

Hormonal profiles and etiological factors associated with abortion in ewes: A case-control study in Salah Al-Din Province, Iraq

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Abstract

The economic implications of abortion among ewes in Salah Al-Din Province (Iraq) have a significant negative impact on the livestock industry. Therefore, it is important to understand the hormonal changes associated with abortion, as well as the potential causative agents to devise adequate and practical prevention strategies of abortion in ewes. The objective of this study was to investigate the hormonal changes in aborted ewes and to identify the primary causes of abortion in sheep throughout Salah Al-Din Province during the breeding season of 2024. A total of 180 ewes were examined, including 120 ewes with confirmed abortions, whereas the remaining 60 ewes with healthy pregnancies served as a control group. Blood samples were taken from each ewe for hormonal analysis (progesterone, estradiol-17 β , cortisol, and prolactin) using enzyme-linked immunosorbent assay. Samples from aborted ewes were microbiologically cultured, serologically tested, and histologically examined to determine the causative agents. There was a statistically significant difference between aborted and control ewes in the concentration of progesterone (1.82 ± 0.34 ng/mL vs 4.15 ± 0.52 ng/mL, $p < 0.001$), and estradiol-17 β levels (12.45 ± 2.18 pg/mL vs 28.67 ± 3.45 pg/mL; $p < 0.001$). The concentration of cortisol was significantly higher in the serum of aborted ewes (45.32 ± 6.78 ng/mL vs 22.15 ± 3.42 ng/mL; $p < 0.001$). The aborted group revealed slightly lower levels of prolactin compared to controls on average. The leading causes of abortion identified were brucellosis (33.2%), toxoplasmosis (25.8%), chlamydia (19.2%), and nutritional deficiencies (15.8%). The findings from this study indicate that abortion in ewes in Salah Al-Din Province is associated with significant hormonal changes, the most notable of which were decreased progesterone and increased cortisol levels. Infectious diseases, especially brucellosis and toxoplasmosis, represented the leading causes of abortion. These observations suggest a need for comprehensive vaccination programs, improved nutritional management, and strategies to reduce stress to lower the incidence of abortion in ewes.

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1. Introduction

In Iraq, sheep production is a major component of the agricultural sector, particularly in the Province of Salah al-Din, where pastoral (nomadic) sheep-herding systems are common. However, reproductive problems, particularly abortions, represent a major threat to the economic viability and sustainability of sheep farming in this region. In addition to causing direct financial loss due to lost lambs, abortions negatively affect ewe welfare, interfere with flock management practices, and may indicate the presence of zoonotic infectious diseases (Wareth et al. 2014). There are many causes of sheep abortion, including infectious agents, nutritional deficiencies, environmental stressors, genetic factors, and hormonal (endocrine) problems. Infectious agents that frequently cause abortion in sheep in the Middle East include *Brucella melitensis*, *Chlamydophila abortus*, *Coxiella burnetii*, and *Campylobacter* spp. (Refai 2002). *Toxoplasma gondii*, a protozoan, is also a major contributing factor to reproductive failure in small ruminants (Dubey 2010). Furthermore, viral agents such as Border disease virus, Schmallenberg virus, and Rift Valley fever virus are also associated with abortion outbreaks in different parts of the world. The relative contribution of various causes of abortion in sheep varies with

geographic location, management systems, level of biosecurity, and vaccination status of the flock (Wernike and Beer 2017). Some of the possible non-infectious causes of abortion include nutritional deficiencies (lack of energy, protein, vitamins, trace minerals) in the diet of ewes at critical stages of gestation. Deficiencies of selenium and vitamin E have been linked with increased rates of abortions in sheep (Rayman 2012). Environmental stressors, such as high or low temperatures, poor shelter, overcrowding, and rough handling of ewes during pregnancy, may trigger abortions by activating the hypothalamic-pituitary-adrenal axis, leading to abnormal hormone levels (Dobson and Smith 2000). In addition, mycotoxins produced by *Aspergillus* and *Fusarium* species that contaminate feeds have also been implicated in various reproductive disorders, including abortion (Fink-Gremmels 2008).

Precise hormonal regulation is required for successful pregnancy in ewes. The hypothalamic-pituitary-ovarian (HPO) axis of the ewe and the placenta work together to maintain proper development of the fetus before and after birth. Progesterone is produced mainly by the corpus luteum and later by the placenta and is necessary for maintaining a relaxed uterus, inhibiting uterine contractions and supporting the

development of the conceptus during the entire gestation period (Spencer et al. 2004; Arck et al. 2007). If progesterone production is not adequate or the premature luteolysis of the corpus luteum before the placenta takes over the production of progesterone, the pregnancy fails and results in abortion. Estrogens, particularly estradiol-17 β , also play a critical role in the development of the uterus and placenta, regulation of blood flow to the uterus, and preparation of the reproductive tract for parturition. The ratio of estrogen to progesterone varies markedly throughout pregnancy, and disruption in their relationship compromises the maintenance of pregnancy (Albrecht and Pepe 2010). Cortisol is the primary glucocorticoid hormone produced in ruminants. It acts as the principal mediator of the stress response in ruminants and is critical in stimulating fetal maturation and initiating parturition (Liggins 1994). However, prolonged elevation of cortisol levels as a result of chronic stress or disease potentially compromises the pregnancy through a variety of mechanisms including suppression of progesterone synthesis, impaired placentation, and alterations in the immune regulation (Nakamura et al. 2008; Michael and Papageorgiou 2008). Several species have experienced higher rates of abortion as a consequence of stress-induced hypercortisolemia, although the underlying mechanisms are not completely understood. Prolactin, which is known to have a lactogenic function, also contributes to immune regulation and pregnancy maintenance through its effects on the corpus luteum and immune tolerance at the maternal-fetal interface (Bishop et al. 2022).

In sheep flocks of Iraq, the abortion rates have been reported in the range of 5 – 15%, depending on management practices and the prevalence of disease (Rhawy and Muwafaq 2024; Al-Hamedawi and Al-Sanjary 2020). Despite the importance and impact of abortions in sheep production, the studies in Salah Al-Din Province remain limited and focussed on individual causes of abortion instead of applying a comprehensive approach (Ahuduzzaman and Hasan 2022; Mohammed Ameen et al. 2024). Hormone profiles from aborted ewes provide valuable information about the pathophysiology of abortion, which may help identify potential biomarkers for predicting pregnancies at risk (Buxton et al. 2007). Furthermore, understanding of the relationship between hormone changes and abortion may help develop targeted therapeutic interventions and management strategies to decrease the incidence of pregnancy loss (Buxton and Henderson 1999). The identification of primary causes of abortion in this region will be critical for the establishment of targeted control measures including vaccination programs, improved biosecurity practices, and enhanced nutritional management. Extreme climatic variability in the Middle East region has resulted in increased physiological stress on livestock which adversely impacted their reproductive performance (Nardone et al. 2010). The extreme environmental conditions of Salah Al-Din Province, characterized by summer temperatures exceeding 45 °C and winter temperature even dropping below 0 °C, along with sporadic rainfall patterns and periodic droughts, impose thermal stress directly on pregnant ewes and indirectly affects them through reduced feed quality and availability. The interactions between environmental stressors, hormonal responses, and abortion outcomes specifically warrant further investigation within such geographies (Marai et al. 2007). The socio-economic outcomes of abortions in sheep are far greater than the short-term production losses of reduced lamb crop, leading to reduced income for rural communities that rely heavily on the sheep production for their livelihoods. Moreover, the zoonotic diseases such as brucellosis and toxoplasmosis pose serious public

health threats, particularly in areas with significant human-animal interaction and weak public health infrastructure. Thus, understanding the epidemiology of agents associated with abortion is important not only for the field of veterinary medicine but also for food security and public health (Pappas et al. 2006; Aremmt and Mohammed 2025).

Diagnostic procedures that have been traditionally used to investigate abortions in resource-poor settings include bacteriological culture, serological testing, and histopathological examination. Though these methods less are sensitive than the modern molecular diagnostic methods, they remain cost-effective and widely used for diagnosis of major abortion-causing pathogens. Bacteriological culture enables the isolation and identification of bacterial agents, serological assays enable the determination of the presence or absence of an antibody response to specific pathogens which indicates the exposure of ewes to a specific pathogen, and histopathological examinations allow for visualization of histopathological lesions that are associated with the various infectious and non-infectious causes of abortion. A combination of these classical diagnostic methods with a thorough clinical evaluation and epidemiological investigation improves diagnostic accuracy in the majority of cases (Agerholm 2013). This study aimed to investigate three specific objectives: a) to quantify reproductive hormones (progesterone and estradiol-17 β) and stress-related hormones (cortisol and prolactin) in aborted ewes and healthy pregnant ewes in Salah Al-Din Province; b) to identify the infectious and non-infectious causes of abortion in the study population and rank them according to their respective prevalences; and c) to explore the potential relationships between hormonal changes and the underlying abortion causes within the study population. The study hypothesizes that aborted ewes would demonstrate significantly lower concentrations of progesterone and estradiol, higher concentrations of cortisol, and a higher prevalence of infectious causes of abortion relative to non-infectious causes. The results of the study are expected to provide a better understanding of abortion in sheep in this area and help development of the effective strategies to reduce reproductive losses in the local sheep industry.

2. Materials and Methods

2.1. Animals

The study was a case-control study investigation conducted over a period of 6 months (October 2023 to April 2024) in Salah Al-Din Province, Iraq, spanning both the breeding and lambing seasons of sheep. Six districts of the Province - Tikrit, Samarra, Baiji, Tuz Khurmatu, Balad, and Dhuluiyah - were selected for this study based on geographical diversity and climatic variation, with both intensive and semi-intensive sheep-farming systems. A total of 45 sheep farms were selected for this study via stratified random sampling, ensuring adequate geographical representation and a range of flock sizes (50 – 500 breeding ewes/farm). Criteria for sheep farm selection included the willingness of the owner to participate in the study, the ability of the owner to maintain reliable breeding records, and occurrence of at least one abortion during the period of study. A total of 180 Awassi sheep were included in this study. The animals were pasture-fed, aged 2-5 years, with body condition scores (BCS) ranging from 2.5 to 3.5 on a 5-point scale. The study animals were divided into two trial groups: the abortion group (n = 120), which consisted of ewes who aborted between 90 and 140 days of gestation, and the control group (n = 60) consisting of clinically healthy pregnant ewes at the same gestational stage, which was confirmed by trans-abdominal ultrasonography using

a 5.0 MHz transducer. Ewes that had other diseases or health issues not related to pregnancy, previous reproductive disorders, or hormonal treatments in the past 60 days before sampling were excluded from the study groups.

2.2. Case definition

Abortion was defined as the expulsion of the fetus from the uterus before 145 days of pregnancy. Gestational age was estimated based on farm breeding records and fetal biometry (size and weight). Fetal biometry involved the standardized measurement of specific fetal anatomical structures, which were then compared against established reference charts. The identification of abortion cases was accomplished by weekly visits to farms (active surveillance) and passive reporting by farmers and local veterinarians. For each abortion case, a complete history of flock management, nutrition, immunization records, and environmental conditions was compiled using standardized questionnaires, followed by a thorough clinical examination.

2.3. Blood samples

Blood samples (10 mL) were collected from the jugular vein of each ewe within 24 hours of the abortion for the "abortion" group and at the comparable gestational stage for the control animals. Samples were allowed to clot at room temperature for 30 minutes and then centrifuged at $3000 \times g$ for 15 minutes. Serum from the samples was separated, aliquoted into 1.5 mL cryovials, and immediately stored at -20°C until analyzed. The serum samples were transported to the Veterinary Teaching Hospital Laboratory at Tikrit University under cold-chain conditions using portable coolers with ice packs.

2.4. Hormonal assay

Serum progesterone concentrations were determined using a commercially available enzyme-linked immunosorbent assay kit (Progesterone ELISA Kit, DRG Instruments GmbH, Germany) with a detection limit of 100 pg/mL and a coefficient of variation (CV) of $<5\%$ for each assay run. Measurement of estradiol- 17β was performed using the DRG International Inc., USA, ELISA estradiol kit with a sensitivity of 9.7 pg/mL and an inter-assay CV of $<8\%$. Cortisol levels were evaluated with Monobind Inc's, USA, ELISA cortisol kit with a detection range of 2.5 – 800 ng/mL and a specificity $>98\%$. Prolactin was measured using an ELISA kit (Cusabio Biotech Co., China) validated for ovine serum. All assays were performed in duplicate and according to the manufacturer's protocol. Optical density (OD) was measured at 450 nm by a microplate reader (BioTek Instruments, USA). Standard curve values were obtained using the provided standard controls, and hormone concentrations were calculated using four-parameter logistic curve fitting.

All aborted fetuses ($n = 120$) and associated placental tissues were aseptically collected when available ($n = 120$), transported on ice, and received in the laboratory within 4 hours of collection. Gross pathological examination was performed, and tissue samples from the fetal liver, spleen, lung, brain, and placental cotyledon were collected for microbiological analysis. The collected tissue samples were stored in sterile containers at 4°C and processed for bacteriological culture within 24 hours of collection.

2.5. Bacteriological examination

Bacteriological analyses were performed using blood agar, chocolate agar, and selective media—including modified Brucella agar supplemented with antibiotics for isolation of *Brucella* species and

Campylobacter blood-free selective agar for *Campylobacter* spp. Cultures were incubated at 37°C under appropriate atmospheric conditions for 5 to 7 days. Bacterial identification was based on colony morphology, Gram staining, as well as biochemical tests (oxidase, catalase, urease, and carbohydrate fermentation). Presumptive identification of the isolates of *Brucella* was based on the characteristic small, smooth, and translucent colonies on Brucella agar, with Gram-negative coccobacilli morphology, positive for oxidase, catalase, and urease reactions, and hydrogen sulphide production, along with CO_2 requirement for growth on solid media containing the dyes basic fuchsin and thionin. *Campylobacter* isolates were confirmed by characteristic darting motility observed on wet mount preparation, positive oxidase and catalase tests, hippurate hydrolysis, and cephalothin resistance. For the identification of other bacterial pathogens, standard biochemical test batteries were utilized, including triple-sugar iron agar, respiratory citrate utilization, indole production, methyl red-Voges Proskauer test, and carbohydrate fermentation profiles.

2.6. Serological examination

Serological testing of samples for individual pathogens was performed using commercially available test kits. *Brucella* antibodies were detected by the Rose Bengal plate test, with confirmation by competitive enzyme-linked immunosorbent assay (IDEXX Brucellosis Serum X2 Ab Test). *Toxoplasma gondii* IgG antibodies were detected by an indirect ELISA kit (IDEXX Toxotest) as per the manufacturer's recommendations, with a value above the cutoff identified as positive. For anti-*Chlamydomphila* antibodies, a commercial ELISA kit (IDEXX Chlamydiosis Total Ab Test) was used for identification.

2.7. Microscopical examination

Following the preliminary findings, histopathological examination was conducted using Gram, Giemsa, and modified Ziehl-Neelsen stains. The examination of tissue sections was done by an experienced veterinary pathologist to identify characteristic lesions attributable to the specific infectious agents. Lesions were graded based on the severity, such as necrotizing placentitis, suppurative inflammation, granulomatous lesions, parasitic cysts, and microorganisms. The placenta impression smears and fetal stomach contents were directly examined under the microscope. The Ziehl-Neelsen staining method was used to detect *Chlamydomphila* organisms and Giemsa staining to identify *Toxoplasma* tachyzoites or tissue cysts. Smears were prepared from fresh tissue, air-dried, fixed in methanol, and stained according to standard methods. The presence of characteristic intracellular organisms was considered supportive evidence for the respective infections.

2.8. Minerals evaluation

To evaluate the nutritional status of pregnant ewes, serum concentrations of selenium, copper, and zinc were measured using atomic absorption spectroscopy. Serum samples were also analyzed for vitamin E (α -Tocopherol) concentrations using High-Performance Liquid Chromatography. Environmental and management factors were evaluated through a structured questionnaire completed by the farm owners. The questionnaire included items on housing conditions, stocking density, feeding practices, water quality, exposure to extreme weather, and potential stressful events during pregnancy.

2.9. Statistical analysis

Statistical analyses were performed using SPSS® version 26.0 (IBM Corporation, USA). Normality of the data was assessed using the Shapiro-Wilk test and by visual inspection of Q-Q plots. Independent samples t-tests for normally distributed data and Mann-Whitney U tests for non-normally distributed data were used to compare hormone concentrations between the aborted and control groups. Results were presented as mean $\pm$ standard deviation for parametric data and as median (interquartile range) for non-parametric data. Chi-Square or Fisher's exact tests were conducted to compare categorical variables, including causes of abortion. Correlation analyses (Pearson or Spearman) were used to assess the correlation between hormone concentrations and specific etiological factor(s). Multiple logistic regression was used to identify independent predictors of abortion. Statistical significance was set at $p < 0.05$, and Bonferroni correction was applied where appropriate for multiple comparisons.

3. Results

A total of 180 ewes were enrolled in this trial, including 120 aborted ewes and 60 healthy pregnant controls. The average age of ewes in the abortion group was 3.4 ± 1.1 years, which did not differ significantly from that of the control group (3.2 ± 0.9 years; $p = 0.24$). Similarly, body condition scores of the two groups did not differ significantly at the time of examination (abortion group: 2.8 ± 0.4 ; control group: 2.9 ± 0.3 ; $p = 0.17$). The gestational age (GA) of aborted ewes ranged from 92 to 138 days (average GA = 114.6 ± 12.8 days). Table 1 illustrates differences in serum hormone levels of aborted ewes ($n = 120$) versus control ewes that were healthy and pregnant ($n = 60$). Aborted ewes had significantly lower progesterone concentrations than healthy controls (1.82 ± 0.34 ng/mL vs 4.15 ± 0.52 ng/mL, $p < 0.001$). Similarly, they had lower concentrations of estradiol-17 β compared to the control group (12.45 ± 2.18 pg/mL vs 28.67 ± 3.45 pg/mL, $p < 0.001$). On the other hand, ewes that aborted had significantly higher levels of cortisol than the control ewes (45.32 ± 6.78 ng/mL vs 22.15 ± 3.42 ng/mL, $p < 0.001$). The aborted group produced slightly lower levels of prolactin compared to controls on average (86.43 ± 14.25 ng/mL vs 92.18 ± 12.67 ng/mL, $p = 0.008$).

Table 1. Serum hormone concentrations in aborted ewes compared to healthy pregnant controls

Hormone	Aborted ewes (n = 120)	Control ewes (n = 60)	P value
Progesterone (ng/mL)	1.82 ± 0.34	4.15 ± 0.52	<0.001
Estradiol-17 β (pg/mL)	12.45 ± 2.18	28.67 ± 3.45	<0.001
Cortisol (ng/mL)	45.32 ± 6.78	22.15 ± 3.42	<0.001
Prolactin (ng/mL)	86.43 ± 14.25	92.18 ± 12.67	0.008

Data presented as mean $\pm$ standard deviation

Table 2 displays the causes of abortions in sheep (ewes) from Salah Al-Din Province. The majority of the abortion cases were attributed to a pathogenic (infectious) agent, with brucellosis (cause: *Brucella melitensis*) being the most common cause of abortion (with 47 cases, or 33.2% of the total). Other common pathogens that caused abortion include toxoplasmosis (*Toxoplasma gondii*), which caused 31 abortions (25.8%) and chlamydiosis (*Chlamydophila abortus*), with 23 abortions (or 19.2%). Nutritional deficits resulted in abortion in 19 cases, accounting for 15.8% of all abortion cases.

As depicted in Table 3, serum hormone levels in aborted ewes were measured in relation to the cause of abortion and were found to be significantly different ($p = 0.01$) among the four groups being studied.

Table 2. Distribution of abortion causes in ewes in Salah Al-Din Province

Cause of abortion	Number	Percentage
Brucellosis (<i>Brucella melitensis</i>)	47	33.2
Toxoplasmosis (<i>Toxoplasma gondii</i>)	31	25.8
Chlamydiosis (<i>Chlamydophila abortus</i>)	23	19.2
Nutritional deficiencies	19	15.8

The level of progesterone was lowest in lambs that aborted due to brucellosis (1.52 ± 0.28 ng/mL), while the level was highest in those that aborted due to nutritional deficiency (2.14 ± 0.42 ng/mL). Likewise, the level of estradiol-17 β was lowest in lambs that aborted due to brucellosis (10.32 ± 1.85 pg/mL) and highest in those that aborted due to nutritional deficiency (14.23 ± 2.67 pg/mL). Lambs that aborted due to chlamydiosis had the highest cortisol levels (46.82 ± 7.15 ng/mL), while lambs that aborted due to nutritional deficiency had the lowest (41.56 ± 5.82 ng/mL). The four groups of lambs did not display significant differences in prolactin (82.15 ± 13.42 ng/mL in brucellosis and 89.45 ± 13.68 ng/mL in nutritional). Overall, the $p = 0.01$ indicates significant differences in hormone levels between lambs that aborted based on the cause of abortion.

Table 3. Serum hormone concentrations according to abortion causes

Abortion cause	Progesterone (ng/mL)	Estradiol-17 β (pg/mL)	Cortisol (ng/mL)	Prolactin (ng/mL)
Brucellosis	1.52 ± 0.28^a	10.32 ± 1.85^a	43.28 ± 5.94^{ab}	82.15 ± 13.42^a
Toxoplasmosis	1.68 ± 0.31^a	11.78 ± 2.12^a	44.67 ± 6.23^{ab}	85.34 ± 14.87^a
Chlamydiosis	1.95 ± 0.36^b	13.45 ± 2.34^b	46.82 ± 7.15^a	88.76 ± 15.23^a
Nutritional deficiency	2.14 ± 0.42^c	14.23 ± 2.67^b	41.56 ± 5.82^b	89.45 ± 13.68^a
p-value	<0.01	<0.01	<0.01	0.08

Different superscript letters within the same column indicate statistically significant differences
Data presented as mean $\pm$ standard deviation

Table 4 presents the comparison of serum levels of trace minerals and vitamin E between the group of nutritionally deficient aborted ewes ($n = 17$) and the group of healthy control ewes ($n = 60$). All measurements taken in the deficient aborted group are statistically significantly lower ($p < 0.05$ for each indicator) than the corresponding measurements for the control ewes. The average concentration of selenium in the deficient aborted ewes (42.3 ± 8.7 μ g/L) was less than half that of control ewes (95.4 ± 12.3 μ g/L) and, furthermore, was considerably less than the reference range of 80–120 μ g/L. Additionally, the average concentration of copper (8.2 ± 1.5 vs. 14.7 ± 2.1 μ mol/L), zinc (11.3 ± 2.4 vs. 15.8 ± 2.8 μ mol/L), and vitamin E (1.8 ± 0.4 vs. 3.5 ± 0.6 mg/L) were also significantly lower in the deficient aborted group.

Table 4. Serum trace mineral and vitamin E concentrations in aborted and control ewes

Parameter	Aborted ewes (n = 17)	Control ewes (n = 60)	Reference value
Selenium (μ g/L)	42.3 ± 8.7^a	95.4 ± 12.3^b	80-120
Copper (μ mol/L)	8.2 ± 1.5^a	14.7 ± 2.1^b	12-20
Zinc (μ mol/L)	11.3 ± 2.4^a	15.8 ± 2.8^b	14-24
Vitamin E (mg/L)	1.8 ± 0.4^a	3.5 ± 0.6^b	3.0-5.0

Different superscript letters within the same row indicate statistically significant differences ($p < 0.05$)
Data presented as mean $\pm$ standard deviation

Table 5. Correlation between hormone concentrations and abortion causes				
Abortion cause	Progesterone	Estradiol-17β	Cortisol	Prolactin
Brucellosis	r = -0.68**	r = -0.59**	r = 0.52**	r = -0.41*
Toxoplasmosis	r = -0.61**	r = -0.54**	r = 0.48*	r = -0.38*
Chlamydiosis	r = -0.60**	r = -0.52**	r = 0.46*	r = -0.36*
Nutritional	r = -0.44*	r = -0.42*	r = 0.39*	r = -0.28
*p<0.05; **p<0.001				

than in both the control group and the established reference ranges. Therefore, these results indicate that nutritional deficiencies, particularly those involving selenium, copper, zinc and vitamin E, are associated with decreased levels of these essential micronutrients and may also contribute to the incidence of abortion in these ewes.

Correlation analysis revealed significant relationships between hormonal parameters and abortion causes. Table 5 summarizes the correlation coefficients between hormone concentrations and major etiological factors.

Multiple logistic regression analysis identified independent predictors of abortion risk. Table 6 presents the regression results.

Table 6. Multiple logistic regression analysis of abortion predictors			
Variable	Odds ratio	95% CI	P value
Low progesterone (<2 ng/mL)	8.4	4.2-16.8	<0.001
Elevated cortisol (>40 ng/mL)	5.7	2.8-11.6	<0.001
Brucellosis seropositivity	12.3	5.4-28.1	<0.001
Toxoplasma seropositivity	7.8	3.6-16.9	<0.001
Low estradiol-17β (<15 pg/mL)	4.2	2.1-8.4	<0.001
Selenium deficiency (<60 μg/L)	3.6	1.5-8.7	0.002
CI: Confidence interval			

4. Discussion

This research analyzed the hormonal and other causes related to sheep abortions in Salah-Al-Din Province, Iraq. Sheep that had abortion revealed lower levels of serum progesterone (P4) and estradiol 17-β (E2) than the control group and an increased level of cortisol indicating that hormones that maintain pregnancy were disrupted within these sheep. In combination with the infectious agents that were found predominately in these sheep (brucellosis and toxoplasmosis), these findings show that abortion is a multifactorial occurrence within this area, which will require coordinated preventative measures. Average levels of P4 were 1.82 ng/mL ± 0.34; while in the control group, average levels were 4.15 ng/mL ± 0.52; thus, the abortions sheep averaged 56% lower than control sheep. P4 levels in both groups averaged below the 2-3 ng/mL threshold needed for mid-gestation (Boscos et al. 2016), which would suggest a common final pathway of luteal dysfunction that provides a mechanism for the occurrence of abortion in these sheep. The strong negative correlation between P4 and brucellosis (r = -0.68) and toxoplasmosis (r = -0.61) indicates that brucellosis and toxoplasmosis are responsible for the dysfunction of the corpus luteum through inflammatory substances such as prostaglandin F2α (Loped-Gatius 2022) and cytokines (TNF-α, IFN-γ) that inhibit P4 synthesis (Gao et al. 2021).

Aborted ewe average E2 levels were 12.45 pg/mL ± 2.18; while the control ewes averaged 28.67 pg/mL ± 3.45, an average of 57% lower

than the control sheep, indicating placental failure. Estrogens are important to the development of the placenta, uterine blood flow, and immune modulation (Albrecht and Pepe 2010). The low E2 levels also may result in a disruption of P4 receptor functionality (Azeez et al. 2021) and create a shift in immune component balance to reduce Th2 responses (Rackaityte and Halkias 2020), which otherwise would support pregnancy. Cortisol was significantly higher in aborted ewes (45.32 pg/mL ± 6.78) than in control ewes (28.96 pg/mL ± 4.88); therefore, increased cortisol can possibly suppress P4 synthesis by inhibiting the function of the corpus luteum. Cortisol levels were approximately 22.15 ± 3.42 ng/mL and exhibited a significant relationship with abortion (r = 0.74). Cortisol has also been shown to inhibit progesterone production via inhibition of 3β-hydroxysteroid dehydrogenase (Kater et al. 2022), facilitate the regression of the corpus luteum by stimulating the production of prostaglandin F2α (Brooks et al. 2014), and enhance uterine contractions (Spencer et al. 2026). Additionally, environmental stressors in Iraq such as summer temperatures over 45°C stimulate the hypothalamic-pituitary-adrenal axis and reduce feed intake, leading to pregnancy loss (Cheng et al. 2022; Marai et al. 2007).

Brucellosis was the most common cause of abortion accounting for 33.2% of cases and is consistent with reports from the area (Abedi et al. 2020; Bagheri et al. 2020). Brucellosis causes necrotizing placentitis resulting in fetal death. The second most common cause was Toxoplasma (25.8%), which was linked to the presence of cats on 89% of the farms and to the persistence of oocysts in the environment (Dubey 2016). Chlamydiosis was responsible for 19.2% of the abortions (Nietfeld 2001). Nutritional deficiencies related to selenium and vitamin E accounted for 15.8% of the abortions, with selenium deficiency being found in 64.7% of those abortions (Rayman 2012). Logistic regression analyses identified predictors of abortion that were independent of one another and included: brucellosis (OR = 12.3), low progesterone (OR = 8.4), Toxoplasma (OR = 7.8), high cortisol (OR = 5.7), low estradiol (OR = 4.2), and selenium deficiency (OR = 3.6).

Deficiencies of copper and zinc are likely a considerable factor in ovine abortion in Salah-Al-Din Province. Copper is necessary for cytochrome c oxidase, superoxide dismutase, and lysyl oxidase, as well as being a cofactor for numerous enzymes. A deficiency of copper causes embryonic death, placental abnormality, and fetal hypoxia by decreasing the formation of blood vessels (angiogenesis) and weakens the membranes of the placenta (Suttle 2018). Additionally, subclinical copper deficiency could predispose the animal to infectious placentitis due to its effect on neutrophil function (López-Alonso and Miranda 2020). The very high levels of molybdenum in the soils of Iraq could lead to secondary copper deficiency (Suttle 2018). Zinc is involved in over 300 metalloenzymes and is required for numerous biological functions including DNA synthesis, steroid production, and immunity. When animals are zinc deficient, LH/FSH secretion, and the activity of 3β-hydroxysteroid dehydrogenase (an enzyme involved in progesterone production) are decreased (Prasad 2014). Additionally, zinc deficiency enhances the immune response to pro-inflammatory cytokines produced by Brucella and Toxoplasma, leading to placentitis and fetal loss (Hostetler et al. 2015). Also, zinc is an important antioxidant and zinc deficiency leads to increased oxidative damage to trophoblasts (Suttle 1986). Salah-Al-Din Province has calcareous, high pH soils with minimal organic matter that have yielded low copper and zinc bioavailability (Al-Jubouri and Al-Hadithi 2017). It is likely there is

a high incidence of multiple trace mineral deficiencies since 64.7% of nutritional abortions had a selenium deficiency. A comprehensive supplementation program should include copper, zinc, selenium, and vitamin E, with the amounts being determined by serum or liver mineral analysis.

5. Conclusions

This study demonstrated that abortion in ewes in Salah Al-din Province of Iraq is associated with significant hormonal disruptions caused by decreased concentrations of progesterone and estradiol-17 β , along with increased cortisol levels. The major causes of abortion in ewes were infectious diseases, such as brucellosis and toxoplasmosis, while nutritional deficiencies and environmental stressors also contributed significantly to reproductive losses in ewes. In order to lower the incidence of abortion in sheep populations, these findings emphasize the necessity of integrated control strategies that combine efficient vaccination programs, better nutritional management, increased biosecurity measures, and mitigation of environmental stress.

Declarations

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