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PREVALENCE OF ENTEROTOXEMIA (PULPY KIDNEY DISEASE) IN GOAT: A COMPREHENSIVE REVIEW

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ABSTRACT

Goat is considered as poor man's cow and is among the earliest small ruminant species to be domesticated and are reared for meat and milk purpose, at least since 2500 B.C. in the Middle East. Goats contributes largely to the livelihood of livestock keeping households of low- and medium-input farmers, many of whom have few resources beyond their small holdings and livestock. It has been observed that maximum production can be obtained by protecting them from different prevalent diseases like enterotoxaemia. Enterotoxaemia is a fatal disease of small and large ruminant's animal species; severe outbreak causes huge economic losses to livestock holders. This disease is also known as pulpy kidney disease due to systemic lesions observed on kidney as it causes nephritis and hydro nephrosis. Enterotoxaemia in goats occurs in four forms, i.e. Per acute, acute, subacute and chronic form. Severe outbreak of this disease observed in warm wet weather at the time of start of monsoon season every year and is having worldwide distribution. Factors which are responsible for exposing the animals towards the enterotoxaemia are sudden changing in diet as animals diet change from poor nutrient pastures to the rich nutrient pastures and changing in environmental temperature as warm wet weather is an ideal environment for the multiplication and toxins production of disease-causing microorganism. It can be diagnosed by detection of specific antibodies, clinical signs and post-mortem lesions. Infected animals can be treated by parental injection of specific chemotherapeutic agents or antitoxins and can be controlled by changing in dietary schedule and vaccination. Still, the pathology and pathogenesis of goat enterotoxaemia is not well understood, with limited studies available in goats. This review provides details information regarding the epidemiology, pathology and pathogenesis of enterotoxaemia in goat which might be helpful for future studies.

1. INTRODUCTION

Goats contributes largely to the livelihood of livestock keeping households of low- and medium-input farmers, many of whom have few resources beyond their small holdings and livestock (Boyazoglu et al., 2005). Goats in the world are clustered in 570 breeds.

In developing countries, the trend of rearing goat is very high because it is used for various purposes like meat and milk, and it is good producer, high capability to reproduce, less requirements of nutrients, good habit of feeding, having profitable market value, at the time of need farmers can easily sale out, although they are meat animals with appropriate size to be slaughter (Hossain et al., 2004).

Goat keeping has been a traditional activity since the ancient time and primary source of livelihood of people of having limited income resources. Famers always prefer to rear this animal because high capability to

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reproduce, consume multiple feedstuffs which are easily available in the market, being a small ruminants easily keep in small yards, having a profitable market value and affordable initial purchasing cost (Sinn et al., 1999). Goats are multipurpose animals, producing meat, milk, skin and hair. Their primary function is meat production, although in temperate countries milk has become of greater importance; skins are a valuable by-product, especially in countries with large goat population. Goat meat is relished in all countries of Asia, Africa and Middle East where there is a tradition for meat consumption from both sheep and goats (Dhanda et al., 2003). Goat milk is prescribed for children, old and sick as it is easily digestible and has medicinal value (Haenlein et al., 2004).

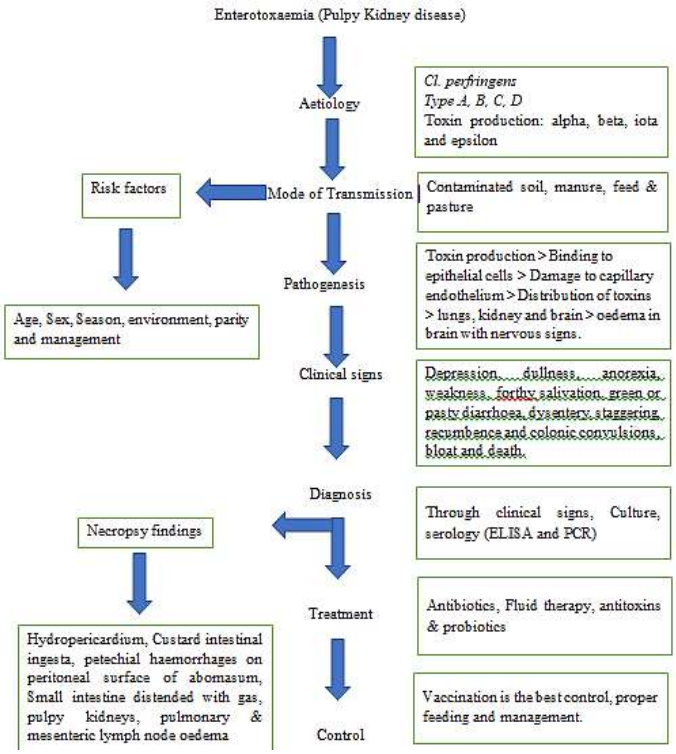

Figure 1. Flow diagram of Enterotoxaemia

Introduction to Enterotoxaemia

Enterotoxaemia is an infectious disease observed in goat, sheep, lambs and kids (Stiles et al., 2013). This disease is also known as pulpy kidney disease, characterized by diarrhoea and dysentery. When animals are supplied with green grasses, concentrate ration will leads towards excessive growth of microflora of intestine and development of enterotoxaemia (Quinn et al., 2002). Very huge economic losses occur due to the outbreak of this disease throughout the world (Bokori-Brown et al., 2014). It is firmly believed that optimum production cannot be achieved without protection from the different livestock disease particularly enterotoxaemia (Chandran et al., 2010;Wang et al., 2011). The outbreaks of these diseases are disasters for the farmers and may put them out of their business by imposing excessive economic losses (Gad et al., 2011). Enterotoxaemia is a devastating disease that affects sheep and goats all over the world. Despite the fact that there are significant differences between caprine and ovine enterotoxaemia, documentation and research on the condition in goats is limited. Simultaneously, caprine enterotoxaemia continues to cause economic losses for goat farmers around the world. Still, the pathology and pathogenesis of goat enterotoxaemia is not well understood, with limited studies available in goats. This review provides details information regarding the epidemiology, pathology and pathogenesis of enterotoxaemia in goat which might be helpful for future studies.

Aetiology

The bacteria which is responsible for enterotoxemia in goat and sheep is *Clostridium perfringens* type D. This disease occurs in young ones of sheep when they will feed with concentrate, same condition may be observed in goat and sheep after the young stage (Radostitis et al., 2007). *Clostridium perfringens*, a gram-positive spore-forming anaerobic bacterium, has been implicated as one of the major pathogens in the development of humans and animal intestinal diseases (Songer, 2010).

Two dissimilar forms of disease causing pathogen has been observed one the dormant and second one the active form. Organisms go through the dormant stage when there is shortage of required nutrients. In this inactive form pathogen can survive for long period even for years (Mueller-Spitz et al., 2010). Pathogen is not having the capability to form precursor for protein which are needed for the synthesis of their various body parts, bacteria will take these essential precursor for protein formation by destructing the group of cells of host through the secretion of various enzymes and toxins (Shimizu et al., 2002). The toxin types will causes redness of mucosal membrane and haemorrhage in cardiac muscles, due to the development of glycosuria condition animals will unable to sight. Transudate fluid will found in abdominal, chest and outer most layer of heart. Nervous sign may be observed due to effect of toxin of central nervous system (Upadhayay, 2005).

Clostridium Perfringens bacterium is rod shaped, survive in the absence of oxygen and gram positive, being an opportunistic parasite it is a normal microflora of animals and human body found in their gastrointestinal tract, this pathogen is found in two different farms such as spores and vegetative farm, during un favourable condition in soil and water this bacterium can be found in inactive or spore farm. The clostridium species which are responsible for developing enterotoxemia in animals are *Cl.perfringens*, in caprine

ovine Type D *Cl.perfringens* is responsible for developing the disease which is characterized by bloody diarrhoea, inflammation of intestine and muscular degeneration (Silva et al., 2009). On the basis for production of major toxins such as iota, epsilon, alpha and beta, this pathogen has been classified as Type A, Type B, Type C, Type D and Type E, when animals are being expose to various risk factors like feeding of animals on green grasses, high energy rich sources, excessive colostrum feeding in lamb and kids, these pathogens will gate opportunity to multiply inside the intestine lumen and leads the animals towards the enterotoxaemia. Type D *Cl.perfringens* is responsible for causing enterotoxaemia in small ruminants like goat and sheep (Uzal & Songer, 2008).

Among clostridia species the *Cl.perfringens* is one of the universal microorganism. Commonly found in the gastrointestinal tract of animals and human beings and dormant farm is also found in soil. Being an anaerobic pathogen it can survive without oxygen and is a gram positive bacillus (Uzal et al., 2016). It has been classified into type A, B, C, D, and E on the basis of production of important toxins such as iota, epsilon, alpha and beta (Siqueira et al., 2012). Different types of *Cl.perfringens* will secrete various toxins, which are responsible for developing specific intestinal infection in specific host (Ohtani et al., 2016).Among the various types of *Cl.perfringens* species Type D produce epsilon, Type C produce beta, Type E produce iota and Type B produce beta as well as epsilon toxins. Type D *Cl.perfringens* is responsible for developing enteritis in caprine and ovine (Silva et al., 2016).

Colony, morphological and biochemical characteristics of Clostridium perfringens

Clostridium perfringens bacteria produced smooth, large, regular convex and slightly opaque colonies and zone of complete hemolysis surrounded by wider zone of incomplete hemolysis on sheep blood agar (Karthik et al., 2017;Fransico et al., 2008;Nazki et al., 2017). When morphologically *clostridium perfringens* observed under electron microscope it was found gram positive bacilli (Rod shaped) (Haq et al., 2016;Rahimoon et al., 2021). Previous studies revealed that *Clostridium perfringens* was positive when they performed different biochemical testes such as Methyl Red Test, Geletin Liquefaction Test and Triple Sugar Iron Test. Whereas Catalase, Oxidase, Urease, Indole, Citrate and Voges Proskauer were negative for negative *Clostridium perfringens* (Haq et al., 2016;Miah et al., 2011).

Epidemiology

Outbreak of enterotoxaemia associated with Type D *Cl.perfringens* is observed in animals having complex stomach particularly goat and sheep throughout the world (Radostitis et al., 2007). During the start of monsoon season, frequent disease outbreaks of enterotoxaemia in sheep and goat is encountered every year in Pakistan, in spite of frequent vaccinations against C. perfringens Type D (Kumar *et al*. 2014). Per acute sickness repeatedly observed in unimmunized goat and sheep (Nasir et al., 2013).In case of Per acute form of enterotoxemia death of animals occurs due to the releasing of the essential toxins, such as alpha,beta,iota and epsilon secreted by a bacteria named *Clostridium perfringens* (Uzal & McClane, 2011).

Risk Factors

Over eating disease can affect the caprine and ovine at any stage of age but mostly frequent outbreak of disease occurs in the animals of having age of 4-10 weeks and in the animals which are being reared for fattening may be suffer from this intoxication at the age of 6 months to 1 year. Clinical signs will be appear in the affected animal when bacteria will multiply and produce their toxins and these toxins will diffuse inside the blood stream through intestinal (Jemal et al., 2016).

Mostly the animals which are suffering this intoxication will be died if the concentration of bacterial and their toxins load will be high in the systemic circulation, as this condition found in animals when they will suffer from par acute form of disease. Alive diseased animals will show the sign of dysentery, diarrhoea and nervous disturbance. when animals are being changed from low nutrient diet to a very rich nutrient diet their microflora will not adjusted in partially digested and over availability of nutrients in the intestine they will gate opportunity to multiply and produce their harmful toxins in intestine lumen (Quinn et al., 2002).

Transmission

Various strains of disease causing agents are normally found in environment and animal manure, from where these pathogens will be ingested by the animals , progressive multiplication of bacteria and production of their toxins occurs inside the body of animals when animals will provide with adequate amount of nutrients through feed as the presence of extra amount of nutrients in the intestine will facilitate growth of disease causing agents in the intestine of affected animal , as when new born lambs provide with adequate amount of colostrum , it will provide suitable environment for the multiplication *Clostridium perfringens* bacteria inside the lumen of intestine (Jemal et al., 2016).

Pathogenesis

Progressive development of disease occurs when enterotoxemia causing agent will penetrate inside the lumen of small intestine, after penetration it will secrete

various toxins, these toxins will gate absorb in to the systemic circulation in order to reach the various organs of the body for causing damages like enteritis ,destruction of villi of small intestine and epithelium and necrosis of various body organs, these toxins also causes nephritis and development of oedematous condition in renal system, abdominal cavity and chest cavity (Upadhayay, 2005).

Type D *Cl.perfingens* pathogens are the normal microflora of small and large ruminants animal species like bovine, caprine and ovine (Uzal *et al.* 2004). Although ,being an opportunistic pathogens when animals are being expose to the various risk factors like excessive feeding of protein rich diet , feeding of succulent green grasses and excessive feeding of colostrum, these microflora will gate opportunity to increase their numbers and will produce various toxins, these toxins will causes inflammation of intestine and then they will diffuse towards the systemic circulation for producing multi systemic effect (Uzal & Kelly, 1996).Toxins will be diffused from the villi of the small intestine towards the lumen of blood vessels in order to reach the systemic circulation for damaging various body organs (Ma et al., 2011).

Excessive feeding of green feedstuffs, concentrates and sudden alteration in feeding and anoxic atmosphere of small intestine leads towards the occurrence of enterotoxaemia (Javed et al., 2009). The causative agent of this disease is a usual microflora of gastrointestinal tract, present in a very minute quantity. Harmful illness occurs due to exposure of animals to various risk factors which will facilitated the growth of *Clostridium perfringens* inside the intestine lumen (Diab et al., 2011).

Clinical Signs

Clinical signs in sheep and goats are colic, diarrhoea and neurological symptoms. Post mortem lesions are widespread vascular congestion, with cerebral, cardiac, pulmonary, and renal oedema (Uzal et al., 2004). In case of per acute farm of the disease animals mostly die however most of the animals may be observed uncomfortable and decrease in their feed intake. There will be foamy salivary glands secretion, loss of fluid, dysentery, grinding of teeth, animal unable to stand, intestinal spasmatic pain, loss of consciousness and animal death (McGavin et al., 2007). In caprine and ovine pathological changes and nature of occurrence of disease will be totally change (Uzal & Songer, 2008).

In caprine and ovine animal species the disease can be identified by diarrhoea dysentery, inflammation of intestine, almost very similar clinical signs of enterotoxaemia in both of the animal species has been observed. This disease can be appear in acute and subacute farms in goat and sheep (Smith & Sherman, 2009). Pulpy kidney disease in goat and sheep is identified with the help of pathological lesions such as oedematous and inflamed renal system, excessive flow of blood inside the intestine lumen , oedematous fluid in outer layer of heart, chest and cavity, flow of blood in second part of large intestine, muscle tissues and cardiac tissues (Javed et al., 2009).

Diagnosis

The diagnosis of a disease is based on the epidemiological features especially the type of diet, clinical and pathological features, Act of knowing the cause of disease will be based on detailed information of animal from animal honour, decrease in the tone of rumen post-mortem lesions, different laboratory tests and identification of bacteria (Upadhayay, 2005). Tentative act of knowing the cause of disease may be done by the observation of pathological lesions, objective evidence, post-mortem findings and other pathological lesions in various organs of the animal body (Javed et al., 2009).

This illness may be identified by the confirmation of intestine lesions, diarrhoea and dysentery, these signs will indicates the presence of Type D *Cl.Perfringens* in feces, as this pathogen is responsible for causing of inflammation small intestine and colon, further diagnosis may be confirmed by culture of gastrointestinal tract content and culture of renal system and by identification of pathogen by performing various biochemical testes,and detection of high level of sugar in the urine would indicates the enterotoxemia in affected animals (Fernandez-Miyakawa et al., 2003).

Necropsy findings will be very helpful in diagnosing this illness. Hence, departed patients must be send for necropsy examination and abnormal organs and tissues should be submitted for laboratory diagnosis. After performing necropsy if erosion of internal lumen of small and large intestine, huge accumulation of watery blood inside the intestine lumen, softness of nervous tissues and renal tissues observed would indicates the occurrence of enterotoxemia in diseased animal (Pugh 2002).

Treatment

This disease can be treated by parentally injecting the penicillin, prognosis will be very poor if penicillin injected parentally after the appearance of clinical signs, for good prognosis diseases animals may be treated by oral administration of sulphonamide an antimetabolite antimicrobial along with the serum having antibody against *Cl.Perfringens* (Shank, 2001).Young ones of goat usually treated by administration of five mille litre of D antitoxins by sub cut route, penicillin may be given orally, to neutralize acidity alkaline agent may be given orally, sometimes carminatives may be given to expel the gasses from stomach. In order to restore hydration diseased animals should be provided with fluid therapy, as administration of antimicrobials causes death of

normal microflora in the intestine so probiotic should be administer for maintaining the normal microflora in the intestine of diseased animal (Bath et al., 2005)

2. CONCLUSION

Enterotoxaemia is an infectious and highly fatal bacterial intoxication occurs in small ruminants like goat and sheep, huge economic losses occurs due to severe outbreak of this disease in the season of monsoon every year in Pakistan. Factors which are responsible for exposing the animals towards the enterotoxaemia are sudden changing in diet as animals diet change from poor nutrient pastures to the rich nutrient pastures and changing in environmental temperature as warm wet weather is an ideal environment for the multiplication and toxins production of disease causing microorganism. Infected animals can be treated by parental injection of specific chemotherapeutic agents or antitoxins and can be controlled by changing in dietary schedule, timely vaccination and by keeping the animals free from stress.

3. CONFLICT OF INTEREST

All authors have declared that there is no conflict of interests regarding the publication of this article.

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Table: 01. Clostridium perfringens types and their toxin production (M Lebrun et al., 2010)

Cl. perfringens type	Toxin production	Animal species affected	Syndrome
Type A	Alpha toxin	Cattle, lamb fowl , Pig	Enterotoxaemia, necrotic entritis
Type B	Alpha, Beta & Epsilon toxin	Neonatal calves, foals, Adult sheep Newborn lambs	Haemorrhagic enteritis, Haemorrhagic Enterotoxaemia, Dysentery
Type C	Alpha & Beta toxin	Neonatal pigs, lambs, calves, goats & foals	Necrotic or haemorrhagic, Enterotoxaemia,
Type D	Alpha & Epsilon	Adult sheep, Lambs (as pulpy kidney disease), calves, Adult cattle Fowl	Acute enterotoxaemia Enterotoxaemia Enterotoxaemia Necrotic entritis

Table: 02. Biochemical characteristics of *clostridium perfringens* (Rahimoon et al., 2021)

Cl.perfrigens	M.R	GLT	TSI	Cat.	Oxid	Ure	Ind	V.P
	+ ve	+ ve	A/A	- ve	- ve	- ve	- ve	- ve

Whereas: M.R = Methyl Red; GLT = Gelatin liquefaction test; TSI = Triple sugar iron ;Cat. = Catalse; Oxid. = Oxidase; Ure = Urease; Ind = Indole; V.P = Voges proskauer

Table: 03. Epidemiology of Clostridia infection.

Cl. perfringens type	**Animals affected**	**pathogenesis**	**Year**	**authors**	**Country**
Type A,B,C,D,E	Calves	Enteritis and enterotoxemia	1999	Petit and others	France
Type A, E	calves	Diarrhea	2000	Garmory and others	USA
Type A	Cattle	Enterotoxemia	2000	Manteca and others	Belgium
Type A	calves	Enterotoxemia	2001	Manteca and others	Belgium
Type A	Dairy cattle	Haemorrhagic bowel syndrome	2002	Dennison and others	USA
Type A,C,D	Cattle	Diarrhoea	2003	Efuntoye and Adetosoye	Nigeria
Type A ,C ,E	Calves and adult cattle	Sudden death, enterotoxaemia, enteritis	2003	Bueschel and others	USA
Type A	Calves and adult cattle	Enterotoxemia	2004	Schotte and others	Germany
Type A	Beef cows	Jejunal haemorrhage syndrome	2004	Abutarbush and others	Canada
Type A	Dairy and beef cattle	Jejunal haemorrhage syndrome	2005	Abutarbush and Radostits	Canada
Type A	Roe deer	Enteritis	2006	Johansson and others	Sweden
Type A	Dairy cattle	Haemorrhagic bowel syndrome	2006	Ceci and others	Italy
Type D	Goat	Enterotoxemia	2021	Muhammad Mohsen Rahimoon and others	Pakistan

Table: 04. Risk factor of Clostridia infection.

Risk Factors	Description	Citation
Age	• Pulpy kidney is a disease which can affect sheep at any age, but is most frequent in lambs of 4-10 weeks of age and in fattening stock from which 6 months to 1 years of age. • Sheep Age of one year are more affected with enterotoxemia fallowed by six month and two year of age.	• Buven *et al*., 1970; Quinn *et al.*, 2002; Jemal *et al.*,2016 • Haq *et al.*, 2016 Abildgaard *et al.*, 2009
Sex	• Female animals affected more as compre to male animal • Compsrasion of prevelnce of enetrotoxemia in male and female of goat and sheep. The males of both species are less infected with enterotoxemia as compare to female.	• Rahimoon *et al*,. 2021 Quinn *et al*., 2002; • Haq *et al.*, 2016 Abildgaard *et al.*, 2009
Environmental	• Changes in internal intestinal environment i.e excessive feeding of animal with nutrient rich diet provide suitable environment for microbes to produce lethal toxins. • when the intestinal environment is altered by sudden changes in diet or other factors, C. perfringens proliferates and produces potent toxins	• Jemal et al.,2016 • Uzal and songer., 2008
Husbandry /Managment	• The husbandry conditions in which the disease occurs include grazing on lush Lambs on well-fed, heavy milking ewes are particularly susceptible.	• Jemal et al.,2016 • Quinn et al., 2002
Feed	• Sheep's changed from a low to a high plane of nutrition may be vulnerable to the pulpy kidney disease • Over-consumption of large amounts of milk leads towards the development of enterotoxaemia in young calves	• Jemal et al.,2016; Uzal and songer., 2008 • Jang *et al*., 2010
Stress	• When animals are being expose to various stress factors i.e temperature, parasitic infestation, changing in feeding plan etc leads toward occurrence of enteritis. • Inadequate colostrum intake, chilling and stress develops enterotoxaemia in young calves	• Rahimoon et al,. 2021; Uzal and songer., 2008 • Jang *et al*., 2010