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Paramphistomum Cervi: Morphology, Life Cycle, Prevalence, Molecular Characterization, and Treatment Insights: A Comprehensive Review

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Abstract: *Paramphistomum cervi, normally referred to as the rumen fluke or not unusual belly fluke, is a parasitic flatworm that infects the rumen and reticulum of ruminant animals worldwide. This overview article provides an outline of the superiority, molecular characterization, treatment, and manipulates measures associated with Paramphistomum cervi. The superiority of this parasite is enormous, affecting numerous domestic ruminants consist of sheep, farm animals, and goats. Recognising Paramphistomum cervi's molecular characteristics, such as its morphology, life cycle, and host interactions, is crucial for devising effective control strategies. Diagnostic techniques, including fecal examination and postmortem examination, are essential for accurate detection of Paramphistomum cervi infections. The article further explores the pathogenesis of this parasite, including the pathological changes it induces in affected animals' rumens and reticula. There is also discussion of the financial effects of Paramphistomum cervi infections on cattle productivity. Additionally, treatment options and anthelmintic drugs available for controlling Paramphistomum cervi infections are highlighted. The review concludes with an assessment of ongoing research. Overall, this review article provides a comprehensive analysis of Paramphistomum cervi, shedding light on its impact on animal health and providing valuable insights for the scientific and veterinary community.*

Introduction:

A genus of parasitic flatworms called Paramphistomum is part of the digenetic trematode family. Its phylum is Platyhelminthes. It comprises flukes, which mostly parasitize ruminants used for livestock as well as certain wild species. They induce a dangerous condition in cattle and sheep known as paramphistomiasis, sometimes termed aphistomosis. Felix Fischoeder created the generic name in 1901 to replace the Aphistoma genus, which was already extant at the time. According to (Lotfy *et al*., 2010), notable paramphistomum species include P. cervi, P. cotylophorum, P. cracile, P. gatoi, P. grande, P. hiberniae, P. ichikawai, P. epiclitum, P. explanatum, P. leydeni, P. liorchis and P. microbothrioides. According to literary sources, trematodes pose a serious epizootic threat not only to ruminants but also to people (Ooms *et al*., 1995; Mas-Coma *et al*., 2005; Samn, 2017; Bibik *et al*., 2020). When helminth infections in animals were being investigated as an epizootic condition in the Russian Federation, it revealed the existence of a variety of trematodes transmitted by fish and mollusks, including fascioliasis, paramphistomiasis, dicroceliosis, opisthorchiasis, clonorchiasis, and others (Gorohov *et al*., 2014; Puzanova, 2019). Due to its detrimental effects on ruminant welfare and health, gastrointestinal parasitic infection is a global problem that is lowering bovine productivity. (Dyab *et al*., 2018; Paul *et al*., 2020; Abdelhamid *et al*., 2021). Animal health and product performance are hampered by parasitic illnesses, which are a common concern on a global scale (Horal & Dawes., 2006). Multifactorial gastrointestinal parasites like nematodes, trematodes, and cestodes are attractive to small ruminants (Waal., 2010). In this regard, there are numerous sources of rumen fluke infection brought on by immature samples, resulting in serious economic losses and animal mortality (Horak and Clark, 2000). Several domestic and wild animals are infected by these trematodes (Rolfe *et al*., 1994). Chronic diseases in species are often related to parasitic infections caused by a variety of trematode species. Trematodes, which are commonly referred to as "flukes," are endoparasites that affect many organs in their hosts, including sheep, goats, and farm animals, as well as other livestock foraging and predators. The body of the mature fluke has a pair of suckers that act as a feeding mechanism and help it attach to the outermost layer of the host's internal systems (Kahl *et al*., 2021).

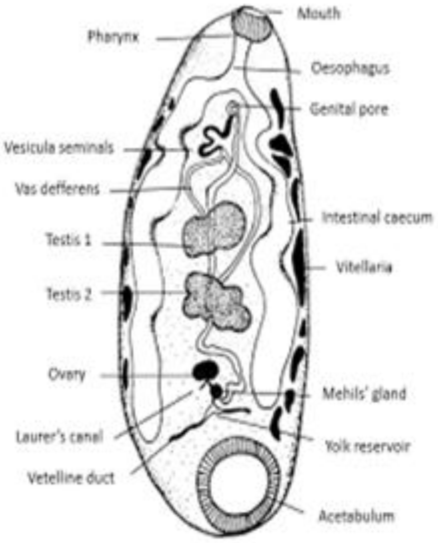

Fig: 1 General diagram of a rumen fluke

This parasitic disease causes significant losses mortality in domestic animals in entire world (Njoku and Nwoko, 2009; Raza *et al*., 2009; Ozdal *et al*., 2010; Melaku and Addis, 2012 and Iqbal *et al*., 2013). The main reason why the global population of domestic animals is declining is because of parasitism (Farooq *et al*., 2012; Elele *et al*., 2013 and Swarnakar et al., 2014a & b). Although paramphistomosis is present around globe, tropical and subtropical areas, particularly in the African continent, Southeast Asia, Australia, Eastern Europe, and the Russia, have the condition at its highest incidence (Boray, 1959, 1969; Horak, 1971; Gupta *et al*., 1978). Depending on the area, several parasite species induce paramphistomosis. Russia, Bulgaria, Poland, France, and Italy have all recorded Paramphistomum cervi sightings whereas Sardinia, Yugoslavia, and Hungary have had P. microbothrium sightings (Horak, 1971). P. ichikawai and Calicophoron calicophorum are two paramphistome types found in Australia and New Zealand that harm cattle and sheep (Brotowidjoyo and Copeman, 1979). Fischoederius elongates, Fischoedrius cobbaldi, Gastrothylax crumenifer, Cotylophoron cotylophorum, Paramphistomum cervi, Paramphistomum explanatum have all been identified in Asia. These species have also been found in China, India, and Ceylon. (Boray, 1959; Hanna *et al*., 1988; Wang *et al*., 2006). To provide the groundwork for upcoming molecular investigations, examination of the morphology and histology of P. cervi using Borax carmine and H and E staining procedures was carried out. During slaughter at several local abattoirs in the Gujarati cities of Anand, Ahmedabad, and Vadodara, 350 sheep between the ages of one and two were tested for the detection of gastrointestinal helminths; 17 of the sheep tested positive for Paramphistomes. During the examination, it was observed that there is very little change in the form and proportions of the parasite and its internal cavities, which differ even between adult and immature worms of the same species, making it nearly impossible to recognise and differentiate amphistome species. While morphology cannot be fully understood using a stereo microscope, the parasite's histology investigation can provide strong confirmation (Chaoudhary *et al.*, 2015). The prevalence of Paramphistomum cervi in ruminative animals has been observed to range from 25.1 to 92% in various parts of Pakistan at various periods. (Iqbal *et al.*, 1993; Ali *et al.*, 2000; Raza *et al.*, 2007; Ijaz et al., 2008; Al-Shaibani *et al.*, 2008; Kakar and Kakarsulemankhel, 2008). In Pakistan where hygienic standards are not too good, parasitism is a real problem, to the health of man and livestock. Losses due to helminthes are greater than is generally realized. Losses in form of death, decrease in milk production, poor quality of meat and decreased fertility are worth mentioning. Fascioliasis and paramphistomiasis are a global hazard for livestock welfare. Fascioliasis is the major factor affecting livestock development in Pakistan and same may be true for Paramphistomiasis (Mirza *et al.*, 2009). Paramphistome parasites belong to family Paramphistomidae, and all have ruminants as definitive host and fresh water snail as an intermediate host. The intake of encysted metacercariae adhering to plants or gliding in water causes infection of the ultimate host. Due to the ultimate host's consumption of metacercariae, the rumen fluke can be discovered in the gastrointestinal tract, where it attaches to the mucosa and matures just before migrating to the rumen (Waal *et al.*, 2010). The infection causes coarse furred, weakness, loss of appetite; weight loss, intestine ulcers, inter-mandibular swelling, and these are the cause of economic losses and high mortality (Chandrasekharan *et al.*, 1982). A review of parasitic studies in Pakistan (Iqbal et al., 1993) revealed that most parasite incidence surveys were carried out at organizations such as Faisalabad and Lahore. However, in some places, the livestock population should be tested for the existence of stomach-borne helminthes. To determine the incidence of Paramphistomum cervi in executed goats, cattle, sheep, and buffaloes in Pakistan's Muzaffar Garh district a survey was carried out. According to the survey P.cervi infection affected 22% of ruminants in Tehsil Jatoi, District Muzaffar Garh. Species wise prevalence for sheep, goats, cattle and buffaloes was 28.57, 23.80, 17.64 and 20.00% respectively (Raza *et al.*, 2009). The prevalence of Paramphistomum cervi infestation in Balochi, Babrik, and Harnai sheep types from Balochistan (Pakistan) was investigated between September and December 2010. 1,200 rumen samples from sheep that had been killed in Quetta City and its vicinity were analysed for this reason. The findings demonstrated a significant difference in gender, age, species, and seasonality of P. cervi infection in livestock. During the course of the trial, animals had an overall P. cervi infection of 17.83 percent. Animals greater than the age of two had a higher frequency of infestation (23.5%). when age was taken into account. In comparison, the community of people under the age of a year had a lower percentage of parasitization (16.66%). In terms of sex, it was shown that females (22.33%) were more infected than males (17.83%). When taking into account the time of year, P. cervi prevalence peaked in October at 19.25%, followed by November at 15.75%, September at 12.75%, and December at 12.5% (Tehmina *et al.*, 2014). 200 sheep that were slaughtered at roughly a year of age were the subject of a research, and incidence of trematodes was noted from May to August 1995 at several abattoirs in Lahore. According to the data collected on the gastro-intestinal trematodes, the months of May were particularly common for Paramphistomum cervi in (14%), Fasciola hepatica (20%), and Dicrocoelium dendriticum (4%). P. cervi (20%), F. hepatica (28%), and D. dendriticum (6%) were the most common infections in June. P. cervi, F. hepatica, and D. dendriticum all had percentages of 34%, 44%, and 14% in July and 30%, 36%, and 10%, respectively, in August. Trematode incidence was seen in sheep at a rate of 65% overall (Hashmi *et al.*, 2003). In order to ascertain the incidence and severity of the condition, a 12-month research on paramphistomosis was conducted in the southeast of Iran. In the Zabol abattoir, 1000 cattle, including 450 Sistani breed and 550 Brahman breed animals of various sexes and ages, were randomly examined for paramphistomidae flukes from December 2012 to October 2013. Of the 1000 cows that were necropsied, 369 had paramphistomes, with the rate of infection being much greater in the Brahman breed (51%), compared to the Sistani breed (19.3%). The stained trematode species identified were Cotylophoron cotylophorom, Paramphistomum cervi,Gastrothylax crumenifer, Explanatum explanatum and Carmyerius spatiosus, in that order: 40, 20, 20, 15 and 5% (Khedri *et al*., 2015). To track the seasonal prevalence of Paramphistomosis, The small bowels of slain sheep were collected from slaughter houses once a week (Abattoirs in Kermanshah, Sanandaj, Tabriz, and Urmia). A total of 2,421 sheep corpses were investigated, of which 0.041% tested positive for Paramphistomum infection (743 male (30.69%) and 1,678 female (69.31%). Summer (July to August) and autumn (November to October) were the two seasons with the greatest infection rates among sheep infected with Paramphistomum species (6.7, 2% and 3.8, 2.3%), respectively (Tehrani *et al*., 2015). From May 1989 to April 1992, 30 rumens were studied each month to determine the seasonal patterns of infection and their connection to the environmental conditions that led to Paramphistomum cervi in cattle. Three municipalities in Tabasco's Sierra region were chosen for cattle: Jalapa, Taepa and Tacotalpa. P.Cervi was discovered all year long, with prevalence ranging from 3.33 to 96.67% and an average yearly prevalence of 39.10%. Infection's peak time was evident in Jalapa. The highest mean intensity nevertheless was discovered at Taepa. The same infection prevalence across the three locations demonstrates the regional pattern of P.cervi infection. Summer, fall and the first few weeks of winter were the most common times that cattle become infected (Rangel *et al*., 2003). Cattle mortality is estimated to be 80 to 90 percent in some parts of India, Australia and the South African Republic (Boray, 1959; Soulsby, 1987). In Gujrat, India, a study was done on the histology and morphology of the rumen fluke of water buffaloes. Key morphological discoveries included the following: The rumen flukes had paramphistomum-type acetabulums, liorchis-type pharynxes, and leydeni-type genital atriums.

These physical traits were present in flukes during both the winter and summer. These observations led researchers to the conclusion that the rumen flukes found on Gujarati buffalo belonged to the species P. cervi (Chourasia *et al*., 2014). Adult paramphistomes have always been thought to be rather innocuous in cattle in Europe. However, recent studies have shown that European Paramphistome species, most frequently Paramphistomum daubneyi, can cause serious gastrointestinal sickness, a decline in productivity, or perhaps mortality as well (Dorchies et al., 2002). Van province is located at 37^0,39^0 latitudes in north direction 43', 26' and 42^0,44^0 longitudes in east direction 40', 30'. This region, which has borders with eastern Iran, is located at an altitude of about 1.725 metres. 40 (8.95%) and 42 (12.4%) of the 447 cattle and 948 sheep have been tested for paramphistomosis at abattoirs during one-year research period from May 2006 to April 2007 in van province respectively. (4.43%) of the animals underwent a gut examination and diagnosed positive for paramphistomum infection. Only two sheep were reported to have paramphistomum spp. at both the rumen and the reticulum, but every parasite in cattle was discovered in the rumen (Ozdal *et al*., 2010). Investigations on the frequency of paramphistomosis in animals such as goats at numerous abattoirs in Bangladesh found that the three amphistome species, Cotylophoron cotylophorum, Gastrothylax crumenifer and Paramphistomum cervi—have a high incidence of 73%. 60% of the goats developed infections with more than one kind of amphistomes (Uddin *et al*., 2006). Paramphistomosis was found in 36.2% of sheep and 30.9% of goats during an inspection of an Indian abattoir in Jammu. The prevalence was significantly influenced by the time of year. In comparison to the summer and winter times of year, the periods of rain and post-rainy seasons yielded a higher proportion of positive animals (Godara *et al*., 2014). Paramphistomosis symptoms start to show 16–32 days after infection. They include decreased appetite and lethargy at first, followed by diarrhoea, a slight temperature, hydropsy, low blood, reclination and starvation. Under experimental circumstances, severe catarrhal diarrhoea might arise from gastrointestinal Paramphistomosis after uptake of up to 50,000 metacercariae (Boray, 1959; Millar *et al*., 2012). The trematodes' migration routes in the abomasum and small intestine, as well as their attachment points in the rumen, have undergone pathological-anatomical modifications. The intestinal mucosa is inflated, reddish, and there are petechial haemorrhages in some places. Deep between the villi, flukes can be found as young adults. In the vicinity of the pylorus, the abomasal mucosa is catarrhically irritated (Samson *et al*., 2018 and Rolfe *et al*., 1994). Between October 2014 and December 2015, Cattle faeces from four predetermined slaughterhouses in Owerri, Imo State, Nigeria, including Afor Egbu, Afor Enyiogugu, Afor Ajala, and Afor Ogbe, have been investigated utilizing direct smear, formal either concentration, and chloride of sodium buoyancy procedures to determine the incidence of paramphistomiasis. The eggs of P. cervi were identified, and the gender of the cattle became apparent. Dentition was used to determine the age ranges of cattle, starting with young calves (2 years) and old cattle (>2 years) being the most recent. 467 (16.1%) of the 2,900 animals evaluated were affected. The highest infection rate was at the Afor Ogbe Abattoir, where 247 animals were affected, or about 14.8%. This was followed by the abattoirs in Oriagu, where 71 animals were affected, or about 23.1%, Afor Ajala, where 65 animals were affected, or about 15.6%, Egbu, where 50 animals were affected, or about 15.8%, and finally Afor Enyiogugu, where 34 tested positive, or about 17.8%. Males had somewhat higher infection intensity than females.

Because the virus was age dependent, age was a key determinant. Adult cattle were infected at a rate of 16.1%, while young cattle were affected at a rate of 7.5%, since older cattle had more illnesses than younger calves, which were less than two years old. It was discovered that the incidence of infection fluctuated seasonally, increasing with more precipitation and declining over the summer (Njoku-Tony *et al*., 2017). On the basis of faecal, liver/rumen, and other examinations, to ascertain the frequency of amphistomosis an investigation was carried out in animals such as buffalo that had been slaughtered in Ahmedabad, Gujarat. Buffaloes were transported to the local abattoir in Ahmedabad district, Gujarat, and 798 stools and 790 rumen test specimens overall were collected. For the duration of a year from the beginning of March 2013 to the end of February 2014, the monthly, seasonal, and overall prevalence were looked at, and the findings were assessed. By examining both faeces and liver samples, it was determined that the total prevalence rate was 27.69% (211) and 28.86% (228), respectively. It was highest in winter, in the months of November and December, followed by monsoonal period, and least in summer, in the month of April. This study's findings suggest that amphistomosis is a serious parasitic infection that affects buffaloes in Ahmedabad and significantly generates losses and reduces output and health, particularly in the months of November and December (Vandip *et al*., 2014). A longitudinal parasitological study of 1,325 specimens of sheep faeces was performed to determine the incidence of trematodes that were allowed to graze naturally in Kashmir Valley, India, was carried out. Of the 28.98% of sheep with at least one illness, different parasite levels were seen. Fasciola gigantica and Fasciola heaptica were the most prevalent species, accounting for 23.92% and 9.96% of the total population, respectively. However, Dicrocoelium dendriticum and Paramphistomum cervi were also found, with respective populations of 4.45% and 2.71%. The months of summer had the greatest infection rates, at 13.94%, followed by those of autumn, at 7.38%, of spring, at 6.06%, and of winter, at 1.41%, according to seasonal variations. The age categories of sheep with the highest (42.8%) prevalence of trematode parasites were 2-4 (37.7%) and 0-2 years (18.79%), respectively (Mir *et al*., 2008). Between September 2004 and September 2005, a random selection of 367 sheep of the Ovis species was made from Imo State's Okigwe, Orlu, Obowo, Ihitte Uboma, and Mbaise districts the frequency of Paramphistomum cervi 96 (26.2%) of the 367 animals tested developed a severe infection. The greatest infection rate was recorded in Okigwe at 34.5%, while the lowest rates were recorded in Afor-ogbe, Orlu, Orieagu, and Achingali at 30.0, 20.4, 18.4, and 16.7%, respectively. Age, however, was shown to be extremely significant (p0.01), mature animals are more likely to get infected than younger ones. Sex did not demonstrate a significant link with the infection (Njoku *et al*., 2009). To precisely understand possible risk factors and how climatological changes affect five important intestinal parasites, a meta-analysis was conducted in Bangladesh: species of Paramphistomum, Schistosoma species, Moneizia species, Strongyloides species, and Trichuris species. The research published in English between 2000 and 2020 were chosen by screening in four internationally renowned databases, including Web of Science, Scopus, PubMed, and Google Scholar. By the analysis of 29 investigations the maximum prevalence was found in Paramphistomum species at 26%; 95%, followed by Strongyloides species at 9%; 95%, Trichuris species at 10%; 95%, Schistosoma species at 19%; and Moneizia species at 8%; in addition, the overall prevalence was noted as 15%; 95% with a CI of 19-33; 5-12; 4-17; 7-31; 5-10; and 11-18 respectively (Hasan *et al*., 2022). A total of 178 dead buffaloes between the ages of four and six were evaluated in 2018. Each buffalo underwent an instant postmortem inspection before having flukes removed with sterilised forceps from its infected reticulum and rumen and put in a saline solution. 23 randomly selected and visually identifiable adult Paramphistomum were used for species-level recognition using specific primers for isolated portions of their 18S rRNA genomes. By utilizing BLAST on the NCBI website, comparable sequences were found using the cleaned sequences (810 bp). The novel Paramphistomum species isolated sequences and GenBank downloaded nucleotides were synced using CLUSTAL in the BioEdit Genome Aligning Tool. Additionally, MEGA X was used to create a phylogenetic tree using the greatest likelihood approach. The 18S rRNA sequence was determined to be 98% identical to Paramphistomum epiclitum and other Paramphistomum species of India and to Paramphistomum cervi of China. Paramphistomum cervi was discovered by molecular analysis to be the parasite species of Pharamphistomum (Rafiq *et al*., 2020). Although structural and histological studies and broad recognition of the paramphistomes are sufficient, structural similarities necessitate molecular methods for exact recognition (Rinaldi *et al*., 2005). Molecular markers are frequently employed in conjunction with the mitochondrial DNA and the 18S rRNA segment of ribosomal nuclear DNA (rDNA) to identify various trematodes (Patwardhan *et al*., 2014; Prasad *et al*., 2009). Nuclear ribosomal DNAs (rDNAs) of eukaryotes are arranged in short tandem repeats or microsatellites. 18S, 5.8S, and 28S ribosomal RNA are three genes that make up a transcriptional unit that is a component of each repeat, an intergenic spacer and a pair of internal transcribed spacers, known as ITS1 and ITS2, are present in between the transcriptional units (Long, E.O and Dawid, I.B; 1980). Different ribosomal DNA fragments can be employed as genetic markers to determine phylogenetic study at distinct taxonomic levels since they evolved at varied speeds (Dai *et al*., 2012; Orosova *et al*., 2010; Yamada *et al*., 2011; Wang *et al*., 2012). The present work identified and characterised the whole rDNA sequence of P. cervi in order to better understand the structures and phylogeny of Digenea trematodes as well as to discover unique genetic indicators for studying intraspecific and interspecific alterations in the Paramphistomatidae. In GenBank, all five full rDNA sequences have been deposited. Five full rDNA sequences had lengths of 8,493, 9,908, 10,056, 10,167, and 10,221 bp, respectively. The ribosomal DNA for 5.8S was 157 base pairs long, for 28S it was 4,186 base pairs long, and for ITS2 it was 286 base pairs long in the five P. cervi samples used in this investigation, were identical. 5.8S, 28S, and ITS2 ribosomal DNA intraspecific changes in P. cervi resulted in zero percent. Guanine +Cytosine ratio ranged from 51.74% to 51.82% for 28S rDNA, 51.75% for ITS2, and 54.14% for 5.8S. However, interspecific variations in ITS2 ranged from 1.4% to 6.3% among members of the Paramphistomatidae family.according to a comparative investigation. As a result, the ITS2 sequence provides a valuable identifier for species-level taxonomic research on the Paramphistomatidae family (Zheng *et al*., 2014). Considering the disease's clinical signs and previous history, paramphistomosis is tentatively diagnosed. It is possible to collect and examine animal faeces for the presence of parasite eggs that may exist to provide additional proof. However, this approach frequently leads to confusions (Horak 1971; Bida and Schillhorn van Veen, 1977; Kelly and Henderson, 1973). The rumen and bile ducts must be treated quickly once paramphistomosis is discovered early in order to prevent lasting damage (Wang et al., 2006). By routinely administering a variety of medications to animals in endemic locations, paramphistomosis can be partially controlled. To treat paramphistomosis in livestock, including cattle, sheep, and goats, a number of medications have been evaluated and suggested (Reddy and Hafeez, 1986; Rolfe and Boray 1988; Gupta *et al*., 1981). Bithionol sulfoxide had been shown to be fairly successful despite rumen flukes being drug-resistant (Prasitirat *et al*., 1996). For scientists from multiple countries, Understanding the intricate microscopic makeup of trematode organs and tissues is crucial. Additionally crucial are histochemical and pathomorphological analyses of the host-parasite interaction involving trematodes, as well as research into how anthelmintic drugs affect the destruction of this association (Periago *et al*., 2008). Histochemical techniques were used to recognise the mucoproteins, common proteins, and hexosaminoglycans in the lesions, tegument, and intestines that serve as the foundation for the physiological morphogenesis of helminthes (Bibik *et al*., 2019; Bibik *et al*., 2020). Controlling paramphistome infection often involves the use of chemotherapeutic anthelmintic medications. Due to the careless application of these drugs, antihelmintic resistance has emerged (Verma *et al*., 2006). Therefore the objective of this paper is to review different literature on the emerging problem of rumen fluke with the underlining on Prevalence, epidemiology, molecular characterization and diagnosis.

Life Cycle:

Rumen flukes are known to live for a number of years. Rumen fluke life cycles include a pair of hosts. Mammals, often ruminants, are the final hosts, with snails serving as intermediate hosts. Ingestion of encysted metacercariae that are either floating in the water or clinging to plants causes infection of the final host (Gonzalez *et al*., 2013). Depending on the temperature, miracidia hatch from these eggs after 12 to 21 days when faeces are discharged into the water. In snails, mature sporocysts bearing rediae take 11 days to develop. Rediae are released from the snail, and after an additional 10 days of maturity, they contain several cercariae. For a further 13 days or more, cercariae must be freed from rediae in order to proliferate within the snails (Vihan 2010). The long, thin tail and two eyespots of mature cercariae allow them to cling to aquatic plants and encyst into metacercariae (Jones *et al*., 2017). The infectious larva is being ingested by the mammalian hosts. When the larva enters the duodenum and jejunum, its cysts are removed (Arrue *et al*,. 1970). Young flukes move from the gastrointestinal canal to the rumen beforehand. Once there, they undergo additional maturation after adhering to the rumen mucus, begin producing eggs, and finish their life cycle. Development and migration to the rumen may be postponed for a number of extra months when fluke infestations are massive (Daugschies *et al*., 2018).

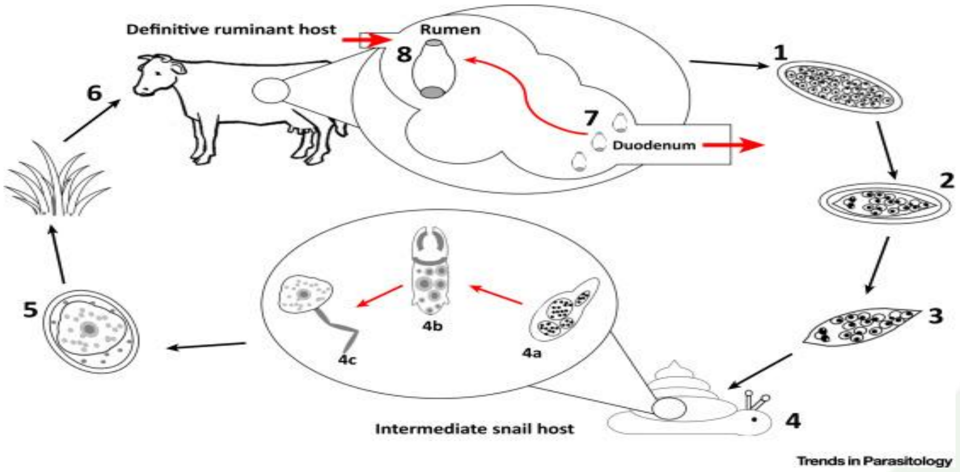

Fig: 2 Life cycle of rumen flukes

Discussions:

A survey found that 54.47% of buffaloes had gastrointestinal parasite illnesses overall in various parts of the district of Khushab in Punjab, Pakistan. Comparing the prevalence of infection to the proportion of parasite infestation in adult animals, it was shown that young cattles had a higher frequency of infection (61.78%) (Deeba *et al*., 2019). This outcome is associated according to the findings of (Mir *et al*., 2013), who found that dairy cows infected with mixed helminths had a 51.29 % infection rate. The infection is also correlated with the state of the body's health, and research shows that the animals in poor health had the highest prevalence (93.75%). The findings concur with those of (Awraris *et al*., 2012), who discovered that animals in poor bodily condition had significant helminth burdens (57.7%), Contrary to Regassa *et al*. (2006), who discovered that the presence of the parasite and the animal's physical state did not substantially correlate with one another. Younger animals may have reduced resistance to infection because they have had less exposure to various helminthes species, as compared to adults (Bilal *et al*., 2009; Raza *et al*., 2012; Zaman *et al*., 2014). The same results were made by (Bachal *et al*., 2002), who discovered that male calves (45.12%) had a greater prevalence of helminthes than female calves (48.30%) in a research (Deeba *et al*., 2019) about the incidence of intestinal parasitic organism diseases among buffalo population. States in the various climate zones throughout the world and animal species claim, prevalence and species caused paramphistomosis exhibit variance. There was a 3.45%-15% variation in the frequency of paramphistomosis in cattle, with an annual average of 8.95%, according to (Ozdal *et al*., 2010). P. cervi prevalence in cattle was reported to be 39.10% by Tabasco researchers (Rangel-Ruiz *et al* 2003). According to reports (Mage *et al*., 2002; Szmidt-Adjidéa *et al*., 2000), In France, the prevalence of paramphistomosis in cattle ranged from 5.2% to 44.7%. According to Soulsby (1982), paramphistomosis outbreaks typically take place during drier months. (Hassan *et al*., 2005) discovered that in domestic ruminants, the prevalence was highest during the monsoon and post-monsoon seasons during the months of July to October with a prevalence rate of 8.06%, and it was lowest during the winter months of November and December with a prevalence rate of 0.49%. Summer, which is defined as the months of March to June with a prevalence rate of 2.92%, was found to be the second most common season. Peak fluke loads and symptomatic paramphistomosis were seen in calves in a subtropical region of eastern Australia in the summertime and the beginning of winter (Rolfe *et al*., 1991). Between 0.72 and 84.1% of domestic animals globally had gastrointestinal parasites, according to the results of a meta-analysis (Hasan *et al*., 2022), but it was stated to be as 15% overall (Dagnachew *et al*., 2011). More specifically, the incidence rate was found to be as 55.6% in Ghana (Squire et al., 2018), and 60% in Ethiopia (Cheru *et al*., 2014). By identifying numerous risk variables such period, species, gender, age, and season, the focus of the present systematic review was the frequency of gastrointestinal parasites. According to parasite species, species of Paramphistomum, which range from 17.83% in Pakistan, had the greatest incidence (26%) (Tehmina *et al*., 2016). Furthermore, when examining the subgroup of species based on big ruminants, the frequency was higher in buffalo than cattle. Additionally, earlier studies confirmed that buffalo had a prevalence rate of 75% compared to cattle's (56.25%). (Bilal et al., 2009). According to the study (Gadahi *et al*., 2009; Poddar *et al*., 2017), which revealed that goats were more vulnerable to gastrointestinal parasite illnesses than sheep. The prevalence of Paramphistomum infection varies by region. Area and worm burden do not significantly correlate ($p > 0.05$). The presence of an intermediary host and the existence of conductive environments that support the survival and development of this parasite in water bodies, particularly well-developed channel systems, may be the causes of P. cervi infection in all districts of central Punjab (Iqbal *et al*., 2013). In the three towns under study, the prevalence was often assessed to be over 30%, with numbers reaching as high as 96.67%, while only a few months of the year had modest incidence. Teapa had the most parasites in the diseased cattle, but Jalapa offered the most affected animals overall. The present infection rates are among the highest when compared to prevalence data from other nations, with comparable or different paramphistome species. In particular, this study found a lower incidence of P. cervi than had previously been reported for Mexico (Rangel-Ruiz *et al*., 2003). Animal P. cervi infections were most prevalent during the rainy seasons of July to October and the cold seasons of November to February (Rangel-Ruiz *et al*., 2003). Similar incidents to those recorded in India and Cameroon happened in May, during the dry season (Asanji, 1989; Varma *et al*., 1989). According to Rangel-Ruiz *et al*., (1999), the infection behaviour of P. cervi was comparable to that of F. hepatica in that (a) it persisted all year long; (b) There were no discernible changes in the intensity average's transient prevalence among the three municipalities; (c) a decline in infection rates was seen in the second year of the trial; (d) There was no discernible association between the mean intensity and the meteorological factors according to the correlation analysis. However, the following distinctions were also noted: (a) In Teapa, P. cervi and F. hepatica both had the highest mean intensities; (b) The rainy and windy seasons had the greatest mean intensity values for P. cervi, whereas the dry season and the beginning of rainy season saw the highest mean intensity data for F. hepatica (Rangel-Ruiz *et al*., 2003). According to Horak (1971), Periodic outbreaks of chronic parasite gastroenteritis with significant levels of illness and death, particularly in young animals, are the hallmark of paramphistomiasis. However, the effects of P. cervi on hepatic paramphistomiasis have not been well investigated, and their part in the aetiology of the condition has not been reported. According to reports (Buttler and Yeoman, 1962; Horak, 1967), paramphistome infection causes cattle fatalities. Asian buffaloes have been reported to be afflicted, and Patnaik (1964) found Paramphistomum explanatum in the diseased animals. P. leydeni and P. daubneyi have also been noted in Vendae, Paris, P. ichikawai-related species were also discovered in this area. However, they regarded this as a distinct species or equivalent to P. cervi (Albaret *et al*., 1987). Pakistan is primarily an agricultural nation, with 70% of the people currently employed in agriculture. 80% of all cattle in the nation are grazed on 30% of all land holdings. Bullocks play a significant role in Pakistani crop production. Despite this, the nation has struggled to get the necessary amounts of milk and other animal products, including cereals. Massive attention is being paid to the production and use of animal products in human diets, and the necessity to advance animal husbandry is generally understood. In Pakistan, there is a lack of knowledge on the illness, the severity of the infection, the pathology, and the histology of this bug. The investigation of this issue has received very little attention (Mirza *et al*., 2009). The frequency of helminths was highest in sheep, then in goats, cattle, and buffaloes. The higher prevalence of helminths in sheep and goats correlates well with a higher proportion of time spent on grazing as compared to cattle and buffaloes, which are comparatively grazed less and are mostly maintained in stalls for eating. The research area's diverse climate, which ranges from tropical to subtropical, is favourable for the growth of helminths with indirect life cycles' larval forms or intermediate hosts (Raza *et al*., 2007). An exceptionally warm and humid summer is favourable for the development and existence of nematode free-living stages (Grant, 1981). Sheep were found to have the highest frequency of Paramphistomum cervi in this investigation. Sheep helminth infection rates vary significantly over the world. The incidence rate of Paramphistomum cervi was not significantly different among animals of four different species, showing that it is not species-dependent. Sheep had an overall P. cervi infection rate of 20.08%. The results obtained in the study were somewhat less significant than prior studies (Uddin *et al*., 2006), which showed that P. cervi was 65.28 percent prevalent in Black Bengal goats executed at multiple abattoirs in the Bangladeshi city of Mymensingh. In the current study, Balochi and Harnai species sheep showed higher/similar frequency (21.5%), whereas Babrik sheep breed showed lower incidence rate of 17.75%. In the current study, September, October, November, and December had the greatest prevalence rates of parasites, with prevalence rates of 25, 66, 21, 17, and 16, 66%, respectively (Tehmina *et al*., 2014).

Trematoda class members exhibit a variety of distinctive characteristics that aid in separating them from other class members. Body covered in integument with frequently bearing spines, papillae, or tubercles, well-developed reproductive system, having alimentary system consisting of oral and posterior suckers with absence of anus except in Fasciola species, and major feature of this class animals having two hosts: primary host (sexual reproduction) and intermediate host (asexual reproduction). These structures are crucial to the survival of the group of animals. Ultrastructure is the study of a biological sample's nano or tiny structure at extremely high magnification via electron microscopy. These investigations aid in the provision of morphological knowledge and guidance for the preparation of the medication for their treatment (Sanger *et al*., 2017). Understanding potential risk factors related to cattle amphistomiasis is necessary to develop and execute effective control measures and management programmes that can lead to the control and elimination of the disease. Along with helping with clinical diagnosis, it is also a helpful tool for figuring out the epidemiology and trends of the disease. During ante-mortem faecal inspection for amphistomum eggs and post-mortem investigation of the rumen and reticulum for the presence of adult amphistomum, the current study revealed that the total frequency of amphistomidae flukes at Zabol, southeast of Iran, was 19.5% and 34.6%, respectively. The study's findings were in line with other studies on adult flukes, which discovered that Mazandaran, Northern Iran, had a reported paramphistomidae fluke infection rate of 33.9% (Eslami *et al*., 2011), and 36.9% in South-Eastern Iran (Khedri *et al*., 2015) (Hajipour *et al*., 2021). Molecular research sheds light on the biology and evolutionary relationships between different parasites. These studies are trustworthy for identifying and describing a number of disease-causing chemicals based on their genetic makeup. The 18S ribosomal RNA pattern of the Paramphistomum cervi generated in this investigation was found to be nearly identical to the P. cervi from the surrounding nations (China and India), this might be attributable to similar geographical, climatic, and trans-boundary host migratory variables (Rafiq *et al*., 2020). Due to the findings of a prior research, the obtained sequence's BLAST results showed that it was 100% identical to P. cervi from China and 98% identical to P. epiclitum and various Paramphistomum species from India. This indicates a shared phylogenetic past (Rinaldi *et al*., 2005; Sindičić *et al*., 2017). Amphistomosis is the primary impediment to successfully growing cattle for farmers with limited resources in tropical parts of the world, which is very prevalent in ruminants (Sanabria and Romero 2008). Despite significant technological improvement, the parasites' morphology continues to serve as the foundation for taxonomical research and recognition (Choudhary *et al*., 2015; Salib et al. 2015). Genetic techniques have not been widely used to corroborate our knowledge of species/sub-species level categorization based on structural parameters for the amphistomes (Sanabria *et al*., 2011). Sequence analysis of the nuclear multi-copy ribosomal DNA genes encoding for ribosomal structural RNAs has frequently been used in evolutionary research and the identification of trematodes since rDNA is mostly consistent with greater variability in sections (Ma *et al*., 2015). An investigation's findings are consistent with the idea that ITS-2+ is a useful genetic identifier for differentiating paramphistome species and may be utilised to categorise samples according to taxonomic groups Paramphistomatidae. It might be used to create molecular clinical techniques to examine the incidence of P. epiclitum in both definitive and intermediate hosts (Jadav *et al*., 2018).

Conclusion:

In conclusion, this review article has provided a comprehensive overview of Paramphistomum cervi, an important parasitic trematode that affects numerous ruminant species worldwide. Through the examination of available literature, we have explored various aspects of P. cervi, including its global prevalence, morphological characteristics, molecular characterization, and treatment options. The worldwide prevalence of P. cervi indicates that it is a significant parasite of concern in many countries, particularly those with extensive livestock farming. Its ability to infect a wide range of ruminant hosts highlights the need for effective control measures to minimize its impact on animal health and productivity. The morphological description of P. cervi has provided valuable insights into its structural features, facilitating its identification and differentiation from other related trematodes. This knowledge is crucial for accurate diagnosis and effective management strategies. Furthermore, the molecular characterization of P. cervi has shed light on its genetic diversity, population structure, and phylogenetic relationships. Such information is essential for understanding the parasite's evolutionary history and transmission dynamics, aiding in the development of targeted control measures.

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