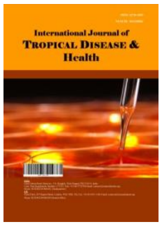

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Diagnosis Challenges and Control Strategies of Transboundary Diseases Presenting with Respiratory Signs in Small Ruminants in Developing Countries: Emphasis on Contagious Caprine Pleuropneumonia and Peste Des Petits Ruminants

A. C. Chota[1,2*], G. M. Shirima[2] and L. J. M. Kusiluka[3]

[1]Tanzania Veterinary Laboratory Agency, P. O, Box 9254, Nelson Mandela Road, Temeke Veterinary, Dar S Salaam, Tanzania.
[2]Nelson Mandela African Institution of Science and Technology, P. O. Box 447, Tengeru, Arusha, Tanzania.
[3]Mzumbe University, P. O. Box 1, Mzumbe, Tanzania.

Authors' contributions

This work was carried out in collaboration among all authors. Author ACC searched the articles and selected the eligible articles to include in the review. Author ACC collected the metadata, did an analysis and prepared the first draft of the review paper. Author GMS while supervising the author ACC, advised on the review paper concept, assisted in all stages of the review paper preparation and scrutinized the review paper drafts and the final draft. Author LJMK while supervising the author ACC, scrutinized the review paper drafts and the final draft of the review paper. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To review the diagnosis challenges and control strategies of the diseases presenting with respiratory signs. The emphasis being more on two transboundary animal diseases of small ruminants; contagious caprine pleuropneumonia (CCPP) and peste des petits ruminants (PPR). Clinical signs and postmortem lesions associated with the two diseases were also explicated.

**Corresponding author: Email: chotaandrew73@gmail.com, chotaandrew@gmail.com;*

Study Design: Review.
Place and Duration of Study: Department of Global Health, School of Life Science and Bio-Engineering (LiSBE), Nelson Mandela African Institution of Science and Technology (NM-AIST) from December 2017 to June 2020.
Methodology: A comprehensive review was carried out following Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. A total of 506 articles, handbooks, Master's and PhD thesis and conference proceedings were collected and after removal of the duplicates 80.6% (424/526) passed the first stage. Of the remaining search materials, (n=291) were removed including handbooks, master's and PhD thesis which did not originate from the developing countries, 31.4% (133/424) passed the second. Of the articles that passed the second stage, (n=85) were removed from the study, these included all articles that did not involve field diagnosis such as review papers and those not originating from the developing countries, 36.1% (48/133) passed the third stage. In the fourth stage, (n=5) articles which reported on retrospective cases and archived samples were removed and 43 articles were reviewed.
Results: Out of the 526 documents retrieved, 43 were eligible for review as they met all criteria for inclusion. Control strategies were recommended in 44.2% (19/43) of the articles of which most of them 63.2%, 12/19) recommended vaccination as a control strategy. Most of the articles reported definitive diagnosis reached following laboratory involvement as majority of them involved outbreak investigation or research works which is not the case in routine diagnosis. The major clinical signs mentioned in the review articles including fever 60.9% (14/23), oculonasal discharge 87.0% (20/23), respiratory distress 82.6% (19/23), erosive stomatitis 43.5% (10/23), diarrhea 56.5% (13/23) and coughing 30.4% (7/23) have been discussed relating to the definitive diagnosis reached in reporting articles. On the other hand, postmortem lesions including lung consolidation 38.1% (8/21), intestinal hemorrhage 38.1% (8/21), lung congestion 28.6% (6/21), serofibrinous pleurisy 28.6% (6/21), pneumonic lungs 23.8% (5/21) and unilateral lung inflammation 14.3% (3/21), have been discussed in relation to the definitive diagnosis reached.
Conclusion: Despite the similarities in clinical signs and postmortem lesions associated with diseases presenting with respiratory signs, definitive diagnosis of CCPP was reached in cases that involved clinical signs and postmortem lesions confined in the respiratory system whereas, PPR was more diagnosed in cases that presented with clinical signs and postmortem lesions associating the digestive system. However, presence of respiratory signs in the cases the diagnosed PPR may implicate presence of unidentified secondary bacterial infections. Vaccinations being the most advocated approach of control, require a broader look to make sure that polyvalent vaccines are available against the four common diseases. Also, use of treatment to reduce the effect of secondary infecting bacteria may be of help. Furthermore, for effective outcomes of the control strategies, collaborative efforts among countries at risk should be advocated.

Keywords: Control strategy; clinical signs; diagnosis challenges; postmortem lesions.

1. INTRODUCTION

Contagious caprine pleuropneumonia and PPR are highly contagious transboundary diseases of small ruminants mainly in Africa, Middle East and the Indian subcontinent [1,2]. The former, CCPP primarily affecting goats and occasionally sheep and wild ruminants [3], whereas, PPR affects the small ruminants including the wild ungulates [4]. Contagious caprine pleuropneumonia is the disease of the respiratory system [5] whereas, PPR is primarily a disease of the digestive system [6], which in most cases culminates with respiratory system following secondary bacterial infection [7].

Concurrent exposures of the two major transboundary diseases (CCPP and PPR) have been reported in Tanzania [8,9,10]. The outbreaks involved, despite causing significant losses due to mortality and reduced productions, persisted for quite some time resulting in continued losses to the farmers resulting from unsuccessful treatments [8]. Continued losses despite the interventions may suggest presence of other un-attended pathogens that equally cause respiratory problems in goats and sheep.

For quite some time, diagnosis of CCPP has depended on the isolation of the causative agent, *Mycoplasma capricolum* subsp. *capripneumoniae* (*M. capripneumoniae*), but is hampered by the fastidious nature of the pathogens [11,12]. Currently, advanced techniques for detection of CCPP have been developed cum introduction of serological and molecular techniques [13-15]. The advanced molecular techniques provide way of tackling the problem of multiple infections with recently, PPR, Capripox, pneumonic pasteurellosis and CCPP being diagnosed in a one-step Multiplex PCR [16,8]. The Latex agglutination test (LAT) is a simple, rapid and real-time test available for field use to diagnose CCPP [17]. Generally, routine diagnosis of CCPP using isolation and modern diagnostic techniques is impractical, isolation being tedious and time consuming whereas, serology and molecular techniques being expensive and require special equipment which cannot be easily maintained in remote areas.

A number of tests can be deployed in the diagnosis of PPR, which includes virus isolation, serological and molecular techniques [18]. Currently, virus isolation in primary cell cultures is up to 1000 times less effective than in lymphoid cells containing a glycoprotein known as Signaling Lymphocyte Activation Molecule (SLAM). The later paves the way to the use of new cell line (BST-34) technique which performs even better than the known Vero Cells [19,18]. The serological diagnosis of PPR targets the antibodies to the pathogen or pathogen [20,15] and these include the virus neutralization or immunodiffusion. Molecular techniques include those targeting the nucleoprotein (N) or fusion (F) genes [21,22] with the current development of the one-step Multiplex PCR where PPR is diagnosed together with Capripox, pneumonic pasteurellosis and CCPP [16,8]. This paves a way to the promising future diagnosis of concurrent diseases. Diagnosis of PPR through isolation, serology and molecular techniques are expensive and require special equipment which cannot be easily maintained in remote areas.

The current picture shows that significant losses accompanies the persisting diseases in the field, persistence of CCPP in the environment within hours to days but in the infected animals can persist for weeks to months [3]. Similar situation was reported in the outbreak of diseases with respiratory signs in Ngorongoro district where PPR and other three diseases were confirmed [8]. Despite the fact that, [3], associates CCPP persistence to conduciveness of the environment, concentration of the pathogen, type of breed, herd density and immunity of the animals; partial or misdiagnosis which results into delayed correct response or poor control strategy should not be underestimated.

Contagious caprine pleuropneumonia (CCPP) and PPR cause significant losses in resource poor households through mortality, morbidity, costs associated to diseases control and management, and reduced performance in terms of growth and productivity. Morbidity and mortality due to CCPP, in naive animals can be 100% to 80%, respectively but in exotic animals morbidity and mortality can be up to 100% [23]. It is estimated that the total annual loss due to CCPP infections in endemic areas can be up to USD 507 million [24]. Peste des petits ruminants (PPR) cause mortality of up to 100% in naive animals and 20% in endemic areas [25]. Peste des petits ruminants are estimated to cause a loss ranging between USD 1.45 to USD 2.1 billion per annum [26].

Similarity in the clinical signs and gross pathological lesions associated with CCPP and PPR, results in partial or misdiagnosis, making it difficult to design proper control strategies for these diseases. On the other hand, the role played by secondary bacterial infections in the persistence of the outbreaks presenting with respiratory signs is not well elucidated. This paper presents a review of the possible shortfalls on diagnosis made and the limitations on the control strategies advocated in surveys and investigations of diseases presenting with respiratory signs for the purpose of improving control strategies.

2. MATERIALS AND METHODS

A comprehensive review was conducted following the pre-specified protocol created following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [27]. Published papers originating from the developing countries, based on original research data, associated with outbreaks presenting with respiratory signs in small ruminants were eligible for selection. Search engines, including Hinari, Google Scholar and AGRICOLAR, were used to search for the published literatures. In the search, research articles, books, conference proceedings, Master’s and PhD thesis submitted to various universities were downloaded, and then in subsequent steps were scrutinized to limit inclusions, to published literatures originating from the developing countries as per 2018 list

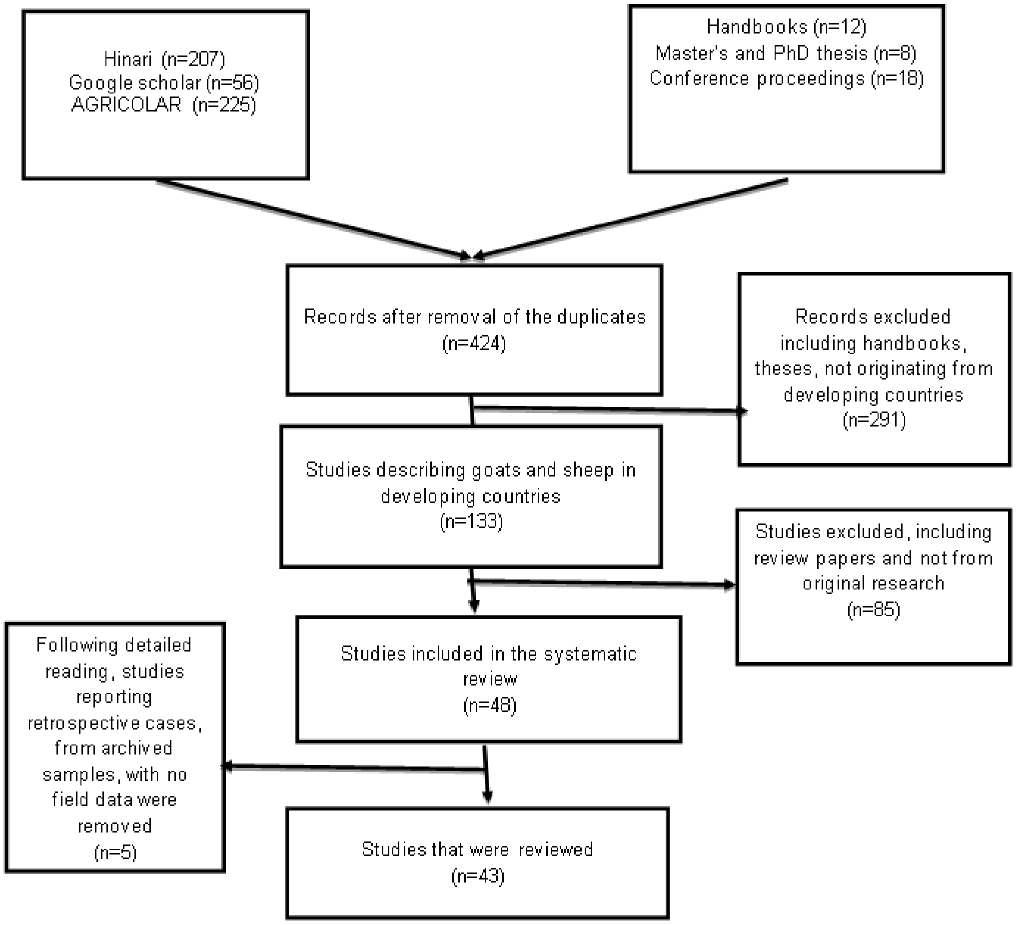

Fig. 1. Selection process of eligible documents for review

[28]. A detailed search strategy and stepwise, inclusion and exclusion criteria are provided (Fig. 1).

2.1 Data Analysis

Data computations and tables' preparations were done in Microsoft Excel® and Microsoft Word® 2010 respectively.

3. RESULTS AND DISCUSSION

Out of 526 documents retrieved, 43 were eligible for review as they met all criteria for inclusion.

3.1 Control Strategies

Generally, disease control recommendations were made by 44.2% (19/43) of the reviewed articles, majority of them, 63.2%, (12/19) recommended vaccinations. Out of the articles that recommended vaccinations, 41.7% (5/12) recommended vaccination against PPR [29,30,31,32,33], 8.3% (1/12) recommended vaccination against CCPP [11] and 50.0% (6/12) recommended vaccination against pneumonic pasteurellosis and pneumonic mannheimiosis [34,35,36,37,38,39]. Vaccination against CCPP still needs to be validated and promoted by stakeholders [40]. However use of antimicrobials as an approach used by livestock keepers to reduce the disease impact was mentioned in 10.5% (2/19) of the articles that mentioned control methods [11,12] whereas, test and slaughter was also recommended in some areas [11]. Nevertheless, [41] suggests, further controlled studies on the role of antibiotics in the carrier state animals which were possibly involved in the recurrence of the diseases after recovery. For effective control of PPR to meet the

Global goal of eradicating the disease by 2030 [42-44] recommends on collaborative efforts between stakeholders and respective zones. On the other hand, [45] suggested that, the complex nature of the respiratory infections does not need a single control strategy which we also believe should be the approach in managing respiratory infections. Use of multivalent vaccines developed from the most prevalent strains of the pathogens, coupled with strategic deworming for control of respiratory diseases [46,37] was also advocated though not implemented yet due to technical and logistic approaches. In this review, we believe this can also be a good approach in controlling the respiratory diseases in small ruminants. However, in order to have a better understanding of the diseases involved in the outbreaks it is important to have a clear picture of the possible diseases involved, which at field level are usually diagnosed using clinical signs and postmortem lesions.

3.2 Distribution of Diseases in the Developing Countries

In 19 articles where diagnosis and control strategies were made and suggested respectively, there was stratification of diseases country-wise. Ethiopia accounted for 31.6% (6/19) of the reported articles, and of these most of them (n=3) addressed diagnosis and control of pneumonic pasteurellosis and pneumonic mannheimiosis [47,45,39] whereas, other articles addressed lungworms and PPR [36], and CCPP [11]. Nigeria, contributed 15.8% (3/18) and of these, (n=2) addressed and diagnosed pneumonic mannheimiosis, pneumonic pasteurellosis and *B. parapertussis* pneumonia and one addressed PPR [30]. Tanzania, accounted for 15.8% (3/19) of the articles, two of them addressed PPR [43,32] and one addressed CCPP, MmmSC and *M. arginine* pneumonia [12]. Of the 19 articles, 10.5% (2/19) were reported from Iran and in both Pasteurella *species* were diagnosed [34,37], similarly, 10.5% (2/19) articles were reported from India and both addressed PPR [31,33]. Egypt accounted for 10.5% (2/10) articles, of those, one addressed PPR [48] and the other one addressed pneumonic pasteurellosis [35]. In Pakistan, PPR was addressed and diagnosed in 5.3% (1/19) of the articles [29].

Diagnosis of CCPP, pneumonic pasteurellosis, pneumonic mannheimiosis and PPR was done using serological, microbiological or molecular methods at zonal and national laboratories [16]. However, the use of the above techniques is practical in advanced laboratories but not in laboratories at district or lower levels as they require skilled technicians and expensive equipment [11,49,50] leaving clinical signs and pathological examinations cornerstone diagnostic methods in the field conditions.

3.3 Major Clinical Signs Reported and Diagnostic Techniques Used in Outbreaks Presenting with Respiratory Signs

3.3.1 Fever

Goats and sheep normal body temperatures are 39.1±0.7°C and 39.4±0.3°C respectively, [51]. Altered body temperatures indicates health problems, this clinical sign has been reported in outbreaks of diseases presenting with respiratory sign in single or concurrence. Fever, was reported in 60.9% (14/23) of the reviewed articles that mentioned clinical signs. In the review, 42.9% (6/14) of the reviewed articles that mentioned fever, reported PPR, these include, [52] with animals at 106±1°F, [53,32,48,21,54] which examined animals with fever and diagnosed PPR using typical clinical and pathological, histopathological and molecular characterizations. Furthermore, 28.6% (4/14) of the reviewed articles reported mycoplasmas. These were, [41] who diagnosed CCPP and *Mycoplasma mycoides* subsp. *mycoides* a causative agent for contagious bovine pleuropneumonia of cattle in pyrexic goats (40°C-41°C). Other three studies, [55,56,57] diagnosed *Mycoplasmas* and *Mycoplasma mycoides capri*. Fever was also reported in 14.3% (2/14) of the reviewed articles which reported pneumonic pasteurellosis and pneumonic mannheimiosis in goat and sheep [47,58]. In 14.3% (2/14) of the reviewed articles, multiple bacterial isolation [45] and co-diagnosis of PPR, pneumonic pasteurellosis, goats and sheep pox, and CCPP in the study conducted in the Democratic Republic of Congo (DRC) were reported [59]. However, in this case, consideration of inclusion of sheep and goat pox in the diagnosis could have been due to the evident lesions for the Capripox virus.

3.3.2 Oculonasal discharges

Discharges that originate from the eyes and the nasal can be detected during pen inspection. The nasal discharges can either be serous (thin, clear and colourless), catarrhal (grey and flocculent), purulent (thick and yellow) or haemorrhagic (red). Discharges may change colour, consistency and amount depending on the underlying disease [60]. In the current review, oculonasal discharge was reported in 87.0% (20/23) of the reviewed articles that mentioned clinical signs. Majority of the reviewed articles, 50.0% (10/20) that mentioned oculonasal discharge reported PPR, and were confirmed using several diagnostic techniques [61,52,53,62,50,43,32,21,54]. Principally, PPR is the disease of the digestive system [6] and clinical signs involving respiratory system occur following secondary bacterial infections [7]. In view of this, there is a high possibility these studies missed the diagnosis of secondary bacterial infections. Oculonasal discharges are anticipated in the infections involving the respiratory system, including CCPP and Mycoplasma pneumonias or other bacterial infections of the respiratory system. Mycoplasmas were mentioned in 20.0% (4/20) of the cases that had oculonasal discharges, these include those by [41] where CCPP and *M. mycoides* subsp. *mycoides* were diagnosed and by [63,56,57] in which *Mycoplasmas* and *M. capri* were reported in goats. Oculonasal discharge was also mentioned in 20.0% (4/19) of the articles that reported pneumonic pasteurellosis and pneumonic mannheimiosis in goat and sheep [47,64,58,22]. In 10.0% (2/20) of the reviewed articles, multiple infections were reported [45,59].

3.3.3 Respiratory distress

This is an indication that an animal has dyspnea and can be diagnosed during flock examinations or individual clinical examination. Respiratory distress has been mentioned in 82.6% (19/23) of the reviewed articles that mentioned clinical signs. Is another common clinical sign to be mentioned, in this review, 52.6% (10/19) of the articles that mentioned respiratory distress reported PPR [61,52,53,30,62,50,43,32,21,54]. Mycoplasmas were reported in 26.3% (5/19) of the reviewed articles [5,12 63,56,57] and 15.8% (3/19) of the reviewed articles reported presence of pneumonic pasteurellosis and pneumonic mannheimiosis [35,47,58] which are due to stress or infections by viruses or mycoplasmas. Co-detections of various diseases that were associated with respiratory distress was reported in 5.3% (1/19) of the articles reviewed [59].

3.3.4 Erosive stomatitis

Vesicular and erosive stomatitis are lesions confined in the digestive systems involving the gums, upper dental pad and ulceration on the tongue [65]. In this review, erosive stomatitis was reported in 43.5% (10/23) of the articles reviewed and the lesion was reported in 90% (9/10) of the outbreaks which confirmed only PPR [61,53,30,62,48,50,43,21,54]. The remaining 10% (1/10) conformed co-detection of PPR and other diseases including sheep and goat pox, and lumpy skin disease [59].

3.3.5 Diarrhea

Diarrhea was associated with PPR and other digestive system diseases like Coccidiosis and intestinal helminthosis [8]. Observation of diarrhea in the outbreaks presenting with respiratory signs suggests presence of concurrent infections with pathogens affecting the respiratory system or secondary infecting bacteria. In this study, 56.5% (13/23) of the reviewed articles that reported diarrhea as a clinical sign, 76.9% (10/13) confirmed PPR [48,30,53,21,54,66,32,43,50,62]. Pneumonic pasteurellosis in co-detection with *Clostridium perfringens* were confirmed in 15.4% (2/13) [35,64] and in 7.7% (1/13), PPR was co-detected together with lumpy skin disease, goat and sheep pox [59].

3.3.6 Coughing

A voluntary or involuntary action that produces a characteristic sound due to opening of the vocal cords and clears the throat from the nasal discharges among other things. The sign is common in diseases affecting the respiratory system and in this review, coughing was observed in 30.4% (7/23) of the reviewed articles that mentioned clinical signs. Coughing was mentioned in 57.1% (4/7) of the articles which eventually confirmed PPR as a definitive diagnosis [61,30,48,66] which is commonly a disease of the digestive system [6]. It is possible, that these diagnoses missed the diseases caused by secondary bacterial infections especially pneumonic pasteurellosis and pneumonic mannheimiosis which are caused by normal commensals of the respiratory tract. In 28.6% (2/7) of the reviewed articles, coughing was associated with pneumonic pasteurellosis and pneumonic mannheimiosis [47,64] which do occur following infections by viruses, mycoplasmas or stressful conditions. Coughing was also mentioned in 14.3% (1/7) of the article that confirmed co-detection of PPR, LSD and Goat and sheep pox, [59] which are all viral diseases affecting digestive and integumentary systems, presence of coughing further, suggests presence of the secondary bacterial infections in the lungs [7].

3.3.7 Other clinical signs

Other clinical signs which were mentioned in the articles reviewed were loss of appetite in 17.4% (4/23) in which PPR, pneumonic pasteurellosis and pneumonic mannheimiosis were diagnosed [58,66,47,50], this loss of appetite could be due to fever or presence of lesions in the buccal cavity due to PPR. Prostration in 13% (3/23) of the reviewed articles which confirmed *M. capri*, PPR, *M. capricolum* [55,66,57]. Conjuctivitis in 13% (3/23) of the reviewed articles which confirmed PPR, CaPV, LSD, *M. capri*, *M. capricolum* and skin pox lesions [59,57,50]. In 8.7% (2/23) of the reviewed articles the authors just reported animals to be “apparently pneumonic” and eventually pneumonic mannheimiosis, pneumonic pasteurellosis, CCPP, *M. arginin* pneumonia, *M. ovipneumoniae* pneumonia were diagnosed [39,67]. Reduced milk production was mentioned in 8.7% (2/23) of the articles that diagnosed *M. capri* pneumonia and *M. capricolum* pneumonia [55,57] whereas, altered milk with flakes, clots, discoloration and reduced amount in 4.3% (1/23) of the articles that diagnose *M. capri* pneumonia [57]. Salivation was mentioned in 8.7% (2/23) of the articles where PPR was diagnosed [53,50] and associated with vesicular lesions in the gums.

3.4 Major Postmortem Lesions Reported in Outbreaks of Diseases Presenting with Respiratory Signs

3.4.1 Lung consolidation

This feature is a solidification of the lung tissue due to accumulation of the fibrinous exudates in the air space that would normally be filled with air [68]. Lung consolidation was reported in 38.1% (8/21) of the articles reviewed that mentioned postmortem lesions. Peste des petits ruminants was confirmed in 50.0% (4/8) of the reviewed articles that presented lung consolidation [62,48,66,50]. Involvement of the lungs in PPR confirmed cases may mean presence of other secondary bacterial infections in the lungs. Mycoplasmas were mentioned in 25.0% of the reviewed articles that reported lung consolidation [11,55] and also 25.0% (2/8) of the articles that reported lung consolidation were associated with pneumonic pasteurellosis and pneumonic mannheimiosis [47,58].

3.4.2 Intestinal hemorrhages

The feature occurred following increased blood in the intestines with engorged blood vessels or filled intestinal lumen. Of the reviewed articles, 38.1% (8/21) reported intestinal haemorrhages with majority 87.5% (7/8) being associated with PPR [48,30,21,54,66,32,50,62]. This is due to the fact that PPR is the disease affecting the digestive system [6]. However, involvement of this lesions in the outbreaks of diseases presenting with respiratory signs, suggests that there were possibly mixed infections. The remaining 12.5% (1/8) of the articles that mentioned intestinal hemorrhage reported pneumonic pasteurellosis [35], the disease caused by a normal pathogen of the respiratory system suggesting that there could have been missed pathogens affecting the digestive system.

3.4.3 Lung congestion

Distension of the blood vessels of the lungs and filling of the alveoli with blood due to infection. In the reviewed articles, the lesion has been mentioned in 28.6% (6/21) of the articles reviewed. Lung congestion was mentioned in 66.7% (4/6) of the articles that diagnosed PPR only [30,48,50,66]. This could also mean, missing of the diagnosis of secondary bacterial infections. On the other hand, this lesion was mentioned in 33.3% (2/6) in which the diagnosis of pneumonic mannheimiosis and pneumonic pasteurellosis was reached [47,64], which could have infected the lung following stress or infection of other mycoplasmas or viruses [7].

3.4.4 Serofibrinous pleurisy

Serofibrinous pleurisy is the inflammation of the pleural membrane which can take different forms including, acute form which is dry or fibrinous [69]. Subacute serofibrinous is characterized with effusion, purulent pleurisy, a suppurative inflammation of the pleura and accumulation of serous fluid in pleural cavity [69]. In the reviewed articles, serofibrinous pleurisy was mentioned in 28.6% (6/21) of reviewed articles that mention postmortem lesions. Serofibrinous pleurisy was mentioned in 66.7% (4/6) of the articles that diagnosed mycoplasmas including CCPP [5,11,12,55]. In the same study, [41], also isolated *Mycoplasma mycoides* subsp *mycoides* the causative agent of contagious bovine pleuropneumonia (CBPP). Furthermore, serofibrinous pleurisy was mentioned in 33.3% (2/6) of the articles that diagnosed pneumonic mannheimiosis complicated with *Bordetella parapertusis* [38] and pneumonic pasteurellosis [64]. All the diseases diagnosed are localized in the respiratory system, except *Mycoplasma capri* which is more associated with the mastitis in goats [57].

3.4.5 Pneumonic lungs

This is the cardinal sign of inflammation. In the reviewed articles, inflamed lungs were mentioned in 23.8% (5/21) of the reviewed articles that mention postmortem lesions. This was associated with 60.0% (3/5) diagnosis of pathogens affecting the respiratory system such as pneumonic pasteurellosis, pneumonic mannheimiosis [49,37,45]. On the other hand, 20.0% (1/5) diagnosed *M. capri* pneumonia and *M. capricolum* pneumonia [56]. In the case which could suggest presence of secondary bacterial infection in the lungs, 20.0% (1/5) of the articles that reported pneumonic lungs lesion diagnosed PPR [54].

3.4.6 Unilateral lung inflammation

Inflammation of the lungs, mainly caused by infectious agents like bacteria, viruses and fungi, in other occasions by environmental pollutants [70,71]. Unilateral lung inflammation was mentioned in 14.3% (3/21) of he reviewed articles. Of these, 33.3% (1/3) were associated with the presence of CCPP, *Mycoplasma ovipneumoniae* pneumonia [5], 33.3% (1/3) pneumonic mannheimiosis and *Bordetella parapertussis* pneumonia [38]. However, 33.3% (1/3) of the articles that presented with unilateral lung inflammation diagnosed PPR [32], which suggests further involvement of opportunistic bacteria [7]. In another study, [72] associated CCPP to over 69% of the bilateral lung inflammation compared to 38% which had unilateral lung inflammation the findings which were contrary to those reported by [73] and [74] who reported that in CCPP, unilateral lung involvement was more as compared to bilateral. In the recent study by [10] reported the asymmetric lung inflammation in concurrent diseases involving CCPP and opportunistic bacterial pneumonia.

3.4.7 Other postmortem lesions

Other postmortem lesions observed in the outbreaks which presented with respiratory signs included buccal mucosa erosions in 14.3% of the reviewed articles, these were associated with the articles which diagnosed PPR [48,50,66]. Presence of respiratory signs in these articles could be due to involvement of opportunistic bacterial pneumonia. Froth in the trachea in 9.5% (2/21) of the reviewed articles, in which, pneumonic mannheimiosis, pneumonic pasteurellosis and *Bordetella parapertussis* pneumonia [38,58] were diagnosed. This lesion is suggestive of other infections which involve the lower respiratory system including mycoplasmas and viruses. The other postmortem lesions were congested urinary bladder, in 9.5% (2/21) of the reviewed articles which were associated with pneumonic pasteurellosis, *Clostridium perfringens and* PPR diagnosis [35,66], Congested and atrophied spleen, in 9.5% (2/21) of the reviewed articles which were associated with PPR diagnosis [62,66], Congested uterus, in 9.5% (2/21) of the reviewed articles which were associated with PPR and CCPP diagnosis [66,75] and in rare cases where suppurative endometritis and suppurative enteritis, in 4.7% (1/21) of the reviewed articles, which was associated with diagnosis of CCPP [75], pericarditis in 4.7% (1/21) of the reviewed articles in which pneumonic pasteurellosis was diagnosed [64] and zebra stripes, a pathognomonic lesions in PPR infection which was mentioned in 4.7% (1/21) of the reviewed articles [50].

3.5 Discussion

The two major transboundary diseases discussed in this review, were diagnosed using advanced technologies which are difficult to be employed in lower level laboratories for routine diagnosis. Despite the use of advanced techniques, there were no considerations of concurrent diseases in many articles in such a way that specific diseases were considered at a time [12,49,38]. In some of the investigated outbreaks clinical signs and postmortem lesions were suggestive of respiratory system involvement [43,21,54] but only diagnosed PPR which is mainly known to involve the digestive system [6]. This suggests presence of secondary bacterial infections especially the normal commensals of the respiratory system [7] which were missed in the diagnosis. When typical clinical signs involving the digestive system were observed, PPR was the mainly diagnosed disease [53,62], but in some outbreaks with typical signs involving the digestive system [35,64] only pneumonic mannheimiosis was diagnosed, this suggests that PPR was missed in the diagnosis. Peste des petits ruminants was also mentioned in the outbreaks where giant cell infiltrations in the lungs were mentioned [66,50], presence of the giant cells in these outbreaks and experimental infections could still be due to presence of pneumonic pasteurellosis or pneumonic mannheimiosis which may set in as a result of stress and compromised immunity caused by PPR infection [7].

From the reviewed articles, outbreaks presenting with respiratory signs both CCPP and PPR should be strongly considered in the differential diagnosis. Occurrence of pneumonic pasteurellosis and pneumonic mannheimiosis are associated with stress and infections caused by viruses and mycoplasmas [7] and thus, secondary bacterial infections have to be taken into consideration as differential diagnoses as well. Contagious caprine pleuropneumonia and other mycoplasma pneumonia are highly associated with postmortem lesions limited in the respiratory systems with *M. capri* pneumonia occasionally involve other systems [55]. On the other hand, presence of respiratory signs associated with typical clinical signs and postmortem lesions involving the digestive system may mean presence of concurrent diseases caused by PPR and secondary bacterial infections or mycoplasmas [8,9,10]. In the recent studies, [59,8,9] the concept of concurrent diseases and the role of secondary bacterial infections in the epidemiology and dynamics of diseases presenting with respiratory signs have been demonstrated. Also, since concurrent diseases are common in small ruminants considering the respiratory system and the variable clinical signs and postmortem lesions in the advent of limited diagnostic tests in the lower settings calls for inclusion of differential diagnosis of the four conditions and refining prominent clinical signs and postmortem lesions for further improvement of field diagnosis.

4. CONCLUSION

The complexity of concurrent infections, the difficulty in diagnosis using clinical and pathological lesions, the challenges in reaching the advanced laboratories and lack of facilities at the lower level diagnostic laboratories results in partial or incorrect information for diagnostic and control strategies. This results into change in the diseases dynamics, continued persistence and spread of infectious diseases. Vaccinations being the most advocated approach of control require a broader look to make sure that polyvalent vaccines are available against the four common diseases. Also, use of treatment to reduce the effect of secondary infecting bacteria may be of help. Furthermore, for effective outcomes of the control strategies, collaborative efforts among countries at risk should be advocated.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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