IMPACT OF TREATMENT WITH ANTI-PARASITE (IVERMECTIN) DURING PREPARTUM PERIOD ON MASTITIS AND POSTPARTUM REPRODUCTIVE PERFORMANCE IN BALADI COWS

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SUMMARY

The current investigation was designed to determine the effect of treatment with anti-parasitic (Ivermectin) on mastitis and postpartum reproductive performance of Baladi cows. Twenty-four Baladi cows were used in this study, the cows were divided into two groups. The G1 (n= 12 cows) were injected two months prepartum with two consecutive doses (15- days in- between) of IVOMEC®Plus solution subcutaneously at the rate of 1ml/50kg live body weight (prescribed by the manufacturer), whilst G2 (n= 12 cows) was used as a control group. The present results revealed that the occurrence of mastitis in treated cows group was significantly (P < 0.05) lower (16.7%) than control cows' group (41.7%). The conception rate in treated cows group was significantly (P < 0.05) higher (66.7%) compared with (33.3%) in control group. The time from calving to conception in treated cows was significantly (P < 0.05) lower (86.5±11.4 days) compared to 123.3±13.2 days in the control group (P < 0.05). The occurrence of anestrous was significantly (P < 0.05) lower (25%). The results of this study showed that Ivermectin injection to pregnant Baladi cows during the last two months of pregnancy (at the rate of 1m/50kg live body weight) was useful in reducing the incidence of mastitis, as well as, in enhancing the reproductive performance of the cows.

Keywords: Ivermectin, mastitis, conception rate, days open, anestrous, Baladi cows.

INTRODUCTION

Endo-and ecto-parasites infestation cause high economic losses in livestock especially farm animals. Economic losses are represented by costs of anthelmintics drugs, higher mortality rate, decline in meat, milk, growth rate and fertility (Mendes et al., 2008). Economic loss was estimated by US \$ 3.2 billion per annum worldwide due to liver worm (Fasciola) as one of endo- parasite in the livestock (Spithill et al., 1999). In Brazil, Grisi et al. (2014) reported that economic losses due to cattle external and internal parasite total loss nearly 14.0 million of US\$ annually. Lawrence and Ibarbura (2007) estimated the economic losses of internal parasites (gastrointestinal nematode) control in beef cattle and reported that there was a 34% decrease in the breakeven price for cattle that were not treated by deworming. Mavrogianni et al. (2012) and Mavrogianni et al. (2014) reported that there is a correlation between endo-parasitic infections and increased frequency of clinical or subclinical mastitis during the first two weeks post-partum in ewes. Food and drugs administration (FDA) has approved Ivermectin as broad spectrum anti-parasitic agent (Gonzalez Canga et al., 2008). Ivermectin is considered to be an effective drug due to its antiparasitic activity against both internal and externalparasites and has multiple applications in veterinary and human medicine (Geary, 2005, Crump, 2017 and Sharun et al., 2019). Sajid et al. (2006) and Jameel et al. (2015) reported that Ivermectin have immune-

potentiating activity in cows. Yates and Wolstenholme (2004), Chaccour et al. (2013) and Suarez et al. (2013) showed that Ivermectin is effectively and widely used against a lot of external and internal parasites. Pregnancy rates were higher in cows after treatment with anti-parasitic drugs (Ivermectin and Eprinomectin) compared with non-treated cows (Loyacano et al., 2002, Kaley et al., 2019 and Volk et al., 2019). Andresen et al. (2017) observed a marked improvement in reproductive performance of cows and heifers after administration of anti-parasites treatment compared to untreated controls group. Infected buffalo cows having the liver worm (Fasciola) needed a long time from calving to conception (Seliem et al., 2010). Dairy cows treated with anti-parasitic drugs needed less time to conception postpartum (Sanchez et al., 2002). Liver fluke infections (Fasciolosis) in cows were accompanied by ovarian inactivity and other infertility problems (Ahmed, 2007). Recently, Ivermectin was used as an antiviral drug because of its effects on a number of RNA viruses including human immunodeficiency virus (HIV)-1 and SARS-CoV-2 (COVID-19) (Wagstaff et al. 2012, Caly et al., 2020 and Kumar et al., 2020). There is no information, on the effect of anti-parasitic treatment on the reproductive performance in Baladi cows that are reared under the environmental conditions of Aswan governorate. The current investigation was planned to study the effect of treatment with the anti-parasitic drug (Ivermectin) on mastitis and some postpartum reproductive parameters of Baladi cows.

MATERIALS AND METHODS

Climatic conditions and farm location:

This study was conducted at a private farm located in a village in Kom Ombou city (32, 31' 23" East and 22, 28' 09" North), Aswan governorate. Average of the ambient temperature was (*Min*.12.3-22.1°C) and (*Max*. 24.2-35.0°C), relative humidity (18-24) during the experimental period which extended from September to April.

Management and feeding of herd:

Twenty- four of Baladi cows were used in the current research. *Alfa*-*Alfa* alongside the concentrate mixture, wheat bran and wheat hay were offered to cows during the experimental period. The cows treated with the Ivomec two months pre-partum after drying. Table (1) shows the specifications of experiment animals. The cows were kept under the ordinary conditions applied on the farm. The cows were kept under semi open sheds and similar environmental and managerial conditions.

Table 1. S	pecifications	(Mean±SE)	of Baladi (cows at s	starting of	treatment	and at calv	ving
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	8	8
Status of cow	Untreated cows	Treated cows
No. of cows	12	12
Body weight (kg) at starting of treatment	305.5 ± 6.5^{a}	315.7 ± 9.4^{a}
Body weight (kg) at calving	310.3±5.4ª	370.6 ± 15.6^{b}
Age (year)	8.5 ± 1.2^{a}	7.4 ± 1.1^{a}
Parity	3-5	3-5
BCS at calving	<3	≥ 3
	1 1 1 1 1 1 CC (T)	0.05

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

Design of the experiment:

The cows at two months prepartum were classified into two groups ((n= 12 cows for each group). The first group (G1) (n= 12 cows) was treated with two consecutive doses of IVOMEC[®] Plus (Ivermectin 1% w/v + clorsulon 10% w/v) two weeks apart. The other group (G2) (n= 12 cows) was used as a control group. The interval between the first treatments and the second was 15 days. The cows were subcutaneously injected with IVOMEC[®]Plus solution behind the shoulder, 1ml/50kg live body weight as recommended by the manufacturer (volume equivalent 10 mg ivermectin and 100 mg clorsulon). According to Mike Catangui (2016) IVOMEC[®] Plus drug was used an anti endo or ecto-parasites (gastrointestinal roundworms, liver flukes, lungworms, cattle grubs, sucking ice, and mange mites). Table (2) shows the classification of (Ivermectin + Clorsulon) combination according to US FDA (Food and Drug Administration) 2015.

Table 2. Specifications of IVOMEC[®] Plus drug (Ivermectin + Clorsulon) adapted to US FDA (Food and Drug Administration) 2015

Drug	Drug Type	Dosage Form	Indications
Ivermectin+ Clorsulon	Anti-parasitic	Subcutaneous	Control of internal/external
			parasites in cows

Detection of heat and pregnancy diagnosis:

The cows were checked for the occurrence of heat twice daily (at 6 am & 6 pm). The sexual behavior of the cows was also visually observed. The cows were naturally mated once the standing behavior of the oestrous cows was observed. Rectal palpation was used (after 60 days post-service), to diagnose pregnancy.

Mastitis diagnosis:

Cows with acute or sub-clinical mastitis were diagnosed using California Mastitis Test according to the steps described by the manufacturer.

Sub-clinical mastitis: Sub-clinical mastitis infected cows do not show any symptoms unless reagents are used. (Kathiriya *et al.*, 2014).

Postpartum reproductive efficiency determination:

Conception rate: estimated as the percentage of animals, that were pregnant from the first service post-partum.

Conception rate = Number of pregnant cows in each group /Total number of served cows in each group x 100

Days open: estimated as the time from parturition to conception in cows

Postpartum ovarian dysfunction determination:

Anestrous cases: Cows did not display any visible signs of estrus during = 60^{th} day postpartum according to Kamal *et al.* (2012).

True anestrous case: Cows considered have true anestrous case when rectal check ovaries are smooth, small and inactive with the absence of corpus luteum and plasma progesterone concentration remain in the basal levels (1ng/ml) (Kamal *et al.*, 2012).

Blood samples and biochemical assay:

Blood samples (10 ml) were collected from cows in estrus, 7th and 21st days post estrus into heparinized tubes from the jugular vein. For plasma harvesting the samples were centrifuged at 3000 rpm for 20 minutes. The separated plasma was stored under

-18°C until the time of analysis. Progesterone (P4) and estradiol-17 β (E₂) hormones were determined by radioimmunoassay kit (Immunotech, France). Progesterone and estradiol-17 β sensitivity values were stated to be 0.03 ng/ml and 4.0 pg/ml, respectively

according to manufacturer labeled information. Intra assay coefficient of variation was 6.2% and 12.2% for progesterone (P4) and estradiol- 17β (E₂), respectively.

Statistical analysis:

The statistical design involved one factor (one-way ANOVA) (treatment effect) on mastitis, postpartum reproductive efficiency and ovarian dysfunction parameters. Chi Square was used to verify the significance of percentage values. The statistical analysis was performed by software (SAS, 2002). Following model was used:

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

Where:

 Y_{ij} = the observation trait; μ = overall mean; T_i =effect of treatment (treated=1 and untreated =2), and e_{ij} = experimental error

Duncan's Multiple Range test (Duncan, 1955) was used to check the significance of the differences between means.

RESULTS AND DISCUSSION

Effect of treatment with anti-parasitic drug on occurrence rate of mastitis in Baladi cows:

Figure (1) indicates the percentage of mastitis in treated cows was significantly (P <0.05) lower (16.7%) than the control group (41.7%). The current result agrees with that reported by Mavrogianni *et al.* (2012) and Mavrogianni *et al.* (2014) who found increased frequency of clinical or subclinical mastitis in the first two weeks post-partum in ewes that suffer from endo-parasitic infections. *Staphylococcus aureus* is considered one of the major pathogenic agents of the udder that causes mainly subclinical infection (mastitis) (Tenhagen *et al.*, 2001, Leitner *et al.*, 2003 and Olde Riekerink *et al.*, 2008). Infections by endoparasites lead to decreasing weight gain, reduced

nitrogen balance, negative affect on metabolism of proteins and suppress immune response in calves(Randall and Gibbs, 1981 and Wiggin and Gibbs, 1990). Ashraf et al. (2018) showed that cows treated with Ivermectin exhibited anti-Staphylococcus aureus activity than other cows. Uhlir (1991) observed that antibody activity is increased after treatment with Ivermectin in rabbits. Backes (2016) reported that white blood cells and lymphocytes were greater in cows treated with anti-parasitic than control cows group. Similar results were reported by Sajid et al. (2006) and Jameel et al. (2015) who stated that treated cows with Ivermectin lead to increase total number of white blood cells and lymphocyte cells in those cows and the reflection of this on the raising of the immunity in animals. Torres et al. (2016) observed that Ivermectin drug was effective against biofilm formation by Staphylococcus aureus. Recently, Heidary and Gharebaghi (2020) discovered that Ivermectin drug has many effects against some diseases and was highly effective against many microorganisms. It worked as antimicrobial, antiviral, and anti-cancer drug. Mastrangelo et al. (2012) reported that Ivermectin acts as an anti-viral agent to flavivirus by inhibiting its replication activity. Recent studies by Lv et al. (2018) and Yamasmith et al. (2018) underlined the effective potential of Ivermectin as an antiviral drug able to reduce viral load in the host. Furthermore, Lim et al. (2013) and Omansen et al. (2015) suggested that Ivermectin acts an antimycobacterial activity against Mycobacterium tuberculosis and Mycobacterium ulcerans. In the light previous studies lower percentage of mastitis in treated cows group than untreated in the present study may be attributed to the anti-microbial effect of Ivermectin (anti- Staphylococcus aureus) in cows udders.



Effect of treatment with anti-parasitic drug on conception rate (%) in Baladi cows:

Figure (2) shows that the conception rate (%) in treated cows was significantly (P <0.05) higher (66.7%) compared with untreated cows (control group) (33.3%). The present findings agree with those reported by Backes (2016) who found that treatment with Long-Acting Eprinomectin (an anti-parasitic

drug) lead to increasing conception rates compared to control group (89 vs. 50%). Higher pregnancy rate (94%) was observed for beef cows that treated with anti-parasitic drugs compared with untreated beef cows 82% (Stromberg *et al.*, 1997). Larson *et al.* (1995) reported that pregnancy rate was higher (56.4%) in beef heifers that treated with Ivermectin than control heifers (25.6%). Pregnancy rate was 72%

and 87% in control cows group and Ivermectin treatments group, respectively in Ontario cow (Kaley et al., 2019). Loyacano et al. (2002) stated that pregnancy rate was higher (78%) in beef heifers that were treated with Ivermectin than no treatment heifers (54%). Volk et al. (2019) reported that beef heifers which treated with Eprinomectin (anti-parasites) recorded greater (84%) pregnancy rate compared with control group heifers (68%). Orellana et al. (1999) reported that treatment with anti-parasites was associated with increasing the conception rate in dairy cows. Seliem et al. (2010) showed that higher pregnancy rate in buffaloes that were treated with anti-Fasciola drugs (67.7%) than control group buffaloes (16.7%). Hammam et al. (2011) found that the pregnancy rate in the healthy treated buffaloes was higher (55.6 %) than buffaloes infected with liver worm (Fasciola hepatica) (30.8 %). Hawkins (1993) and Gross et al. (1999) stated that anthelmintic-treated beef cows recorded higher conception rate and calving rate compared to untreated controls. The present results indicate increase in the conception rate in treated cows by anti-parasitic drug compared to untreated cows which may be due to improve weight gains and general body condition score of treated cows during postpartum period than untreated cows. Larson et al. (1995) reported that treatment of beef heifers with Ivermectin improved weight gains and pregnancy rate during a 60-d breeding season. Barakat et al. (1995) showed that acute infection with nematodes worms (internal parasites) was associated with low

incidences of conception rate and ovarian activity in cows and buffaloes. Somehez et al. (2002) stated that removing external and internal parasites around calving improved the energy balance through the postpartum period and therefore improved the reproductive performance of cows. Maintaining of body weight and body condition score during postpartum period led to increase energy balance and have also positive effect on reproductive performance of beef cows (Hess et al., 2005). Improving of body weight and body condition score of beef heifers which were treated with extended-release Eprinomectin (anti-parasites) during breeding season may be the to improved their reproductive main cause performance (Volk et al., 2019). Marked improvement was showed in reproductive performance of cow and heifers after administration of anthelmintic treatment compared to untreated controls (Andresen et al., 2017). Rehbein et al. (2013) reported that treatment with deworming drugs led to reduce worm burdens and increase weight gains in cattle. Infections with trematode (internal parasite) caused depressed appetite and feed intake in affected sheep hence decreased available energy (Taylor et al., 2007 and Rojo-Vázquez et al., 2012). El-Khadrawy et al. (2008) reported that buffalo-cows with (internal parasites) (Fasciola) recorded lower concentrations of serum Zn, Cu, Fe and Se compared to healthy animals. Ahmed et al. (1998) stated that buffaloes which have lowered Cu or Zn in blood suffered weak growth and infertility.



Effect of treatment with anti-parasite on the time from calving to conception (Days open) in Baladi cows:

Table (3) illustrates that the time from calving to conception in treated cows was significantly (P <0.05) lower 86.5 ± 11.4 days than untreated cows (control group) 123.3 ± 13.2 days. The present findings correspond with those reported by Walsh *et al.* (1995) and Sanchez *et al.* (2002) who found that the interval from calving to conception was less in dairy cows which were treated with anti-parasitic drugs (Ivermectin or Eprinomectin) compared to untreated cows. Orellana *et al.* (1999) stated that treatment of cows with an anti-parasite led to reduced interval from

calving to conception. Seliem *et al.* (2010) showed that infected buffaloes with internal parasites liver worm (*Fasciola*) needed a long time from calving to conception (156.75, days) compared to non-infected group (112.46, day). Mejía *et al.* (1999) stated that treatment of dairy heifers with anti-parasitic (Ivermectin) caused to increased growth rate and earlier onset of ovarian functions. Ballweber *et al.* (1997) suggested that used anti-parasites (Doramectin or Ivermectin) in cattle led to significant increase in weight gain in drug-treated groups relative to untreated groups, ranging from 0.132 to 0.272 kg average daily gain. Lacau-Mengido *et al.* (2000) observed that Ivermectin treated dairy heifers recorded increased serum IGF-1, and this caused to acceleration

of sexual and somatic maturation. Buffaloes having poor body condition score had less number of small and large follicles in their ovaries hence low incidence of good quality oocytes (Ahmed *et al.*, 1999). Observed in ewes having poor body condition lowering LH secretion or decline its pulse frequency. This effect is mediated through glucose level, or insulin growth factor-I (IGF-1) (Snyder *et al.*, 1999). Deficiency of energy is considered as one of most agents detrimental to reproduction of livestock (Dunn and Moss, 1992). McClure (1994) reported that energy deficiency causing to inhibit ovarian function at pituitary synthesis/release of gonadotropin. Level of IGF-1 is very important to ovarian follicular development (Robinson, 1996).

Table 3. Effect of treatment with anti-parasitic on the time from calving to conception (DO) in Baladi cowsTreated cowsUntreated cows

No. of cows	12	12
The time from calving to conception (DO) days:		
X ± S E	86.5 ± 11.4^{a}	123.3 ± 13.2^{b}
a, b: values within the same row having different superscripts are signific)	

a, b: values within the same row having different superscripts are significantly different at (P < 0.051-Conception rate calculate from first service

Effect of treatment with anti-parasite on ovarian dysfunction in Baladi cows:

Figure (3) indicates that the proportion of anestrous cases (%) was significantly (P <0.05) lower (8.3%) in treated cows group than untreated cows (control group) (25%). This may be due to improvement of the body condition score of treated cows compared with non-treated cows. The current result agrees with that recorded by Barakat et al. (2001) who found that cows infected by internal parasites (liver worm) was associated with loss of body condition, decreased fertility and prolonged anestrus period. Ahmed (2006) and Ahmed et al. (2006) observed that infected buffaloes with internal parasites liver worm (Fasciola) recorded prolonged anestrous period compared with healthy animals. Stewart et al. (1992) stated that treatment of beef replacement heifers with Ivermectin led to improved weight gain, feed efficiency, and estrous activity. Barakat et al. (1995) showed that acute infection with nematodes worms (internal parasites) was associated

with low occurrence of ovarian activity in cows and buffaloes. Anthelmintic treated dairy cattle recorded less time to recovering estrous during postpartum period (Sanyal et al., 1992). Liver fluke infections (Fasciolosis) in bovine were associated with ovarian inactivity and other infertility problems (Ahmed, 2007). Simsek et al. (2007) reported that 58% of repeat breeder cows were suffering from liver worm (Fasciola. hepatica). Jeffcoate et al. (1988) and Fernandez-Abella et al. (2006) found that reduction in ovulation rate and ovarian activity in infected ewes with internal parasites. El-Khadrawy et al. (2008) reported that lower concentrations of serum Zn, Cu, Fe and Se in buffalo which infected by liver worm (Fasciola) compared to healthy animals. Kommisrud (2005) suggested that there is a positive correlation between increased pre-partum blood selenium levels and decreased incidence of ovarian cysts and anestrus/silent estrus during the post-partum period in Norwegian dairy herds.



Concentrations of progesterone and estradiol-17 β at estrus, 7th and 21st day post-service in treated and untreated Baladi cows:

Table (4) indicates that concentrations of progesterone and estradiol-17 β at the time of estrus were significantly (P < 0.05) higher in pregnant cows than non-pregnant. The present result agrees with that reported by Waldman *et al.* (2001) who reported that

a strong inverse association between the probability of non-return to estrus and progesterone concentration at the time of estrus in cows. Busch *et al.* (2008) showed that pregnant cows have higher progesterone concentration at day 10 post- service compared with non-pregnant cow. The current result is in agreement with that stated by Lemley *et al.* (2010) who found that increase of progesterone post- service was associated with elevated pregnancy maintenance and improvement in the development of the embryo. Rivera et al. (2011) observed decreased progesterone concentrations during follicle growth in dairy cows lead to low cow embryo quality production. Higher pre- and post- service progesterone concentrations were associated with improvement of the fertility. Progesterone modifies ovarian and uterine function through direct effects or indirect effects on fertilization and early stages from development of embryo (Cerri et al., 2011). El-Khadrawy et al. (2008) suggested that buffaloes having (internal parasites) (Fasciola) recorded lower concentrations of blood Zn, Cu, Fe and Se compared to healthy animals. Kamada, (2017) and Kassab et al. (2020) reported that supplementation of selenium to diet in dairy and beef cows led to increases in progesterone and estradiol concentrations during estrous cycle. Sadek and Shaheen (2015) showed that there is increasing in

serum progesterone in Baladi cows during postpartum after treatment with Ivermectin (anti-parasites) for up to 3 months. Opposite trend showed for estradiol in blood serum and returned to the increasing during three months after treatment. Seliem et al. (2010) observed that increasing in progesterone and decreasing in estradiol in blood serum of buffaloes that treated with (anti-Fasciola-hepatica). Hammam et al. (2011) showed that infected buffaloes with liver worm (Fasciola) had a decrease in estradiol concentrations (28.42+8.64 pg/ml) than the healthy group (39.61+18.23 pg/ml). Lopez-Diaz et al. (1998) found that Friesian heifers infected with liver flukes (liver worm) recorded decline levels of progesterone than healthy animals. They suggested that liver flukes may be able to alter normal metabolism and/or balance of sex hormones.

Table 4. Concentrations of progesterone and Estradiol-17 β at estrus, 7th and 21st day post-service in treated and untreated Baladi cows

Treate	ed cows	Untreated cows		
Pregnant	Non-pregnant	Pregnant	Non-pregnant	
0.37 ± 0.09^{a}	0.24 ± 0.04^{b}	0.25 ± 0.02^{a}	0.17 ± 0.04^{b}	
3.30±0.03 ^a	2.10±0.01 ^b	2.80 ± 0.02^{a}	1.90±0.03 ^b	
7.21±0.12 ^a	0.30±0.01 ^b	5.13±0.12 ^a	0.26 ± 0.01^{b}	
37.30±0.32 ^a	13.60±0.22 ^b	22.10±0.11 ^a	12.30 ^b ±0.31 ^b	
	Treate Pregnant 0.37±0.09 ^a 3.30±0.03 ^a 7.21±0.12 ^a 37.30±0.32 ^a	Treated cows Pregnant Non-pregnant 0.37±0.09 ^a 0.24±0.04 ^b 3.30±0.03 ^a 2.10±0.01 ^b 7.21±0.12 ^a 0.30±0.01 ^b 37.30±0.32 ^a 13.60±0.22 ^b	$\begin{tabular}{ c c c c c c c } \hline \hline Treated cows & Untreal \\ \hline \hline Pregnant & Non-pregnant & Pregnant \\ \hline \hline 0.37 \pm 0.09^a & 0.24 \pm 0.04^b & 0.25 \pm 0.02^a \\ \hline 3.30 \pm 0.03^a & 2.10 \pm 0.01^b & 2.80 \pm 0.02^a \\ \hline 7.21 \pm 0.12^a & 0.30 \pm 0.01^b & 5.13 \pm 0.12^a \\ \hline 37.30 \pm 0.32^a & 13.60 \pm 0.22^b & 22.10 \pm 0.11^a \\ \hline \end{tabular}$	

 $^{,a, b}$: values within the same row having different superscripts are different at (P <0.05).

CONCLUSION

The results of this study showed that Ivermectin injection to pregnant Baladi cows during the last two months of pregnancy (at the rate of 1m/50kg live body weight) was useful in reducing the incidence of mastitis, as well as, in enhancing the reproductive performance of the cows.

REFERENCES

- Ahmed, W.A., S.I. Shalaby and M.M. Zaabal, 1998. Effect of mineral supplementation on some blood biochemical and immunogenetic parameters in buffalo-cows suffering from inactive ovaries. Beni- Suef Veterinary Medicine Research, 8: 149-165.
- Ahmed, W.A., G.M, Nabil, H.H, El-khadrawy, E.M, Hanafi and S.I, Adel-Moez, 2006. Monitoring progesterone level and markers of oxidative stress in blood of buffalo cows with impaired fertility. Egypt. J. Biophys. Biomed. Engineering, 7: 71-83.
- Ahmed, W.M., 2006. Adverse conditions affecting ovarian activity in large farm animals. Proceeding of the 3rd International Conference of Vet. Res. Div., NRC., Cairo, Egypt, 251-253.
- Ahmed, W.M., 2007. Overview on some factors negatively affecting ovarian activity in large farm animals. Global Vet., 1: 53-66.

- Ahmed, W.M., A.S. Abdoon, S.I. Shalaby and O.M. Kandil, 1999.Effect of reproductive status and body condition on ovarian follicles and oocytes quality in buffalo-cows. Buffalo Journal, 15: 333-334.
- Andresen, C.E., D.L. Loy, T.A. Brick, and P.J. Gunn, 2017.Effects of extended-release eprinomectin on cow/calf performance and reproductive success in a fall-calving beef herd. The Professional Animal Scientist, 34:223–229.
- Ashraf, S., U. Chaudhry, A. Raza, D. Ghosh and X. Zhao, 2018. In vitro activity of ivermectin against Staphylococcus aureus clinical isolates. Antimicrobial Resistance and Infection Control, 7:27.
- Backes, E.A. 2016, "Evaluation of Long-Acting Eprinomectin Compared to Conventional Anthelmintics in Cow/Calf Production." Theses and Dissertations. 1677. University of Arkansas, Fayetteville, USA.
- Ballweber, L.R., L. Smith, J.A. Stuedemann, T. Yazwinski and T.L. Skogerboe, 1997.The effectiveness of a single treatment with doramectin or ivermectin in the control of gastrointestinal nematodes in grazing yearling stocker cattle. Vet Parasitol,72:53-68.
- Barakat, A.M., E.M, Hanafi, H. A. Sabra, M.M. Zaabal and W.M.Ahmed, 2001.Effect of parasitic infection on ovarian activity in native Egyptian cows and ewes with special reference to changes

in blood constituents and immunogenetic markers.Zagazig. Vet. J., 29: 121-136.

- Barakat, I.M. and A.M. Selim, 1995. The relation between gastrointestinal nematodes infestation and postpartum ovarian inactivity in buffalocows. Zagzig Veterinary Journal, 23: 35-38. Busch, D. C, J. A. Atkins, J. F. Bader, D. J. Schafer, D. J. Patterson, T. W. Geary and M. F. Smith, (2008). Effect of ovulatory follicle size and expression of estrus on progesterone secretion in beef cows Published online before print December 21, 2007, doi: 10.2527/jas.2007-0570 J Anim Sci., 86: 553-563.
- Caly, L., J.D. Druce, M.G. Catton, D.A. Jans, D.A., K.M. Wagstaff, 2020. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res. 178 (2020) 104787.
- Cerri, R. L. A.,R. C. Chebel, F. Rivera, C. D. Narciso, R. A. Oliveira, W.W. Thatcher and J. E. P. Santos, 2011. Concentration of progesterone during the development of the ovulatory follicle: I. Ovarian and embryonic responses. Journal of Dairy Sci., 94: 3342-3351.
- Chaccour, C. J., K. C. Kobylinski, Q. Bassat, T. Bousema and C. Drakeley, 2013. Ivermectin to reduce malaria transmission: A research agenda for a promising new tool for elimination. Malaria J. 12, 153-161.
- Crump, A., 2017. Ivermectin: enigmatic multifaceted 'wonder' drug continues to surprise and exceed expectations. J Antibiot., 70(5):495–505.
- Duncan, D. B., 1955.Multiple ranges and multiple F. Test. Biometrics, 11:1-24.
- Dunn, T.G. and G.E. Moss, 1992.Effect of nutrition deficiencies and excess on reproductive efficiency of livestock. Journal of Animal Science, 70: 1580-1593.
- El-Khadrawy, H.H., F.M. El Moghazy, M.M. Abd El Aziz.and W.M. Ahmed, 2008.Field investigation on the correlation between ovarian activity and fascioliosis in buffalo-cows. American-Eurasian J. Agri. Environ. Sci., 3(4): 539-546.
- Fernandez-Abella, D., Z. Hernandez and N. Villegas, 2006.Effect of Chiezey et al. 213 gastrointestinal nematodes on ovulation rate of merino Boorola heterozygote ewes (Fec B Fec +) Anim. Res. 55:545-550.
- Geary, T.G., 2005. Ivermectin 20 years on: maturation of a wonder drug. Trends Parasitol., 21(11):530–532.
- González Canga, A., A.M. Sahagún Prieto,1 M. J. Diez Liébana, N. F. Martínez, M. S. Vega and J. J. GarcíaVieitez, 2008. The pharmacokinetics and interactions of ivermectin in humans–a minireview. AAPS J. 10 (1), 42–46.
- Grisi, L., R. C. Leite, J. R. de Souza Martins, A. T. M. B. Renato Andreotti, P. H. Duarte Cançado, A. A. P. L. Jairo Barros Pereira and H. S. Villela, 2014.Reassessment of the potential economic impact of cattle parasites in Brazil. Braz. J. Vet. Parasitol., 23 (2): 150-156.

- Gross, S.J., W.G. Ryan and H.W. Ploeger, 1999. Anthelmintic treatment of dairy cows and its effect on milk production. Vet. Rec. 144, 581–587.
- Hammam, A. M., R. M. El Khateeb, H. A. Amer, S. K.A. Abou-El-Dobal, and W. Scott, 2011.Response of Fasciola free and infected buffaloes to CIDROvSynch treatment during summer season with emphasis on sex hormone and biochemical changes. Journal of American Science;7(9):810-820.
- Hawkins, J.A., 1993. Economic-benefits of parasite control in cattle. Vet. Parasitol. 46, 159-173.
- Heidary, F. and R. Gharebaghi, 2020. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. The Journal of Antibiotics, 73:593-602.
- Hess, B. W., S. L. Lake, E. J. Scholljegerdes, T. R. Weston, V. Nayigihugu, J. D. C. Molle and G. E. Moss, 2005. Nutritional controlsof beef cow reproduction. J. Anim. Sci. 83(E. Suppl.): E90– E106.
- Jameel, G. H., A. A. Ahmed, O. K. Jalil and W. S. Dawood, 2015.Ivermectin activity in treatment of cattle dermatophytosis.Diyala Agricultural Sciences Journal, 7 (1) 30 - 40.
- Jeffcoate, I.A., P.H. Holmes, G. Fishwick, K. Bairden and J. Armour, 1988.Effects of trichostrongyle larval challenge on the reproductive performance of immune ewes, Res. Vet. Sci., 45:234-239.
- Kaley, G. M., P. Menzies, K. G. Bateman and J. L. Gordon, 2019.Efficacy of fenbendazole and ivermectin in treating gastrointestinal nematode infections in an Ontario cow-calf herd. Can Vet J; 60:1213–1219.
- Kamada, H., 2017. Effects of selenium-rich yeast supplementation on the plasma progesterone levels of postpartum dairy cows. Asian-Australas J Anim Sci., Vol., 30 (3):347-354.
- Kamal, M. M., M.M. Rahman, H.W. Momont and M. Shamsuddin, 2012.Underlying disorders of postpartum anoestrus and effectiveness of their treatments in crossbred dairy cows. Asian Journal of Animal Sci., 6 (3): 132-139.
- Kassab, A. Y., H. Hamdon, W. Senosy, H. Daghash and A. Soliman, 2020.Impact of antioxidants supplementation on metabolic status and reproductive performance of Aberdeen Angus cows during seasonal thermal stress in arid subtropical regions. Egyptian J. Anim. Prod., 57(1):1-11.
- Kathiriya, J., B. Kabaria, D. Saradava and D. Sanepara, 2014.Pervalence of subclinical mastitis in dairy cows in Rajkot district of Gujarat. International journal of science and nature., 5 (3): 35-43.
- Kommisrud, E., O. Osteras and T. Vatan, 2005. Blood selenium associated with health and fertility inNorwegian dairy herds. ActaVeterinaria Scandinavia,46: 229-234.
- Kumar, B. S., M. Jeyaraman, R. Jain and T.C. Anudeep, 2020. A wonder drug in the arsenal

against COVID - 19: Medication Evidence from Ivermectin. J. Adv. Med. Med. Res., 32:30-37.

- Lacau-Mengido, I.M., M.E. Mejía, G.S. Díaz-Torga, I.A. Gonzalez, N. Formía, C. Libertun and D. Becú-Villalobos, 2000. Endocrine studies in ivermectin-treated heifers from birth to puberty. J. Anim. Sci., 78: 817-824.
- Larson, R. L., L.R. Corah, M.F. Spire and R.C. Cochran, 1995.Effect of treatment with ivernectin on reproductive performance of yearling beef heifers. Theriogenology, 44:189-197.
- Lawrence, J. D. and M.A. Ibarbura, 2009.Economic analysis of pharmaceutical technologies inmodern beef production in a bioeconomy era.Iowa State University.
- Leitner, G., N. Yadlin, E. Lubashevsy, E. Ezra, A. Glickman, M. Chaffer, M. Winkler, A. Saran and Z. Trainin, 2003. Development of a Staphylococcus aureus vaccine against mastitis in dairy cows. II. Field trial. Vet. Immunol. Immunopathol., 93: 153-158.
- Lemely, C.O., K. A. Vonnahme, L. R. Tager,K. M. Krause and M. E. Wilson, 2010. Diet-induced alterations in hepatic progesterone (P4) catabolic enzyme activity and P4 clearance rate in lactating dairy cows. Published online before print March 11, 2010, doi: 10.1677/JOE-10-0042 J Endocrinol., 205: 233-241.
- Lim, L.E., C. Vilcheze C. Ng, W.R. J. Jr., S. Ramon-Garcia and C.J. Thompson, 2013. Anthelmintic avermectins kill Mycobacterium tuberculosis, including multidrug-resistant clinical strains. Antimicrob Agents Chemother., 57(2): 1040-1046.
- Lopez-Diaz, M., C. Carro and C. Cadorniga, 1998. Puberty and serum concentrations of ovarian steroids during prepuberal period in Friesian heifers artificially infected with Fasciola hepatica. Theriogenology, 50: 587-593.
- Loyacano , A. F., J.C. Williams , J. Gurie , A.A. DeRosa, 2002. Effect of gastrointestinal nematode and liver fluke infections on weight gain and reproductive performance of beef heifers. Veterinary Parasitology, 107: 227-234.
- Lv, C., W. Liu, B. Wang, R. Dang, L. Qiu, J. Ren, C. Yan, Z. Yang and X. Wang, 2018. Ivermectin inhibits DNA polymerase UL42 of pseudorabies virus entrance into the nucleus and proliferation of the virus in vitro and vivo. Antiviral Res. 159: 55-62.
- Mastrangelo, E, M. Pezzullo, T. De Burghgraeve, S. Kaptein, B. Pastorino, K. Dallmeier, X. de Lamballerie, J. Neyts, A.M. Hanson, D.N. Frick, M. Bolognesi and M. Milani, 2012. Ivermectin is a potent inhibitor of flavivirus replication specifically targeting NS3 helicase activity: new prospects for an old drug. J AntimicrobChemother.,67(8):1884-1894.
- Mavrogianni, V.S., E. Papadopoulos, D.A. Gougoulis, E. Gallidis, I.A. Fragkou, D.C. Orfanou, S. Ptochos and G.C. Fthenakis, 2012. Pre-existing gastrointestinal trichostrongyl osispredisposes

ewes to clinical mastitis after experimental mammary infection. In: Proceedings of the 12th Greek Veterinary Congress, Athens, Greece.

- Mavrogianni, V.S., E. Papadopoulos, S.A. Spanos, A. Mitsoura, S. Ptochos, D.A. Gougoulis, M.S. Barbagianni, I. Kyriazakis, G.C. Fthenakis, 2014.Trematode infections in pregnant ewes can predispose to mastitis during the subsequent lactation period. Res. Vet. Sci., 96: 171-176.
- McClure, T.J., 1994. Nutrition and Metabolic Infertility m the Cow. CAB International, Wallingford, Oxon, UK.
- Mejía, M.E., C Libertun, G.S. Díaz-Torga, P. Villafane, N. Formía, D. Becú-Villalobos and I.M. Lacau-Mengido, 1999. Continuous ivermectin treatment from birth to puberty on growth and reproduction in dairy heifers. J. Anim. Sci., 77: 1329-1334.
- Mendes, E.A., W.S. Lima and A.L. de Melo, 2008. Development of F. hepatica in Lymnaeacolumella infected with miracidia derived from cattle and marmoset infections. J. Helminth., 82: 81-84.
- Mike Catangui, PhD, 2016. Dewormers for Beef and Dairy Cattle. Entomologist and Parasitologist, MWI Animal Health Technical Services.
- OldeRiekerink, R.G., H.W. Barkema, D.F. Kelton and D.T. Scholl, 2008.Incidence rate of clinical mastitis on Canadian dairy farms. J Dairy Sci.,91(4):1366-1377.
- Omansen, T.F., J.L. Porter, P.D.R. Johnson, T.S. Van der Werf, Y. Stienstra, T.P. Stinear, 2015. In-vitro activity of Avermectins against Mycobacterium ulcerans. PLOS Neg Trop Dis.,9(3): e0003549.
- Orellana, P., S. Recabarren, A. Lobos, A. Islas, M. Briones and L. Rubilar, 1999. Effects of winter supplementation and anti-parasite treatment on the productive performance of milk herd in the centralsouth region of Chile. Preven. Vet. Med., 38: 207-215.
- Randall, R.W. and H.C. Gibbs, 1981.Studies on the effects of two levels of gastrointestinal helminthiasis on digestion and energy metabolism in calves. Am J Vet Res,42:1730-1734.
- Rehbein, S., D. G. Baggot, E. G. Johnson, B. N. Kunkle, T. A. Yazwinski, S. Yoon, L. G. Cramer, and M. D. Soll, 2013. Nematode burdens of pastured cattle treated once at turnout with eprinomectin extended-release injection. Vet. Parasitol., 192:321-331.
- Rivera, F.A., L.G. D. Mendonça, G. L. Jr, J. E. P. Santos, R. V Perez, M. Amstalden, A. Correa-Calderón and R. C. Chebe, 2011. Reduced progesterone concentration during growth of the first follicular wave affects embryo quality but has no effect on embryo survival post transfer in lactating dairy cows. Published online before print December 22, 2010, doi: 10.1530/REP-10-0375 Reproduction, 141: 333-342.
- Robinson, J.J., 1996. Nutrition and reproduction. Anim. Reprod, Sci., 42: 25-34.

- Rojo-Vázquez, F.A., A. Meana, F. Valcárcel and M. Martínez-Valladares, 2012. Update on trematode infections in sheep. Vet. Parasitol. 189: 15-38.
- Sadek, K. M. and H. M. Shaheen, 2015. The biochemical effects of ivermectin on reproductive hormones and mineral homeostasis in Baladi cows post parturition. Vet. arhiv 85, 95-103.
- Sajid, M. S., Z. Iqbal, G. Muhammad and M. U. Iqbal, 2006.Immunomodulatory effect of various antiparasitics: a review. Parasitology, 132: 301-313.
- Sanchez, J., A. Nødtvedt, I. Dohoo and L. DesCoteaux, 2002. The effect of eprinomectin treatment at calving on reproduction parameters in adult dairy cows in Canada. Prev. Vet. Med., 56: 165-177.
- Sanyal, P.K., D.K. Singh and M.R. Knox, 1992.The effect of peri-parturient anthelminitic treatment on the productivity of dairy cattle in subtropical western India. Veterinary Research Communication, 16: 445-451.
- SAS, 2002. User's Guide: Statistics, Version 9.0 Edition. SAS Institute Inc., Cary, NC, USA.
- Seliem, M. M. E., A.A. Derbala, A.M. Hammam, G.H. Morsy, H.A. Shalaby, M.H. Ibrahim, D. M. Aboelsoued, 2010. The effect of fasciolosis and anti-Fasciola drugs on reproductive performance of buffalo-cows. Proc. 5th Inter Conf. Vet. Res. Div., NRC, Cairo, Egypt, pp. 123 – 130.
- Sharun, K., T.S. Shyamkumar, V.A. Aneesha, K. Dhama, A.M. Pawde and A. Pal, 2019. Current therapeutic applications and pharmacokinetic modulations of ivermectin, Veterinary World, 12(8):1204-1211.
- Simsek, S., A. Risvanli, A.E. Utuk, M. Yuksel, N. Saat and E. Koroglu, 2007.Evaluation of relationship between repeat breeding and Fasciola hepatica and hydatid cyst infections in cows in Elazig district of eastern Turkey. Res. Vet. Sci., 83: 102-104.
- Snyder, J.L., J.A. Clapper, A.J. Roberts, P.W. Sanson, D.L. Hamernik and G.E. Moss, 1999.Insulin-like growth factor-I, Insulin-like growth factor-Ibinding proteins and gonadotropins in the hypothalamic pituitary axis and serum of nutrientrestricted ewes. Biology of Reproduction, 61: 219-224.
- Somchez, J., A. Nodtvedt, I. Dohco and L. DesCoteaux, 2002. The effect of epriomectin treatment at calving on reproduction parameters in adult dairy cows in Canada. Preventive veterinary Medicine, 56: 165-177.
- Spithill, T.W., P.M. Smooker and D. Coperman, 1999.Fasciolagigantica: epidemiology, control, immunology and molecular biology. In: Dalton JP (ed) Fasiolosis. Oxworth, Commonwealth Agricultural Bureau International, Mussoorie, pp 465–525.
- Stewart, W. B., C. A. Piche, K. M. Newcomb, 1992.Effect of antiparasitic treatment in beef replacement heifers.Can Vet J, 33: 394-396.
- Stromberg, B. E., R. J. Vatthauer, J. C. Schlotthauer, G. H. Myers, D. L. Haggard, V. L. Kingand H. Hanke, 1997. Production responses following

strategic parasite control in a beefcow/calf herd. Vet. Parsitol., 68:315-322.

- Suarez, G., L. Alvarez, D. Castells, O. Correa and P. Fagiolino, 2013.Relative bioavailability and comparative clinical efficacy of different ivermectin oral formulations in lambs. BMC Vet. Res. 9, 27-36.
- Taylor, M.A., R.L. Coop and R.L. Wall, 2007.Veterinary Parasitology, third ed. Blackwell, Oxford, 874 pp.
- Tenhagen, B.A., D. Edinger, B. Baumgartner, P. Kalbe, G. Klunder and W.Heuwieser, 2001.Efficacy of a herd-specific vaccine against Staphylococcus aureus to prevent post-partum mastitis in dairy heifers. J. Vet. Med. Ser. A., 48: 601-607.
- Torres, N.S., J.J. Abercrombie, A. Srinivasan, J.L. Lopez-Ribot, A. K. Ramasubramanian and K.P. Leung, 2016. Screening a commercial library of pharmacologically active small molecules against Staphylococcus aureus biofilms. Antimicrob Agents Chemother.,60(10):5663-5672.
- Uhlir, J. 1991. Effect of ivermectin on the development of serum antibody activity in rabbits infested with Psoroptescuniculi (Acari: Psoroptidae). Folia Parasitol (Praha), 38: 79-82.
- US FDA, 2015.Multicriteria-based ranking model for risk management of animal drug residues in milk and milk products. Accessed October 8, 2015. http://www. fda.gov/Food/Food Science Research/Risk Safety Assessment/ ucm443549.htm.
- Volk, M. J., J. M. Kordas, R. S. Stokes, F. A. Ireland, and D. W. Shike, 2019.Effects of spring administration of extended-release eprinomectin on fescue toxicosis, performance, and reproduction of fall-born beef heifers. T. Anim. Sci., 3(1):20-28.
- Wagstaff, K. M., H. Sivakumaran, S. Heaton, D.J. Harrich, D.A. Jans, 2012. Ivermectin is a specific inhibitor of importin α/β -mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. Biochem. J., 443:851-856.
- Waldman, A., O. Reksen, K. Landsverk and E. Ropstad, 2001. Progesterone concentrations in milk fat at first insemination- effects on non- return and repeat- breeding. J Anim. Reprod., Sci., 65: 33-41.
- Walsh, T. A., P.J. Younis and J.M. Morton, 1995. The effect of ivermectin treatment of late pregnant dairy cows in south-west Victoria on subsequent milk production and reproductive performance. Austmlian Veterinary Journal, 72 (6): 201-207.
- Wiggin, C.J. and H.C. Gibbs, 1990.Adverse immune reactions and the pathogenesis of Ostertagiaostertagi infections in calves. Am J Vet Res,51: 825-832.
- Yamasmith, E., F.A. Saleh-arong, P. Avirutnan, N. Angkasekwinai, D. Mairiang, E. Wongsawat, S. Tanrumluk, U. Fongsri, Y. Suputtamongkol, 2018. Efficacy and Safety of Ivermectin against Dengue Infection: A Phase III, Randomized, Double-blind,

Damarany

Placebo-controlled Trial, in 34th Annual Meeting the Royal College of Physicians of Thailand-'Internal Medicine and One Health'. ((Pattaya, Chonburi, Thailand. Yates, D.M, and A.J. Wolstenholme, 2004. An Ivermectin – sensitive glutamate gated chloride channel subunit from Dicrofilariaimmitis. Int. J. parasitol., 43(9) :1075- 81.

تأثير المعاملة بمضادات الطفيليات (الايفرمكتين) أثناء فترة ما قبل الولادة على التهاب الضرع والأداء التناسلي بعد الولادة في الأبقار البلدية

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صممت الدراسة الحالية لتقدير تأثير المعاملة بمضادات الطفيليات (الايفرمكتين) على التهاب الضرع والأداء التناسلي بعد الولادة في الأبقار البلدية. تم استخدام 24 بقرة بلدي في هذه الدراسة، تم تقسيم الأبقار إلى مجموعتين. تم حقن G1 (ن = 12 بقرة) قبل الولادة بشهرين بجرعتين متتاليتين (15 يومًا فيما بينها) بمحلول Plus Plus تحت الجلد بمعدل 1 مل / 50 كجم من وزن الجسم الحي (طبقا لتوصيات الشركة المصنعة)، تم استخدام 22 (ن = 12 بقرة) كمجموعة كنترول. أظهرت النتائج الحالية أن حدوث التهاب الضرع في مجموعة الأبقار المعاملة كان أقل معنويا (0.05 Plus) (ن = 12 بقرة) كمجموعة كنترول. أظهرت النتائج الحالية أن حدوث التهاب الضرع في مجموعة الأبقار المعاملة كان أقل معنويا (0.05 Plus) (ن = 12 بقرة) كمجموعة كنترول. أظهرت النتائج الحالية أن حدوث التهاب الضرع في مجموعة الأبقار المعاملة كان أقل معنويا (0.05 Plus) من مجموعة أبقار الكنترول. (4.11%). كان معدل الحمل في مجموعة الأبقار المعاملة أعلى معنوياً (0.05 Plus) مقارنة (6.60×) مقارنة بـ (3.30٪) في مجموعة البقار الكنترول. كان الوقت من الولادة إلى الحمل في مجموعة الأبقار المعاملة أعلى معنوياً (0.05 Plus) مقارنة بـ (1.63 ± 1.12 يومًا) في مجموعة الكنترول. كان الوقت من الولادة إلى الحمل في الأبقار المعالجة أقل بكثير (3.58 ± 1.14 يوم) مقارنة بـ (1.62 ± 1.32 يومًا) في مجموعة الكنترول. (9.05 Plus) . كانت حالات السكون الجنسي اقل معنويا (0.05 Plus) في الأبقار المعالمة مقارنة بالمجموعة الكنترول (25٪). أظهرت نتائج هذه الدراسة أن حق الأبقار البلدية العشر بالإيفرمكتين خلال الشهرين الأخيريين من الحمل (معدل 1 مل / 50 كجم من وزن الجسم الحي) كان مفيدًا في تقليل الإصابة بالتهاب الضرع، وكذلك في تحسين الأداء التناسلي.