

Clinical and Comparative Efficacy of Antibiotic Therapy for the Management and Treatment of Secondary Bacterial Infection in Peste des Petits Ruminants in Goats and Sheep in Saudi Arabia

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Abstract

Background: Peste des Petits Ruminants (PPR) is a contagious viral disease that affects goats and sheep and cause significant economic losses. It is associated with secondary bacterial infections that further exacerbate the clinical impact of the disease. **Aims and Objectives:** This study aimed to evaluate the morbidity and mortality rates associated with PPR outbreaks and assess the effectiveness of four different antibiotic treatment protocols to manage the secondary bacterial infections in PPR-infected goats and sheep. **Materials and Methods:** The disease was confirmed through real-time polymerase chain reaction (PCR) and clinical signs such as cough, fever, chills, shortness of breath, mucopurulent nasal and ocular discharge, and diarrhea. Positive animals of both species were divided into four equal groups (A, B, C, and D), with each group received a different antibiotic treatment protocol with identical supportive care for all groups: Treatment A: Oxytetracycline Treatment B: Tylosin + Gentamicin Treatment C: Tylosin + Gentamicin + Ceftriaxone Treatment D: Control group (no antibiotic treatment) **Results:** Goats exhibited a higher infection rate (73.24%) compared to sheep (47.26%). Among the treatment groups, Treatment C demonstrated the lowest overall mortality (9.94%) and the highest recovery rate (90.05%). In contrast, Treatment D (the control group) was the least effective with highest mortality rate (43.45%) and the lowest recovery rate (56.54%). Statistical analysis with Chi-square test revealed a highly significant difference in Treatment C ($P < 0.05$). **Conclusion:** Combination therapies, particularly Treatment C (Tylosin + Gentamicin + Ceftriaxone), were found to be the highly effective in the management of secondary bacterial infections in PPR disease.

Keywords: Antibiotic combination therapy, antibiotic treatment protocols in peste des petits ruminants, peste des petits ruminants, peste des petits ruminants clinical diagnosis, small ruminant viral disease

INTRODUCTION

The two important meat sources in Saudi Arabia are sheep and goats (1). Millions of these animals are reared throughout the country at different locations (2). In Saudi Arabia, the PPR is exotic and outbreaks occur variably in animals, especially sheep and goats <1 year and over 4 months of age (3). In Saudi Arabia, the first case of PPR was recorded in 1990 (4) Now, it becomes endemic to the countries of Asia and Africa (5).

Peste des Petits ruminants (PPR) is a highly contagious and important transboundary disease with high economic implications (6). This disease is characterised by erosive stomatitis that may become necrotising, enteritis and pneumonia (7). The disease comes in different forms such as per acute, acute, sub-acute and sometimes chronic. It

has an incubation period of 4–7 days (8). This disease has high economic importance due to its high morbidity and mortality rates (9). It is believed that the morbidity of sheep is low to PPR disease due to an innate immunity to the PPR virus (PPRV) (10). However, in goats, its effects are unquantifiable and the mortality varies between 50% and 80%, whereas morbidity varies between 80% and 90% (11).

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The virus is transmitted through direct contact with body secretions by the infected animal (12). The eyes and nose of the infected animals contain dried discharges. The carcasses of the affected animals are emaciated and sunken eyes. The lining of the nasal cavity will be reddened and congested with creamy yellow exudate (13). The severity of the symptoms of PPR disease is based on the different factors such as age, species, immunity and previous exposure (14).

After initial replication in the oropharynx and local lymphoid, the PPRV spreads through the lymphatic system and bloodstream and target organs such as the lymph nodes, spleen, lungs, gastrointestinal tract, and liver. The virus infects immune cells such as T-lymphocytes, macrophages and dendritic cells, thus impairs the immune defenses (9). The destruction of T- and B-lymphocytes weakens the adaptive immune response and thus facilitates bacterial infections such as pneumonia and diarrhoea (8). Its spreads to the respiratory, gastrointestinal and skin tissues causes bronchopneumonia, severe diarrhoea and skin lesions like stomatitis and 'big head disease'. These symptoms lead to dehydration, weight loss and respiratory distress (15). There is a chance of abortion in pregnant animals. In outbreaks, the mortality rate sometimes exceeds 70%. The infected animals usually die in 10 days after getting the virus (15).

Antibiotics are not effective against the PPRV itself. They are used to control the secondary bacterial infection that often complicates PPR cases. Because PPR is a viral disease, supportive care including antibiotics to treat bacterial infections becomes a crucial component in its management strategies (9).

The literature review has revealed various strategies to combat the PPR disease. Baruti *et al.* (16) used Metronidazole (10 mg/kg), ceftriaxone (7.5 mg/kg) and levamisole (2.5 mg/kg) for 7 days along with supportive care such as rehydration and ulcer treatment. This treatment protocol results in the complete recovery of the affected goats. Another study by Ugochukwu *et al.* (17) compared various drug protocols in Dwarf goats. They found that a combination of Ivermectin, Acyclovir and Oxytetracycline was the most effective treatment that resulted in the lowest mortality (25%) in comparison to a single medication ($\geq 75\%$). Ugochukwu *et al.* (18) conducted yet another study on Dwarf goats and revealed that a combination of Levamisole, Oxytetracycline and Amantadine hydrochloride resulted in 0% mortality. The goats treated with fewer medicines resulted in higher mortality from 25% to 50% and the untreated goats had the highest death rate (75%). Olaogun *et al.* (19) studied a PPR outbreak in a similar goat breed (Dwarf). They treated the animals for 5 days with a combination of multivitamins, sulphadimidine and tylosin and found that despite the treatment, the mortality reached 28%.

The present study aimed to investigate the morbidity and mortality in both species of goats and sheep. In this study, different combinations of treatment trials were applied to both species and then the effectiveness of these trials was judged

in inter and intra-species. In the end, from these results, the most effective treatment that resulted in the lowest mortality was observed.

MATERIALS AND METHODS

Study animals

The trial was conducted during an outbreak of PPR at a sheep and goat farm in the Kingdom of Saudi Arabia. The farm recently purchased 852 female Dwarf goats for breeding purpose and 292 male sheep of different breeds (Sawakni, Najdi and Harri) for fattening purposes. All goats in this study were female and sheep were males. The goats in this study were below the age of 1 year while the age of sheep was between 1 and 2 years with almost same body score for both species. All animals were non-vaccinated.

Confirmation of infection

A positive case of PPR is an animal that tests positive for PPRV infection through the real-time polymerase chain reaction (RT-PCR) and is also showing clinical signs of the disease (mucopurulent nasal and ocular discharge, diarrhoea and respiratory distress). Animals that met the diagnostic and clinical criteria were included in the study. The eligibility criteria for animals required to be included was to exhibit the typical clinical signs of PPR and then to be confirmed positive by the diagnostic method. The procedure of swabs collection, storage and sending to the laboratory was carried out as described by Wieland *et al.* (20) The conjunctival, oral and nasal swabs (two samples from each animal) were collected from these animals and sent to the laboratory for RT-PCR to isolate and sequence the positive samples. The swabs collected as a samples were stored at -80°C before being examined.

The procedure of RT-PCR was conducted according to the guidelines described by Balamurugan *et al.* (21) To detect PPRV in clinical samples using one-step RT-PCR, a 50 μL reaction mixture was prepared containing 5 μL of total RNA extracted from the sample, 20 pmol of each PPRV-specific primer, 10 μL of $5\times$ reaction buffer (that contains MgCl_2 , Tris HCl, KCl and dNTPs) and 2 μL of an enzyme mixture consisted of Ominiscript and Sensiscript reverse transcriptases and HotStar Taq DNA polymerase. Reverse transcription procedure was performed at 50°C for 30 min, followed by the inactivation of reverse transcriptase and then activation of Taq polymerase at 95°C for 15 min. The target genes were amplified with 35 cycles of denaturation at 94°C for 30 s, the primer annealed at 60°C for 30 s and extension done at 72°C for 1 min, followed by a final extension at 72°C for 10 min. Purified PPRV RNA of 10 ng was included as a positive control. The RT-PCR products were analysed by electrophoresis in a 1.5% agarose gel and confirmed the authenticity by digesting the products with restriction enzymes NciI and XhoI for the N gene and DdeI and MboII for the M gene, with a subsequent electrophoresis on a 2% agarose gel. The sensitivity was determined by using serial tenfold

Table 1: Details of drugs used in this experiment

Type of drug/ used for	Brand name	Constituent (s) and composition	Recommended dose by the manufacturer
Antibiotic	Terramycin*/LA	Each mL contains: Long acting oxytetracycline 200 mg	1 mL for 10 kg body weight
Antibiotic	Gentodad 10%	Each mL contains: Gentamicin (as sulphate) 100 mg	1 mL for 20 kg body weight
Antibiotic	TYLO SAV 200	Each mL contains: Tylosin (as tartrate) 200 mg	1 mL for 20 kg body weight
Antibiotic	CEFTRIMAX L.A	Each 100 mL contains: Ceftriaxone sodium 10 g	1 mL for 20 kg body weight
Antiallergic/ antihistamine	ALLERVET	Each mL contains: Chlorphenamine maleate 10 mg	1 mL for 25 kg body weight
Antibiotic	PENDISTREP 20/20	Each mL contains: Procaine benzylpenicillin 200 mg (200,000 I.U) Dihydrostreptomycin sulphate eq. 200 mg base	2.5–5 mL/50 kg body weight
Antibiotic/ antidiarrheal	PHARMA TRIMAZINE 420/80	Each gram contains: Sulphadiazine sodium 420 mg Trimethoprim 80 mg Dextrose monohydrate as excipient	21 mg Sulphadiazine sodium and 4 mg Trimethoprim per kg body weight divided into two doses for a maximum of 5 days
Antispasmodic/ antisialogogue	ATROJAT	Each ml contains: Atropine sulphate BP 1 mg sodium metabisulphite BP 0.1% w/v water for injection BP q.s	For sheep and goat: 0.080–0.160 ml/kg
Pain killer/ antipyretic	FLUNIXIN	Each ml contains: Flunixin meglumine 50 mg 5 mg phenol as preservative	1 ml for 45 kg body weight
Antibiotic/eye drop	TOBRACIN	Each ml contains: Active ingredients: (tobramycin 3 mg benzalkonium chloride as preservative 0.1 mg) Inactive ingredients: (boric acid, tiwen 80, sodium sulfate, sodium HCL or NaOH and highly purified water)	
Herbal spray for wound dressing/ lesions	Topicure	Each 100 mL contains: Serala (pinus longifolia) 15g Tailaparna (Eucalyptus spp.) 12.5g Davadaru (cedrus deodara) 10g Colouring agent: Curcumin as excipients	Topical use
Fluid therapy	Ringer's lactate	Each 1 L contains: Sodium lactate 3.20 g Sodium chloride 6 g Potassium chloride 0.40 g Calcium chloride 2H ₂ O 0.27 g Water for injection to 1000 mL	10–20 mL/kg body weight - up to 40–60 mL/kg body weight
Fluid therapy	Normal saline	0.9% sodium chloride solution	10–20 mL/kg body weight - up to 30–40 mL/kg body weight

dilutions of purified PPRV RNA, that ranged from 1 ng to 10 fg, to establish the lowest RNA concentration that gave a clear positive signal. A positive sample exhibited the expected band size and restriction enzyme digestion pattern, to confirm the presence of PPRV.

Experimental drugs

Experimental drugs used in this study including their brand name, ingredient(s) and manufacturer's recommended dose are described in Table 1.

Experimental design and drugs administration

Positive animals from each species were randomly assigned to four treatment groups (A, B, C and D) to eliminate the biases. The simple randomisation process was employed, and each animal was randomly assigned to one of the treatment groups using the random number generation. The treatment plan was structured into four groups for both sheep and goats: Groups A, B, C and D [Table 2].

Each group received a different combination of antibiotics, while all groups received identical supportive treatments, including herbal spray for oral lesions, antidiarrhoeal medications, fluid therapy, eye drops, antihistamines,

Table 2: Experimental groups and number of animals for both sheep and goats

Groups names	A (treatment group)	B (treatment group)	C (treatment group)	D (treatment group)
Animals species	Goats			
Number of animals	213	213	213	213
Animals species	Sheep			
Number of animals	73	73	73	73

painkillers/antipyretics and atropine sulfate. Groups A, B and C were the treatment groups that received both antibiotics and supportive medications to address the secondary bacterial infections. However, in contrast, the Group D served as the control group, received only supportive treatments without antibiotics [Table 3].

The 852 goats were evenly distributed across the four groups, with each group consisting of 213 goats. Similarly, the 292 sheep were equally assigned to the groups, with each group containing 73 sheep.

Administration of antibiotic(s) and supportive medications (doses and duration) were administered, as recommended by the manufacturer [Table 3].

Explanation of the specific antibiotic combinations chosen *Oxytetracycline (treatment A)*

Oxytetracycline is a broad-spectrum tetracycline antibiotic that is commonly used to treat respiratory infections, enteric diseases and other bacterial infections in goats and sheep. Its can be used in goats (with PPR outbreaks) against common secondary bacterial infections that can result from PPR, such as pneumonia or diarrhoea caused by *Escherichia coli*, *Pasteurella* or *Mycoplasma* species (22).

Tylosin + Gentamicin (treatment B)

Tylosin is a macrolide antibiotic often used to treat respiratory infections and *Mycoplasma*-related conditions in small ruminants. Gentamicin, an aminoglycoside antibiotic, is effective against Gram-negative bacteria, which could be beneficial if secondary bacterial infections in sheep involve pathogens such as *E. coli* or *Salmonella*. Their combination produce synergistic effects, as Tylosin targets *Mycoplasma* species while Gentamicin addresses Gram-negative pathogens to cover a broader range of potential infections during PPR outbreaks (23).

Tylosin + Gentamicin + Ceftriaxone (treatment C)

Ceftriaxone is a third-generation cephalosporin and is broad-spectrum, particularly effective against Gram-negative bacteria, *Staphylococcus* and *Streptococcus* species and it provides good results in treating secondary bacterial infections due to PPRV (24). The goal of this combination is to provide a comprehensive antimicrobial therapy for goats to targeting both Gram-positive and Gram-negative bacteria as well as *Mycoplasma* species.

Statistical analysis

All statistical calculations were made with a 95% confidence interval (CI) and a Chi-square test was performed for the data analysis. The Chi-square test evaluated whether in terms of

mortality there exists a statistically significant difference in treatment effectiveness or not.

Analysis rule

Null hypothesis (H_0): There is no significant difference in mortality rates between different treatments.

Alternative hypothesis (H_1): There exists a significant difference in mortality rates between different treatments.

Decision rule: If the $P < 0.05$ then we will reject H_0 (significant difference) and if the $P > 0.05$ then we will fail to reject H_0 (no significant difference).

RESULTS

Clinical symptoms of the disease

Clinical signs were different among the animals and symptom severity also varied. Initially, the disease started with a serous nasal discharge and fever, although not all animals developed a fever. In later stages, the nasal discharge became mucopurulent and gave a purified odor [Figure 1].



Figure 1: Sheep with mucopurulent nasal discharge infected with Peste des Petits Ruminants virus

Table 3: Tabular explanation of the experimental design

Drugs groups and administration	Goats and sheep groups			
	A	B	C	D
Treatment A: Terramycin*/LA (oxytetracycline)	Yes	No	No	No
Treatment B: TYLO SAV 200 (tylosin) + gentodad 10% (gentamicin)	No	Yes	No	No
Treatment C: TYLO SAV 200 (Tylosin) + gentodad 10% (gentamicin) + ceftimax L.A (ceftriaxone)	No	No	Yes	No
Treatment D: No antibiotic (control group)	No	No	No	No
Sulphad+trimetho oral for diarrhoea (if required)	Yes	Yes	Yes	Yes
Atroject (Atropine sulphate) (If required)	Yes	Yes	Yes	Yes
FLUNIXIN (Flunixin meglumine) (If required)	Yes	Yes	Yes	Yes
TOBRACIN eye drop (if required)	Yes	Yes	Yes	Yes
Herbal spray on oral lesions (if required)	Yes	Yes	Yes	Yes
Fluid therapy for dehydration (if required)	Yes	Yes	Yes	Yes

The pneumonic animals coughed a lot due to bronchopneumonia. The severely affected animals developed areas of necrosis on the mucus membrane of the nasal cavity [Figure 2]. The severe cases have laboured breathing and loud respiratory rales could be heard from a distance. All these animals ultimately die of the condition.

The affected goats isolated themselves from the herd and were often found leaning against fences or walls or sitting with their heads lowered. They appeared stressed and exhausted. As the disease progressed, many goats also developed diarrhoea that led to dehydration and emaciation. It initially contained undigested feed material but later became profuse and watery. It was unresponsive to any treatment. Some cases involved mucus or bloody diarrhoea. Some animals exhibited intense straining with only mucus or blood-stained mucus [Figure 3].

In later stages, stomatitis appeared on the lips and gums, dental pad, tongue, palate and dental pad [Figure 4]. All these areas were involved in some cases and one or more than one area was involved in some cases.



Figure 2: Goat with the areas of necrosis on the mucus membrane of the nasal passage

Several goats went off feed and succumbed to starvation. Eleven cases, in later stages, developed orf-like lesions on the lips [Figure 5]. Swollen lips prevented them from closing their mouths and to grip fodder. Goats with these swollen lips struggled to eat and eventually died of starvation.

In later stages, at the end of the disease, some animals developed mandibular and brisket oedema [Figure 6]. In recovered goats, the edema subsided naturally. However, in severely affected animals that were still undergoing the disease, the oedema spread over the entire face that resembled 'big head disease'.

In contrast, the recovered animals showed localised oedema beneath the mandible or at the region of the brisket similar to the case of liver fluke infection. Both brisket and mandibular oedema were not observed at once in a single animal. Either an animal is having brisket or mandibular oedema only [Figure 7].

Goats that survived the severe respiratory and digestive symptoms became highly emaciated. Some goats become too weak to stand but they continue eating and drinking



Figure 3: Goat with bloody diarrhoea and severe tenesmus (later she died)



Figure 4: A goat with severe stomatitis and lesions



Figure 5: Goat with orf-like lesions

while sitting or lying down. Over the time of 2–3 weeks, they regained strength and resumed normal activity.

After the outbreak, a secondary wave of diarrhoea occurred that was also unresponsive to treatment. The already weakened animals did not survive. They died due to severe dehydration. These diarrhoeic cases were marked by extreme straining. The PPR outbreak had long-lasting effects on the survivors. Even months after their recovery, minor dietary changes in their feed had triggered digestive disturbances such as diarrhoea and indigestion.

During the outbreak, some pregnant goats aborted live fetuses [Figure 8]. All of them experienced retained foetal membranes. Ten days after the start of the outbreak, all goats were administered the first dose of the PPR vaccine (Pestevac®) followed by a booster dose 29 days later. Notably, a male kid was born to a goat that had received its first PPR vaccine dose 21 days prior. Ten days after his birth, the kid developed PPR-like oral lesions but recovered with just the application of herbal spray (Topicure®) inside the mouth.

A thick yellowish-white discharge from the eyes makes them sticky. When it dried up, it strictly binds both eyelids together

and the goat is unable to open its eyes. If these eyes were tried to open forcibly, the animals feels pain [Figure 9].

When their eyes were opened with assistance, the eyelids gave a matting appearance. Some goats developed profuse catarrhal conjunctivitis with congestion and lacrimation, due to the continuous flow of tears and the hairs of the affected area of the face eroded. Corneal opacity was observed in the later stages of the disease and the retina turned to whitish blue like the case of pink eye [Figure 10].

Post-mortem findings

Pharynx and hard palate

In severe cases, the lesions were observed on the pharynx and hard palate. In the start, these lesions were observed to be shallow and reddish, but in later stages, they give the appearance of a pinkish-white colour [Figure 11].

Liver

In some animals, the liver was found to be enlarged and discoloured.



Figure 6: Goats with facial oedema in later stages of Peste des Petits Ruminants, later she died

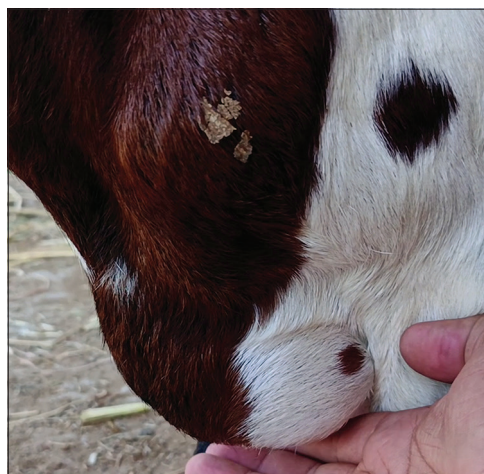


Figure 7: Goat with brisket oedema in the recovery stage, she recovered



Figure 8: Aborted fetus that was alive



Figure 9: Goat in later stages of Peste des Petits Ruminants. She was unable to open her eyes because the thick discharges had tightly sealed the eyelids together. Her facial hairs had fallen where the tears ran off (The green colour was the herbal spray that was applied to repel flies away)



Figure 10: A goat with cloudy eye in the later stages of Peste des Petits Ruminants, her eyes were recovered



Figure 11: The hard palate and other areas of the mouth of a goat died of Peste des Petits Ruminants after a long fight with the disease



Figure 12: Intestines of a sheep died of Peste des Petits Ruminants

Intestines

On the intestines, streaks of haemorrhages were found in some animals [Figure 12].

Respiratory tract

Mucopurulent material was found in the trachea and larynx of severely affected animals. The patches of bronchopneumonia were evident in the lungs [Figure 13].

Occurrence of peste des petits ruminants in both goats and sheep

The results showed that PPR infection was more prevalent in goats (73.24%) than in sheep (47.26%). Despite the higher infection rate in goats, the mortality rates were similar, with 16.83% of goats and 14.84% of sheep died from the disease. These findings suggest that although goats have a higher infection burden, the mortality rates are comparable between the two species [Table 4].

Effectiveness of different treatments in goats

Among the treatments, Treatment C demonstrated the highest effectiveness, with the lowest mortality rate (10.90%) and the highest recovery rate (89.10%). This suggests that the combination of tylosin, gentamicin and ceftriaxone provided



Figure 13: Trachea of a goat containing mucopurulent fluid and lesions

enhanced therapeutic benefits. Treatment B, which included tylosin and gentamicin, also showed promising results with a mortality rate of 16.67% and a recovery rate of 83.33%. It indicated that it was effective but slightly less than Treatment C. Treatment A, which had a mortality rate of 19.23% and a recovery rate of 80.77%, was effective but had a higher mortality rate compared to the tylosin-based regimens. The least effective was Treatment D, with the highest mortality rate (46.15%) and the lowest recovery rate (53.84%) that made it the least beneficial treatment option [Table 5].

Effectiveness of different treatments in sheep

Similar to goats, the results for sheep showed varying success rates across the treatments, with Treatment C proving the most effective. It resulted in the lowest mortality rate (5.71%) and the highest recovery rate (94.29%) that indicated its superior efficacy. Treatment B, which consisted of tylosin and gentamicin, had a mortality rate of 14.28% and a recovery rate of 85.71% that showed promising results but slightly less effective compared to the combination in Treatment C. This emphasises the potential benefits of adding ceftriaxone to

improve treatment outcomes. Treatment D showed the highest mortality rate (31.42%) and the lowest recovery rate (68.57%), proving it to be the least effective treatment for sheep [Table 6].

Treatment-wise analysis in both species

The overall effectiveness of four different treatments for PPR in both goats and sheep was evaluated and summarised in Table 7. Treatment C proved to be the most effective, with

Table 4: Occurrence of peste des petits ruminants in both goats and sheep

Species	Total number of animals	Infected (count)	Infected (%)	Died (count)	Died (%)
Goats	852	624	73.24	145	23.23
Sheep	292	140	47.95	24	17.14

Table 5: Effectiveness of different treatments in goats

Treatment	Infected	Died (count)	Died (%)	Recovered (count)	Recovered (%)
Treatment A	156	30	19.23	126	80.77
Treatment B	156	26	16.67	130	83.33
Treatment C	156	17	10.90	139	89.10
Treatment D	156	72	46.15	84	53.84

Table 6: Effectiveness of different treatments in sheep

Treatment	Infected	Died (count)	Died (%)	Recovered (count)	Recovered (%)
Treatment A	35	6	17.14	29	82.86
Treatment B	35	5	14.28	30	85.71
Treatment C	35	2	05.71	33	94.29
Treatment D	35	11	31.42	24	68.57

Table 7: Treatment-wise analysis in both species

Treatment	Infected	Died (count)	Died (%)	Recovered (count)	Recovered (%)
Treatment A	191	36	18.85	155	81.15
Treatment B	191	31	16.23	160	83.77
Treatment C	191	19	09.94	172	90.05
Treatment D	191	83	43.45	108	56.54

Table 8: Overall treatment-wise statistical analysis

Treatment	Total infected	Total died (count)	Total died (%)	Total recovered (count)	Total recovered (%)	Pearson Chi-square	P (asympt. significant)	Interpretation	Mortality CI (95%)
Treatment A	191	36	18.85	155	81.15	1.19	0.276	No significant difference	13.30–24.39
Treatment B	191	31	16.23	160	83.77	3.85	0.0499	Significant difference	11.00–21.46
Treatment C	191	19	09.94	172	90.05	16.43	5.05E-05	Highly significant difference	5.70–14.19
Treatment D	191	83	43.45	108	56.54	50.47	0.0001	Highly significant difference	36.43–50.49

CI: Confidence interval

the lowest mortality rate (9.69%) and the highest recovery rate (89.89%). In contrast, Treatment D had the highest mortality rate (20.21%) and the lowest recovery rate (79.79%) that made it the least effective treatment. Treatment A and Treatment B showed intermediate effectiveness, with mortality rates of 19.15% and 16.49% and recovery rates of 80.85% and 83.51%, respectively. These findings suggest that Treatment C is the most effective in the reduction of mortality by combating secondary bacterial infections. While Treatment D is the least effective amongst the four treatments [Table 7].

Overall treatment wise statistical analysis in both species

Table 8 presented the results of four different treatments for the treatment of secondary bacterial infections in PPR in terms of mortality rates, recovery rates and statistical significance. The mortality CIs provided insight into the reliability of the mortality estimates for each treatment.

Treatment A had a mortality rate of 18.85%, with a 95% CI ranging from 13.30% to 24.39%. It indicated that the true mortality rate was likely within this range. The $P = 0.276$, which was >0.05 , suggested that there was no significant difference in mortality rates compared to the expected rates. It indicated that Treatment A was not statistically significant.

Treatment B showed a mortality rate of 16.23%, with a 95% CI of 11.00%–21.46%. The $P = 0.0499$ was <0.05 . It indicated that a statistically significant difference existed in mortality rates. It suggested that Treatment B was effective in reducing mortality compared to the expected rate.

Treatment C had the lowest mortality rate (9.94%), with a 95% CI of 5.70%–14.19%. The $P = 5.05E-05$, which was very small, an indication of a highly significant difference in mortality rates. This suggested that Treatment C was the most effective in the reduction of mortality, with a high statistical significance.

Treatment D showed the highest mortality rate (43.45%), with a 95% CI ranging from 36.43% to 50.49%. Although the $P = 0.0001$ was very small, that was positive for a highly significant difference, the high mortality rate suggested that Treatment D was less effective compared to the other treatments.

In summary, Treatment C was the most effective in the reduction of mortality, while Treatment D was the least effective despite showing statistical significance.

DISCUSSIONS

PPR continues to be a significant threat to the livestock industry in Saudi Arabia because the outbreaks have occurred sporadically in this region. The findings of this study confirm previous reports that the susceptibility of goats is higher compared to sheep. However, despite this disparity in infection rates, the mortality rates between the two species were comparable. The findings suggest that goats may harbour a higher infection burden, but the disease outcome in terms of mortality was relatively consistent between the two species.

One of the key aspects of this study was the comparison of four different treatment combinations. The antibiotic combination involving tylosin, gentamicin and ceftriaxone (Treatment C) proved to be the most effective treatment across both species. It resulted in the lowest mortality rate (9.94%) and the highest recovery rate (90.05%) overall. This suggests that the broad-spectrum antimicrobial activity of this combination offers enhanced therapeutic benefits.

Conversely, Treatment D showed the poorest performance. It resulted in the highest mortality rate (43.45%) and the lowest recovery rate (56.54%). This indicates that Treatment D was less effective in treating PPR, possibly due to its inadequate antimicrobial spectrum. This emphasises the need for multi-drug combinations to improve the clinical results.

Moreover, the findings suggest that the antibiotic combination offers a more reliable approach to the management of secondary bacterial infections due to PPRV in both goats and sheep. This aligns with the idea that the use of multiple drugs can be more effective than a single antibiotic in the management of highly contagious diseases like PPR.

The study also revealed some important clinical observations, such as the presence of secondary bacterial infections. For example, animals with severe respiratory symptoms often developed secondary infections, which worsened pneumonia and resulted in higher mortality. In addition, the presence of diarrhoea and emaciation in infected goats highlighted the importance of supportive care, such as fluid therapy and nutritional support. These were provided in this study and may have contributed to the recovery of some animals.

Furthermore, the study noted the long-term effects of PPR on surviving animals. Some goats that survived the acute phase of the disease developed chronic gastrointestinal disturbances, such as diarrhea and indigestion. This indicates that the infection may have lasting effects on the health of the animals even after recovery. This has important implications for the long-term management and care of animals that survive PPR outbreaks.

Statistical analysis was performed using the Chi-square test to determine whether the differences in mortality rates were statistically significant. The study revealed significant differences in the effectiveness of the treatment regimens for managing secondary bacterial infections in PPR. Treatment C showed a highly significant difference ($P = 5.05E-05$). It

indicated the effectiveness of the combination of Tylosin, Gentamicin and Ceftriaxone in the reduction of mortality rates and improvement in recovery. This confirms the clinical observations that Treatment C was the most effective in the treatment of bacterial infections in PPR. In contrast, Treatment D, with the highest mortality rate (43.45%) and lowest recovery rate (56.54%), demonstrated the poorest performance and was also highly significant ($P = 0.0001$). Treatment B (Tylosin + Gentamicin) showed a promising recovery rate of 83.77%, although its P value (0.0499) indicated no significant difference, while Treatment A (Oxytetracycline) also failed to show statistical significance ($P = 0.276$). The observed clinical differences in Treatment C could also be influenced by the factors such as animal immunity, pre-existing infections and environmental conditions, which may have played a role in the treatment outcomes. Nevertheless, the statistically significant findings for Treatment C strongly support its use in the improvement of recovery and the reduction of mortality during PPR outbreaks. In brief, this study emphasises the superior efficacy of antibiotic combination therapy. Specifically, it highlights the use of tylosin, gentamicin and ceftriaxone in the management of PPR in both goats and sheep.

It is essential to note that the antibiotics used in this study were not intended to cure PPR because the disease is caused by a viral agent. However, antibiotics play a key role in the management of secondary bacterial infections (pneumonia and gastrointestinal disturbances) that often complicate PPR cases. This study confirms the importance of antibiotics as supportive care to control secondary bacterial infections.

The use of multiple antibiotics in this study raises the important concerns about the development of antimicrobial resistance (AMR). While antibiotics are essential for managing secondary bacterial infections linked to PPR, their widespread and repeated use could contribute to the emergence of resistant bacterial strains. This phenomenon may reduce the effectiveness of antibiotics in future outbreaks and increase the risk of treatment failure. AMR could complicate the management of PPR and other bacterial infections and pose a significant threat to animal health. Therefore, there is a need to highlight the importance of monitoring bacterial resistance patterns in PPR outbreaks. Future research should focus on the assessment of antibiotic resistance in pathogenic bacteria associated with PPR. There is also a need to explore alternative treatments, such as antiviral therapies or immunomodulatory agents to reduce reliance on antibiotics and limit the risk of AMR development.

Clinical implications

This study highlights the importance of antibiotic combination therapy in the reduction of mortality and improvement of recovery rates for the management of secondary bacterial infections in PPR in both goats and sheep. The findings reinforce the efficacy of antibiotic combination therapy, including ceftriaxone, as it consistently produced the best treatment outcomes. The observed trend suggests that a single

antibiotic may not have been sufficient for optimal disease management in the severe cases of PPR.

Future perspectives

Additional studies are needed to explore the long-term effects of PPR, especially the chronic gastrointestinal issues in surviving animals. Studies focusing on the understanding of the pharmacokinetics of combination therapies will provide insights into the refinement of disease control programs. Future studies are needed to understand the resistance profiles associated with these treatment regimens to ensure the welfare of affected livestock populations.

CONCLUSION

In summary, the results of this study highlight the superior efficacy of antibiotic combination therapy, particularly the combination of tylosin, gentamicin and ceftriaxone in the management of secondary bacterial infections associated with PPR in small ruminants. This combination demonstrated the highest efficacy, with the lowest mortality (9.94%) and highest recovery rate (90.05%) in both goats and sheep. Treatment D, on the other hand, was found to be the least effective, showing the highest mortality (43.45%) and lowest recovery rate (56.54%). Although some treatments did not show statistically significant differences ($P > 0.05$), the clinical results support the use of combination therapies for improved disease control. Future research focusing on AMR, pharmacokinetics of treatment regimens and the long-term impacts of PPR will be crucial for enhancing disease management and ensuring the welfare of affected livestock populations.

Author contributions

- Hafiz Aftab Ahmed: Conceptualisation, data curation, writing original draft, review and editing
- Amir Rashid: Project administration, methodology and validation
- Anas Ashraf: Formal analysis, resources, supervision and statistical analysis
- Hafiz Saleet Ahmed: Investigation (data collection) and writing.

Ethical considerations

This study was conducted under the ethical guidelines for the treatment of animals. The animals involved in this study were managed under strict welfare protocols to minimise distress and suffering. During this study, all necessary steps were taken to ensure the humane handling of animals. The clinical management was carried out by qualified veterinarians, and animal care procedures were adhered to both local and international standards for ethical research. Ethical approval was not required for this study as it involved drug administration to goats and sheep, which are not subject to human participant guidelines.

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Conflicts of interest

Regarding the publication of this study, the authors declare no conflicts of interest. The authors declare that no financial support, sponsorship or commercial interests influenced the research design, data collection or interpretation of results. The authors declare that they are independent researchers with no affiliations that could influence the findings of this study. They do not hold any patents, shares or financial interests in the medications used in this study. The mentioning of specific drug brand names does not imply endorsement and equivalent alternatives may be available in the market. The authors confirm that any pharmaceutical company, government agency or private entity did not fund the study.

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