination of gentamicin and PGF2 had the fewest days to first estrus and higher pregnancy rates (80%) compared with cows treated with two injections of PGF2α (66%)or not treated (33%). Previous studies reported similar pregnancy rates (65.38%) after using PGF2α in treatment of clinical endometritis. Previous reports (Jeremejeva et al. 2012, López-Gatius et al. 2015, Voelz et al. 2018) indicated that the systemic administration of PGF2α significantly improved the pregnancy rate of cows with clinical endometritis, perhaps due to luteolysis of an active corpus luteum in cyclic cows that decreased concentrations of progesterone in serum. Furthermore, the estrogen in serum and increases in contractions of the myometrium are favorable for elimination of uterine infection (LeBlanc et al. 2002) (Sheldon et al. 2006) (Walsh et al. 2007) (Bogado Pascottini et al. 2020) (LeBlanc 2020). In addition, PGF2α causes relaxation of the cervix and expulsion of uterine contents (Hirsbrunner et al. 2003, Pascottini and LeBlanc 2020). Exogenous PGF2α may also enhance immune functions or increase uterine motility that help the uterus to resolve infections in animals that lack active corpus lutea (Hirsbrunner et al. 2003). Regression of CL allows the development of dominant follicle on the ovary and induces ovulation within 72–96 h after PGF2α administration so that the uterus becomes more resistant to infections under

the influence of estrogen (Wulster-Radcliffe et al. 2003). Hence, the use of PGF2α may alter the endocrine state of cows to increase microbial resistance inside the uterus and enhance body defense mechanism including greater phagocytic activity and inflammatory responses in the endometrium (Kaufmann et al. 2010). In contrast, some studies found that PGF2α treatment is not effective in the treatment of endometritis (Choudhary et al. 2016, Mandhwani et al. 2017). The difference findings in different studies may be attributed to the hormonal imbalance at the time of inducing estrus as PGF2α controls the estrous cycle via shortening the luteal phase (Wenzinger and Bleul 2012, Nowicki et al. 2017).

Results of the present study clearly indicate that gentamicin is an effective treatment for endometritis in buffalo cows. The reproductive performance of cows was improved after intrauterine infusion of 10% gentamicin and intramuscular injections of PGF2α and was similar to that for buffalo cows without endometritis. Previous studies found similar effects following intrauterine infusion of 10% gentamicin in repeat breeder cows (LeBlanc et al. 2002, Tison et al. 2017). The current result for days open after intrauterine infusion of gentamicin was similar to that reported previously of 121 days (Daniels et al. 1976, Ensley and Hennessey 1979). The effects of gentamicin are attributed to the bactericidal effects through inhibition of synthesis of bacterial proteins (Mingeot-Leclercq et al. 1999, Khair et al. 2018). Gentamicin is one of the most effective intrauterine antibiotics for treatments of chronic or subclinical uterine infections in cattle (Ocal et al. 2004).

The results from the present study of reproductive performance in buffalo cows treated with gentamicin and PGF2α are similar to those reported previously for treatment of clinical endometritis (Jeremejeva 2015). In addition, similar results were obtained following the intrauterine infusion of oxytetracycline and a PGF2α injection for treatment of clinical endometritis (Sheldon and Noakes 1998, Ahmadi et al. 2018). Intrauterine infusion of cephapirin or systemic administration of PGF2α has improved pregnancy rates of cows with clinical endometritis (Kaufmann et al. 2010, Tison et al. 2017, Brodzki et al. 2018). The improvement may be attributed to luteolysis of the corpus luteum after PGF2α injection in cyclic cows resulting in lower progesterone and higher estrogen in serum and increases in myometrial contractions (Copelin et al. 1988, Stevenson and Phatak 2010). These events are favorable for clearance of uterine infections (Nehru et al. 2019). Regression of the corpus luteum allows growth of dominant follicles which results in estrus and ovulation 72–96 h after PGF2α administration. Under the influence of estrogen, the uterus becomes more resistant to infections (Wulster-Radcliffe et al. 2003). In addition, there are positive effects of PGF2α to enhance of phagocytosis, immune function, chemotaxis, cell-mediated cytotoxicity, and lymphocyte function of the uterus due to leukotriene B4 (Lewis 2003, Lefebvre and Stock 2012).

Altogether, the biochemical changes (CK, AST, total bilirubin, and albumin concentrations) in serum serve as an aid for diagnosing endometritis in the buffalo with more specificity for CK. Furthermore, Gentamicin and/or PGF2α tend to improve reproductive performance and are effective for treatment of clinical endometritis in buffalo cows. Hence, producers should pay close attention to prevention and control programs for endometritis in postpartum buffalo cows from both milk production and reproductive efficiency points of view, but also to decrease culling of high producing cows.

Authors' contributions Mohammed Elmetwally: conceptualization, methodology, validation, formal analysis, investigation, data curation, writing–original draft, writing–review, and editing;
Gehad E Elshopakey: conceptualization, analyses for blood, data analyses, writing, review, and editing;
Wael Eldomany: conceptualization, writing–review, and editing;
Ashraf El-Desouky: conceptualization, writing–review, and editing.
Fuller W Bazer: data curation, writing, review, and editing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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