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Review Article

Neonatal Calf Diarrhea: Current Knowledge and Epidemiological Insights from Morocco

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Abstract

Neonatal calf diarrhea is one of the leading causes of morbidity and mortality in young cattle worldwide, resulting in substantial economic losses in veterinary medicine. This review provides a comprehensive synthesis of current knowledge on neonatal calf diarrhea, addressing the main etiological agents, pathophysiological mechanisms, associated risk factors, as well as the diagnostic, therapeutic, and preventive approaches used for its control. Particular attention is given to the epidemiological situation in Morocco through an analysis of national scientific studies conducted since the 1980s. Moroccan studies highlight the predominant role of bovine rotavirus, bovine coronavirus, *Escherichia coli* F5 (K99), and *Cryptosporidium parvum*, as well as the significant contribution of husbandry practices and passive transfer of colostral immunity to the occurrence of diarrhea in calves. Despite recent advances in diagnostic methods, national data remain fragmented, and studies on the molecular characterization of circulating strains are still very limited. Strengthening epidemiological surveillance, molecular characterization of circulating strains, and integrated control measures combining biosecurity, vaccination, and improved colostral immunity transfer appear essential to achieve sustainable control of this disease in Morocco.

Keywords: Neonatal Calf Diarrhea; Bovine Rotavirus A; Bovine Coronavirus; *Escherichia coli* K99; Enteric Infections; Epidemiology; Cattle Farming; Morocco

Introduction

Cattle farming plays a strategic role in global food security by making a significant contribution to the production of milk, meat, and animal protein. It also represents an essential source of income for many agricultural enterprises and plays a key role in the socio-economic development of rural areas, particularly in developing countries [1,2].

Despite considerable advances in herd management, nutrition, and animal health, neonatal diseases continue to represent a major constraint to the productivity of cattle herds. The first weeks of life constitute a particularly critical period for calves, during which their survival, growth, and future productive performance may be severely compromised by a variety of health disorders [3].

Beyond its direct effects on calf survival, neonatal calf diarrhea imposes a considerable economic burden on cattle production systems worldwide. Economic losses result not only from calf mortality but also from reduced average daily weight gain, delayed age at first calving, impaired future milk production, increased veterinary interventions, antimicrobial treatments, labor requirements, and replacement costs. In addition, recurrent outbreaks may compromise overall herd productivity through increased disease management expenses and reduced production efficiency. Recent studies estimate that neonatal calf diarrhea remains one of the most costly diseases affecting dairy and beef calves, emphasizing that investments in preventive measures, including colostrum management, vaccination, biosecurity, and early diagnosis, are substantially more cost-effective than treating clinical disease [3-6].

In Morocco, several studies have reported neonatal diarrhea as a major cause of pre-weaning mortality, highlighting the significant impact of this disease on the national cattle industry [7-9].

Beyond its impact on animal health and productivity, neonatal calf diarrhea also raises growing public health concerns, particularly in the context of antimicrobial use and the emergence of antibiotic-resistant bacteria [10], as well as the zoonotic potential exhibited or potentially acquired by some of the etiological agents involved in this disease [11,12].

In this context, a better understanding of neonatal calf diarrhea is essential to improve its prevention and control. This review aims to provide a comprehensive overview of neonatal calf diarrhea while critically reviewing the epidemiological situation in Morocco. By compiling and analyzing the available national evidence in light of current international knowledge, this review seeks to identify existing knowledge gaps, emphasize the limitations of the currently available Moroccan data, and highlight priorities for future epidemiological and molecular research in Morocco.

Etiology of neonatal calf diarrhea

Neonatal calf diarrhea is a multifactorial disease involving several infectious agents, mainly belonging to bacterial, viral, and parasitic species. The diversity of the agents involved, together with the frequent occurrence of co-infections, contributes to the clinical and epidemiological variability observed in the field and accounts for the complexity of disease control.

Bacterial agents

Among the bacterial agents involved, *Escherichia coli* is one of the principal causes of neonatal diarrhea, particularly during the first days of life. Certain pathogenic strains, especially enterotoxigenic *E. coli* (ETEC) expressing the F5 (K99) adhesin, are the strains most frequently associated with neonatal disease in calves [13]. Other pathotypes, particularly Shiga toxin-producing *E. coli* (STEC) and enteropathogenic *E. coli* (EPEC), have also been described in cattle, although their involvement in neonatal diarrhea remains less clearly established [14].

Bacteria belonging to the genus *Salmonella*, mainly *Salmonella Typhimurium* and *Salmonella Dublin*, are responsible for enteritis that may be severe in young calves and can progress to systemic forms associated with high mortality [15]. Infected cattle, including asymptomatic carriers, contribute to the dissemination of the infection within the farm environment. Owing to their zoonotic nature, *Salmonella* spp. also represent a major public health concern [16].

Other bacteria, such as *Clostridium perfringens*, *Clostridium difficile*, and *Campylobacter jejuni*, may occasionally be involved in neonatal calf diarrhea, although their role generally remains secondary compared with *E. coli* and *Salmonella* spp. [13,17,18].

Parasitic agents

Protozoa also represent major etiological agents of neonatal diarrhea in calves, with *Cryptosporidium parvum* being considered one of the principal enteric parasites involved worldwide.

Its resistance in the environment and its fecal–oral mode of transmission favor its persistence in cattle farms [19,20].

Other protozoa, such as *Eimeria* spp., mainly *E. bovis* and *E. zuernii*, as well as *Giardia intestinalis*, may also be associated with digestive disorders in young calves [21,22]. Certain nematodes, particularly *Strongyloides papillosus*, are also involved, although more occasionally [20].

Viral agents

For many years, infectious diarrhea in infants and animals was attributed exclusively to bacteria and protozoa until the development of electron microscopy and molecular biology techniques [23]. In 1969, the first evidence of the involvement of a virus in neonatal calf diarrhea was reported following the observation of "reovirus-like" particles in the feces of diarrheic calves. This agent was subsequently identified as a rotavirus. A few years later, its role in severe diarrhea in young children was also demonstrated [24,25]. Subsequently, bovine coronaviruses were also recognized as major etiological agents of neonatal calf diarrhea, either alone or in association with rotaviruses [26].

Bovine rotaviruses, mainly Rotavirus A (RVA), are now recognized as among the principal viral agents responsible for neonatal diarrhea worldwide [27,28]. Their segmented genome promotes genetic reassortment events, contributing to the considerable diversity of circulating strains [29]. Molecular classification is based mainly on the VP4 and VP7 proteins, which are widely used in epidemiological and phylogenetic studies [30].

Bovine coronavirus (BCoV), belonging to the genus *Betacoronavirus*, also constitutes a major etiological agent of neonatal calf diarrhea [31]. The Spike protein, particularly the S1 subunit, plays an essential role in viral attachment and exhibits substantial genetic variability associated with mutation and recombination events [31].

Other enteric viruses, including bovine noroviruses, neboviruses, astroviruses, kobuviruses, toroviruses, and bovine enteroviruses, have also been detected in diarrheic calves [32]. In addition, rotaviruses belonging to groups B (RVB) and C (RVC), although reported much less frequently than group A rotaviruses, have been identified in several countries and have occasionally been associated with cases of neonatal diarrhea or mixed infections in calves [33-35]. However, the pathogenic role and epidemiological importance of all these emerging enteric viruses remain insufficiently characterized compared with those of Rotavirus A and bovine coronavirus [36-38].

Risk factors and modes of transmission

Neonatal calf diarrhea results from complex interactions between the host, the pathogen, and the environment. During the first weeks of life, calves are particularly vulnerable because of the immaturity of their immune system. In this context, the transfer of passive immunity through colostrum constitutes a key protective factor. The quality, quantity, and timeliness of colostrum intake directly influence the immune status of the newborn, whereas failure of passive transfer significantly increases the risk of infection and mortality [4,39]. Maternal immune status, particularly the vaccination of pregnant cows, also contributes to enhancing calf protection through the transfer of specific antibodies in the colostrum [40].

Transmission of the principal etiological agents occurs mainly through the fecal–oral route, either from infected animals or from a contaminated environment. Infectious pressure is favored by inadequate hygiene, high animal density, the mixing of calves of different ages, and poor calving management. In addition, unfavorable climatic conditions, particularly cold and humidity, may increase calf susceptibility by compromising their vitality and early colostrum intake [41]. Thus, the occurrence of neonatal calf diarrhea results from a multifactorial imbalance involving host susceptibility, infectious pressure, and herd management practices. The principal risk factors involved are summarized in Figure 1.

One health perspective

Although neonatal calf diarrhea is primarily recognized as one of the leading causes of morbidity, mortality, and economic losses in cattle production, its impact extends beyond livestock health. Several enteropathogens involved in this syndrome possess recognized or suspected zoonotic potential and may circulate at the animal–human–environment interface, making neonatal calf diarrhea an important One Health concern. Consequently, effective prevention and control require an integrated approach involving veterinary medicine, public health, food safety, and environmental surveillance.

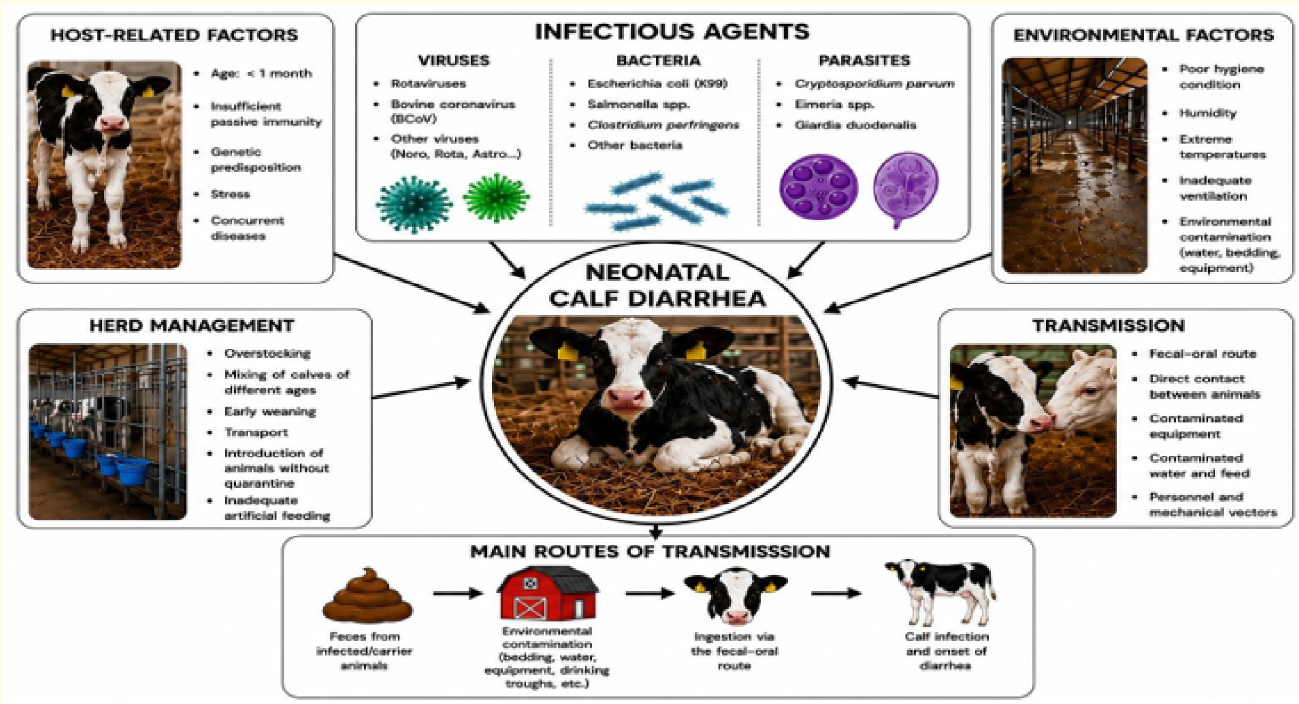

Figure 1: Multifactorial determinants of neonatal calf diarrhea, showing the interactions among host susceptibility, infectious agents, environmental conditions, herd management, and the main routes of pathogen transmission.

Among the pathogens associated with neonatal calf diarrhea, *Cryptosporidium parvum*, pathogenic *Escherichia coli*, and *Salmonella* spp. are well-recognized zoonotic agents, whereas bovine rotavirus is increasingly considered from a One Health perspective because of accumulating evidence of interspecies transmission and genetic reassortment. Infected calves may serve as important reservoirs and shed large numbers of pathogens through feces, contributing to contamination of the farm environment and facilitating transmission to other animals and humans [4,39,42].

Environmental contamination represents one of the major pathways involved in pathogen dissemination. Fecal shedding by infected calves may contaminate bedding, manure, drinking water, soil, feeding equipment, and surrounding farm environments. Under inadequate hygienic conditions, these pathogens may persist for prolonged periods, increasing the risk of indirect transmission between animals and creating opportunities for human exposure through direct contact with infected calves, contaminated materials, food products, or water sources [4,42].

Farm workers, veterinarians, and individuals in close contact with livestock are particularly exposed, while young children, elderly people, and immunocompromised individuals represent the most vulnerable populations [42].

From a public health perspective, *Cryptosporidium parvum* remains one of the most important zoonotic enteric parasites responsible for waterborne outbreaks of diarrheal disease. Likewise, pathogenic *Escherichia coli*, particularly Shiga toxin-producing strains (STEC), and *Salmonella* spp. are recognized causes of foodborne and occupational infections worldwide. Although bovine rotavirus primarily infects cattle, molecular studies have demonstrated that interspecies transmission and genomic reassortment between animal and human rotaviruses may occur, highlighting the importance of continuous molecular surveillance within a One Health framework.

Considering these interconnected risks, the control of neonatal calf diarrhea should extend beyond conventional herd management practices. In addition to improving colostrum management, hygiene, vaccination, and biosecurity, surveillance strategies should integrate molecular epidemiology, antimicrobial stewardship, environmental monitoring, and collaboration between veterinary and public health authorities. Such an integrated One Health approach would contribute not only to reducing disease burden in calves but also to limiting environmental dissemination of enteric pathogens and minimizing potential zoonotic transmission.

Pathogenesis of neonatal calf diarrhea

Neonatal calf diarrhea results from several pathophysiological mechanisms leading primarily to intestinal malabsorption, hydroelectrolytic hypersecretion, and inflammation of the intestinal mucosa. These alterations result in substantial fluid and electrolyte losses, leading to dehydration and, in some cases, severe metabolic disturbances.

Viral infections, particularly those caused by bovine rotavirus and bovine coronavirus, induce destruction of the enterocytes of the small intestine, resulting in villous atrophy and a reduced intestinal absorptive capacity. Bovine coronavirus may also affect the colon, thereby aggravating malabsorption and causing tenesmus and difficulty in defecation in young calves [43,44].

Certain strains of *Escherichia coli* induce intestinal hypersecretion through the production of enterotoxins that disrupt ionic exchanges and promote the secretion of water and electrolytes into the intestinal lumen [45]. Infections caused by *Salmonella* spp. are more commonly associated with inflammation and increased intestinal mucosal permeability, which may progress to severe systemic disease [46]. In addition, *Cryptosporidium parvum* impairs digestive function through its intracellular development within enterocytes, resulting in persistent watery diarrhea [41].

Overall, the pathogenesis of neonatal calf diarrhea is based on the interaction of mechanisms of malabsorption, hypersecretion, and intestinal inflammation, which may coexist during mixed infections and explain the variability in the clinical severity observed. The main pathophysiological events leading to hydroelectrolytic disturbances are summarized in Figure 2.

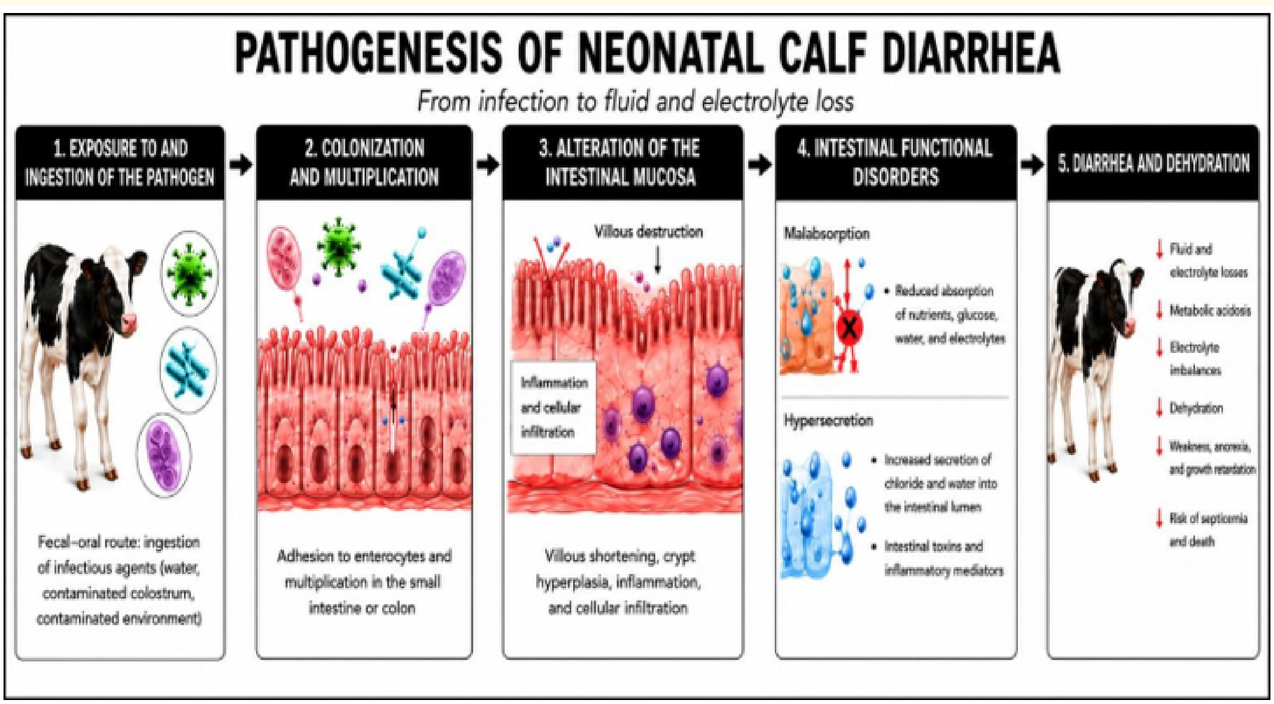

Figure 2: Schematic representation of the pathogenesis of neonatal calf diarrhea, from pathogen exposure and intestinal colonization to epithelial damage, diarrhea, dehydration, and electrolyte imbalance.

Clinical and metabolic consequences

Neonatal calf diarrhea is mainly characterized by the passage of liquid to semi-liquid feces, sometimes associated with mucus or blood, accompanied by depression, anorexia, a reduced suckling reflex, and a progressive deterioration of the general condition [4,39]. The clinical presentation varies according to the etiological agent involved, the age of the calf, and the severity of fluid and electrolyte losses.

The principal enteric agents responsible for neonatal calf diarrhea exhibit variable clinical manifestations, which are sometimes non-specific and frequently associated with mixed infections. The main clinical characteristics reported in the literature are presented in Table 1.

Etiological agent	Main clinical manifestations	References
Escherichia coli	Severe watery diarrhea, rapid dehydration, weakness, occasionally septicemia	[41,47]
Rotavirus	Profuse watery diarrhea, anorexia, dehydration, electrolyte imbalances	[48]
Bovine coronavirus	Severe diarrhea with mucus or blood, dehydration, depression, occasionally respiratory signs	[20,44]
Salmonella spp.	Inflammatory diarrhea, sometimes hemorrhagic, hyperthermia, depression	[20,49]
Clostridium perfringens	Acute hemorrhagic enteritis, abdominal pain, rapid progression	[13]
Campylobacter jejuni	Gastroenteritis and deterioration of the general condition	[18]
Eimeria spp.	Watery or hemorrhagic diarrhea, weight loss, growth retardation	[20,50]
Cryptosporidium parvum	Profuse diarrhea, dehydration, growth retardation	[51]
Giardia intestinalis	Moderate chronic diarrhea	[20]
Strongyloides papillosus	Hemorrhagic enteritis, anemia, dehydration	[20]

Table 1: Summary of the main clinical manifestations associated with the infectious agents involved in neonatal calf diarrhea.

The fluid and electrolyte losses induced by diarrhea lead to dehydration, often associated with hypovolemia and reduced tissue perfusion [52]. These disturbances promote the development of metabolic acidosis, resulting mainly from intestinal bicarbonate losses, lactate accumulation associated with tissue hypoperfusion, and the absorption of organic acids produced in the intestine [53,54]. In severe cases, calves may exhibit generalized weakness, neurological disorders, difficulty standing, and recumbency.

Neonatal calf diarrhea is also frequently accompanied by hypoglycemia and azotemia secondary to reduced feed intake, disturbances of energy metabolism, and renal hypoperfusion [55,56]. Beyond its clinical consequences, neonatal calf diarrhea represents a major cause of economic losses in cattle farming due to increased mortality, growth retardation, reduced zootechnical performance, and the costs associated with treatment and preventive measures [4,39].

Diagnosis of neonatal calf diarrhea

The diagnosis of neonatal calf diarrhea is based on an integrated approach combining clinical observations and laboratory investigations. Owing to the diversity of the etiological agents involved and the frequent occurrence of mixed infections, laboratory analyses remain essential to confirm the etiology and guide therapeutic management [20].

The clinical signs observed are generally non-specific and include diarrhea of variable consistency, dehydration, generalized weakness, anorexia, and a reduced suckling reflex. Severe cases may progress to shock or septicemia [20,57].

The diagnosis of bacterial infections is based mainly on fecal culture, the identification of virulence factors, and molecular techniques such as PCR. In *Escherichia coli*, the detection of the F5 (K99), F41, and F17 adhesins allows the characterization of enterotoxigenic strains associated with neonatal diarrhea [20]. *Salmonella* spp. infections are generally confirmed by bacterial culture and PCR [20,57], whereas infections caused by *Clostridium perfringens* are diagnosed by anaerobic culture combined with toxin detection using immunological (ELISA) or molecular (PCR) techniques [20].

For viral infections, particularly those caused by bovine rotavirus and bovine coronavirus, several diagnostic methods are used, including Ag-ELISA, virus isolation, conventional PCR, and RT-qPCR. The latter is currently considered the reference method because of its high sensitivity and its ability to detect and characterize circulating viral strains.

The diagnosis of parasitic infections is based mainly on coproscopic examinations for the detection of *Cryptosporidium parvum* oocysts and coccidial oocysts in fecal samples [20].

In addition, rapid immunochromatographic tests are now widely used in the field for the simultaneous detection of several enteric pathogens, particularly group A rotaviruses, bovine coronaviruses, *Cryptosporidium parvum*, and *Escherichia coli* F5 (K99). Easy to perform and providing results within a few minutes, these tests constitute particularly useful screening tools for cattle farms. However, their diagnostic performance remains variable depending on the target pathogens and the conditions of use, which may require confirmation by more sensitive laboratory methods such as PCR or ELISA [4].

Despite advances in diagnostic methods, several limitations remain, including mixed infections, the high cost of molecular techniques, and variable access to specialized laboratories. Furthermore, the detection of a pathogen does not always allow its involvement in the clinical expression of the disease to be established with certainty [20].

The diagnosis of neonatal calf diarrhea requires the integration of clinical examination with appropriate laboratory investigations to identify the etiological agent(s) involved. Because each diagnostic technique presents specific advantages and limitations in terms of analytical performance, cost, turnaround time, and field applicability, the choice of method should be guided by the clinical context, available laboratory facilities, and the objectives of the investigation. A summary of the principal diagnostic methods currently used in neonatal calf diarrhea is presented in Table 2 [4,41,58].

Sensitivity and specificity are expressed qualitatively because diagnostic performance varies according to the pathogen investigated, sample quality, stage of infection, and laboratory protocol. Molecular methods, particularly real-time PCR and sequencing, currently provide the highest analytical performance and are increasingly used for epidemiological surveillance and molecular characterization of enteric pathogens [4,41,58].

Treatment of neonatal calf diarrhea

The therapeutic management of neonatal calf diarrhea is based primarily on the correction of dehydration, electrolyte imbalances, and metabolic acidosis. Rehydration therefore constitutes the cornerstone of treatment, whether administered orally or intravenously depending on the severity of the clinical presentation [20,58].

Oral electrolyte solutions are used primarily in calves presenting with mild to moderate dehydration and retaining a functional suckling reflex. They restore fluid and electrolyte balance, correct metabolic acidosis, and provide an energy supply through the presence of glucose and alkalinizing agents such as bicarbonate, acetate, or citrate [41,58,59]. Whereas temporary withdrawal of milk feeding was previously recommended for diarrheic calves [15], current knowledge supports maintaining milk feeding in addition to rehydration in order to prevent energy deficiency and promote repair of the intestinal mucosa [41,59,58].

In severely affected calves presenting with marked metabolic acidosis, shock, or prolonged recumbency, intravenous fluid therapy is required to rapidly restore tissue perfusion and correct metabolic disturbances [60,61]. Several intravenous solutions may be used, including isotonic sodium chloride, sodium bicarbonate, and lactated or acetate Ringer's solutions [61].

Adjunctive treatments may also be administered to improve animal comfort and promote recovery. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as meloxicam and flunixin meglumine, help reduce pain, intestinal inflammation, and the systemic effects associated with endotoxemia [58].

Antimicrobial therapy should be used judiciously and primarily when bacterial infections associated with septicemia, hyperthermia, or severe deterioration of the general condition are suspected or confirmed [58]. The main classes of antibiotics used include sulfonamides, beta-lactams, tetracyclines, fluoroquinolones, aminoglycosides, and colistin. However, the emergence and spread of antimicrobial-resistant bacteria constitute a major challenge for both animal and public health, highlighting the need for prudent antibiotic use, ideally based on the results of antimicrobial susceptibility testing [62].

Antimicrobial resistance and stewardship

Although antimicrobial therapy plays an important role in calves presenting with systemic illness or suspected septicemia, its widespread and sometimes inappropriate use has contributed to the emergence of antimicrobial resistance (AMR), which has become a major challenge for both veterinary and public health. Consequently, AMR is now recognized as a One Health concern because resistant bacteria and antimicrobial resistance genes can circulate among animals, humans, and the environment [63,64].

Among the bacterial pathogens associated with neonatal calf diarrhea, pathogenic Escherichia coli and *Salmonella enterica* have received particular attention because of their increasing resistance to multiple antimicrobial classes. Numerous studies have reported resistance to β-lactams, tetracyclines, sulfonamides, aminoglycosides, fluoroquinolones, and polymyxins, with multidrug-resistant (MDR) isolates becoming increasingly common in dairy calves. Long-term surveillance studies have shown that resistance to tetracyclines and sulfonamide–trimethoprim combinations remains particularly widespread among enteropathogenic *E. coli*, while antimicrobial-treated calves harbor significantly higher levels of resistance than untreated animals, indicating that antimicrobial exposure promotes the selection of resistant strains [65]. In addition, systematic reviews have identified preweaned calves as important reservoirs of antimicrobial-resistant *E. coli* and *Salmonella*, highlighting their role in the persistence and dissemination of resistance genes within dairy farms [66].

The emergence and spread of AMR are influenced not only by antimicrobial use but also by management practices. Frequent treatments, feeding waste or non-saleable milk containing antimicrobial residues, inadequate hygiene, and environmental contamination all favor the maintenance of resistant bacterial populations. Because the intestinal microbiota of young calves is still developing, resistant bacteria can establish and persist more readily in the gastrointestinal tract. Consistent with these observations, recent epidemiological studies have shown that farms with higher antimicrobial use are more likely to harbor MDR *E. coli*, whereas improved bedding management and husbandry practices are associated with lower resistance rates [63,67].

These findings emphasize the importance of antimicrobial stewardship in calf production. Current recommendations advocate restricting antimicrobial therapy to calves with systemic signs of bacterial infection rather than uncomplicated diarrhea, for which supportive care remains the cornerstone of treatment. Whenever possible, antimicrobial selection should be guided by bacterial culture and antimicrobial susceptibility testing to optimize therapeutic efficacy and ensure appropriate treatment. Likewise, preventive measures, including adequate colostrum management, improved hygiene, biosecurity, appropriate nutrition, and vaccination, remain the most effective strategies for reducing disease incidence and the need for antimicrobial use at the herd level [63,64].

Furthermore, despite the frequent use of antimicrobials in diarrheic calves, evidence supporting their routine administration remains limited. A recent systematic review concluded that available clinical studies are highly heterogeneous and provide insufficient evidence of clear therapeutic benefits in uncomplicated neonatal calf diarrhea, further supporting the recommendation to reserve antimicrobial treatment for clinically justified cases [64].

Overall, the prudent use of antimicrobials, continuous surveillance of resistance patterns, evidence-based therapeutic decisions and preventive herd health measures are essential to preserve the efficacy of antimicrobials while limiting the dissemination of resistant bacteria across the interface between animals, humans and the environment. Therefore, the successful management of neonatal calf diarrhoea primarily relies on the early correction of dehydration and metabolic disturbances. Antimicrobial therapy should only be used in clinically justified situations within an integrated antimicrobial stewardship framework.

Prevention of neonatal calf diarrhea

The prevention of neonatal calf diarrhea is based on an integrated approach combining hygiene measures, biosecurity, herd management, and the enhancement of passive immunity in newborn calves. Its objective is to reduce infectious pressure and limit the transmission of the principal enteric pathogens [20].

The management of the farm environment constitutes an essential component of disease prevention. Housing calves in individual pens during the first weeks of life, the rapid isolation of sick animals, and rigorous management of calving areas all contribute to limiting environmental contamination. Likewise, adequate ventilation, together with regular cleaning and disinfection of housing facilities and farm equipment, significantly reduces the environmental infectious load [20].

The health management of pregnant cows also plays a major role in disease prevention. A balanced diet, appropriate dry-period management, and the implementation of hygienic measures at calving contribute to reducing the risk of neonatal infection. Maternal vaccination represents another major preventive strategy and is discussed in greater detail below.

In newborn calves, the early administration of a sufficient quantity of high-quality colostrum constitutes the most important preventive measure. Umbilical disinfection, the reduction of stress factors, and the maintenance of appropriate husbandry conditions, particularly with regard to hygiene, temperature, and ventilation, also contribute to the prevention of enteric infections. In certain high-risk situations, prophylactic treatments targeting parasitic infections may also be considered [20].

Maternal vaccination strategies

Maternal vaccination, combined with adequate colostrum management, hygiene, and biosecurity, is one of the most effective strategies for preventing neonatal calf diarrhea. Commercial vaccines are generally multivalent formulations targeting the major enteropathogens, particularly bovine rotavirus A (RVA), bovine coronavirus (BCoV), and enterotoxigenic *Escherichia coli* F5 (K99). Administered during late gestation, they stimulate the production of pathogen-specific antibodies that are transferred to calves through colostrum, providing passive protection during the first weeks of life. Vaccines such as Rotavec® Corona, ScourGuard®, Bovigen™ Scour, Fencovis®, and Lactovac® are widely used, although their composition varies according to national regulations [68,69].

Maternal vaccination has been shown to increase colostral antibody concentrations, enhance passive immunity, and reduce pathogen shedding and disease severity. However, its impact on diarrhea incidence and calf mortality remains variable because of differences in herd management, infectious pressure, vaccine formulations, and circulating pathogens. Consequently, vaccination should be integrated with good colostrum management and biosecurity rather than considered as a standalone preventive measure [68,69].

A major challenge is the genetic diversity of RVA. Since most commercial vaccines are based on a limited number of reference strains, mainly G6P[5], antigenic differences between vaccine and field strains may reduce vaccine effectiveness. Nevertheless, maternally derived antibodies can still provide partial cross protection by reducing disease severity and pathogen shedding [68,69].

In Morocco, Rotavec® Corona is the vaccine most commonly used for maternal immunization against neonatal calf diarrhea. Although it targets the principal enteropathogens historically reported in Moroccan cattle farms [70], recent studies have identified several circulating RVA genotypes, including G6P[5], G6P[14], G10P[5], and G10P[14]. Because data on vaccine coverage and field effectiveness remain limited, continued epidemiological and molecular surveillance is needed to evaluate vaccine performance under local conditions [71,72].

Future vaccines should incorporate broader antigenic diversity, improve mucosal immunity, and provide better protection against pathogens insufficiently covered by current formulations, particularly *Cryptosporidium parvum* and emerging enteric viruses [68].

Epidemiology of neonatal calf diarrhea in Morocco

Although neonatal calf diarrhea has been extensively investigated worldwide, published data from Morocco remain scarce and fragmented. Most of the available information originates from veterinary theses conducted during the 1980s and early 1990s, whereas only a limited number of peer-reviewed epidemiological and molecular studies have been published over the past decade. Therefore, the following section aims not only to summarize the available Moroccan evidence but also to critically assess its strengths and limitations, identify the major knowledge gaps, and highlight the need for updated epidemiological and molecular investigations to better characterize the current situation of neonatal calf diarrhea in Morocco.

Historical data and early investigations

The first Moroccan data on neonatal calf diarrhea originated primarily from several Veterinary Medicine theses conducted at the Hassan II Institute of Agronomy and Veterinary Medicine between 1982 and 1994. These pioneering studies identified the principal agents involved in this disease, notably bovine rotavirus, bovine coronavirus (BCoV), *Escherichia coli* F5 (K99), and *Cryptosporidium parvum*, as well as several risk factors associated with herd management conditions.

Benlamlih [73] was among the first to demonstrate the circulation of rotavirus and coronavirus in Moroccan cattle farms, reporting their prevalences of 26.7% and 18%, respectively, in diarrheic calves. The study also highlighted the importance of mixed infections and the role of poor hygienic conditions in the spread of these pathogens. Chakroune [74] confirmed the predominant role of rotavirus by reporting a prevalence of 39% in diarrheic calves, whereas Jelti [75] showed that *E. coli* F5 (K99) was detected in 30.8% of affected calves compared with only 4.8% of healthy calves.

Subsequently, El Yousfi [76], through the follow-up of 550 calves from several farms, reported an overall diarrhea frequency of 25.6% and a mortality rate reaching 6%. This study confirmed the involvement of rotavirus, detected in 50% of diarrheic calves, as well as *E. coli* K99 and *Cryptosporidium* spp. In the same year, Benani [9] showed that the most severe clinical forms were generally associated with mixed infections and unfavorable herd management conditions. Finally, Kichou [77] confirmed the importance of *E. coli* K99, reporting an isolation rate of 29.1% in diarrheic calves, and documented a high frequency of multidrug resistance among the isolated strains.

Taken together, these studies established the foundations of current knowledge on neonatal calf diarrhea in Morocco. They highlighted the major role of bovine rotavirus, bovine coronavirus, *Escherichia coli* F5 (K99), and *Cryptosporidium parvum*, while emphasizing the importance of young calf age, hygienic conditions, and herd management practices in the occurrence of this disease [78]. These initial observations were subsequently consolidated and updated by studies published in scientific journals, providing more recent data on the distribution of enteropathogenic agents and the associated risk factors in Moroccan cattle farms.

Published epidemiological studies on neonatal calf diarrhea in Morocco

Among the first published studies on neonatal diarrhea in ruminants in Morocco, Fassi Fihri., *et al*. [8] conducted an epidemiological survey in the Rabat–Kénitra, Marrakech, and Agadir regions to evaluate the involvement of rotavirus and *Escherichia coli* F5 (K99) in calves aged 1 to 25 days. The authors reported infection rates of 29.7% for rotavirus and 26.9% for *E. coli* F5 (K99), confirming the major role of these two agents in the etiology of neonatal calf diarrhea. The study also showed that approximately 35% of diarrhea cases could not be attributed to the investigated pathogens, suggesting the involvement of other enteric pathogens. Finally, the authors emphasized the importance of monitoring antimicrobial resistance among *E. coli* strains circulating in cattle farms.

Nearly thirty years later, Zouagui., *et al*. [40] updated the epidemiological data through a survey based on immunochromatographic tests conducted in 78 cattle farms involving 1,932 calves younger than two months of age. The overall prevalence of neonatal calf diarrhea was 10%, with variations among the regions studied. Rotavirus was the most frequently detected pathogen (37.2%), followed by bovine coronavirus (25%) and *E. coli* F5 (21.9%). The authors also highlighted the importance of mixed infections and the impact of herd management conditions, particularly the inadequate hygiene observed in a large proportion of the farms.

Overall, the epidemiological studies published in veterinary medicine confirm the predominant role of bovine rotavirus among the agents responsible for neonatal calf diarrhea in Morocco. They also emphasize the role of bovine coronavirus and *Escherichia coli* F5 (K99), as well as the importance of colostral immunity transfer, mixed infections, and herd management practices in the occurrence and severity of diarrheic episodes.

Molecular characterization of bovine rotavirus in Morocco

Beyond epidemiological investigations, several recent studies have focused on the genetic diversity of bovine rotavirus A circulating in Morocco. These studies have provided the first molecular data on the genotypes present in Moroccan cattle farms and have contributed to a better understanding of the dynamics of viral circulation.

Ennima., *et al.* [71] reported the circulation of the G6P[5] and G10P[14] genotypes in different Moroccan dairy farms. These findings constituted the first molecular characterization data on bovine rotavirus A in Morocco and confirmed the presence of genotypes that are widely distributed in cattle populations worldwide.

Subsequently, Alaoui Amine., *et al.* [72] demonstrated additional genetic diversity by identifying the G6P[14], G10P[14], and G10P[5] genotypes in cattle and goats raised under extensive and nomadic production systems. The results also suggest the occurrence of interspecies viral exchanges and highlight a risk of zoonotic transmission, as well as the potential emergence of new genotypes in regions where close contact exists between humans and animals. This risk was further supported by an experimental study showing that a rotavirus strain isolated from an 18-month-old child hospitalized with severe diarrhea was able to induce similar clinical signs in an experimentally inoculated ewe. This study also represents the first complete genomic analysis of Rotavirus A strains originating from nomadic livestock systems in Morocco. To date, the G6P[5], G6P[14], G10P[5], and G10P[14] genotypes represent the main Rotavirus A strains identified in Morocco. However, the limited number of available studies does not yet allow a comprehensive assessment of the virus's genetic diversity at the national level. These findings highlight the need to strengthen molecular surveillance to better understand the evolution of circulating strains and assess their compatibility with vaccination strategies implemented in cattle farms.

Overall, the studies conducted in Morocco highlight the predominant role of Rotavirus A in neonatal calf diarrhea, often in association with bovine coronavirus, *Escherichia coli* F5 (K99), and *Cryptosporidium parvum*. They also emphasize the importance of factors related to the animal, colostral immunity, and herd management practices in the expression of the disease. Although molecular data remain limited, they reveal a considerable genetic diversity among circulating strains and suggest the occurrence of interspecies viral exchanges that may favor the emergence of new variants, thereby highlighting the value of an integrated One Health approach for the surveillance of bovine rotavirus in Morocco.

In conclusion, the evolution of knowledge on neonatal calf diarrhea in Morocco reflects the gradual transition from the first epidemiological investigations conducted during the 1980s to more recent molecular characterization approaches. The main milestones of this evolution are summarized in Figure 3.

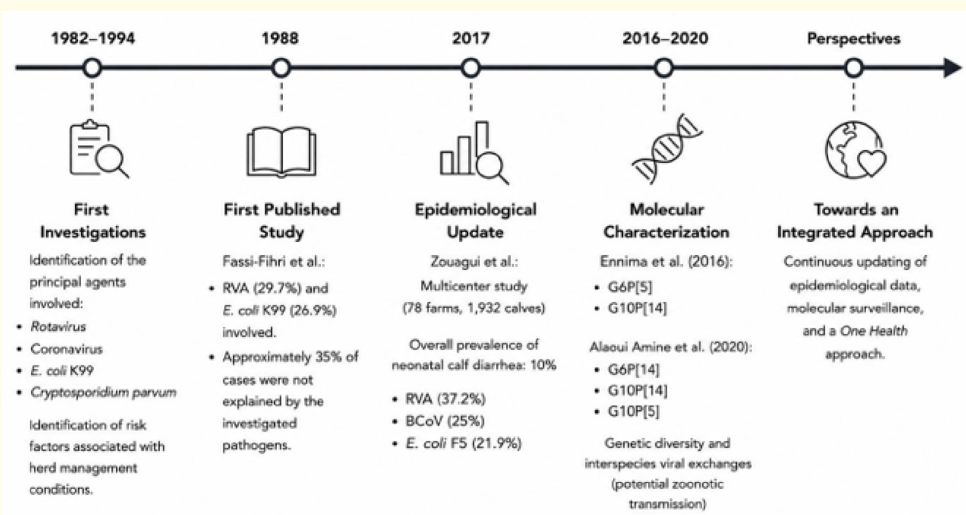

Figure 3: Timeline illustrating the evolution of knowledge on neonatal calf diarrhea in Morocco.

The Moroccan epidemiological situation in the context of current international knowledge

To better interpret the available Moroccan data, it is essential to place them in the context of current international knowledge. Although neonatal calf diarrhea has been extensively investigated worldwide, epidemiological information from Morocco remains relatively scarce and fragmented. Nevertheless, the available evidence indicates that the epidemiological profile observed in Moroccan cattle farms shares many similarities with that reported in other regions of the world.

The predominance of bovine rotavirus A, bovine coronavirus (BCoV), *Escherichia coli* F5 (K99), and *Cryptosporidium parvum* in Morocco is consistent with findings reported in Europe, Asia, Africa, and Latin America, confirming the cosmopolitan distribution of these major enteropathogens. Likewise, the principal risk factors identified in Moroccan studies including young calf age, inadequate passive transfer, poor hygiene, overcrowding, and suboptimal herd management practices resemble those described internationally [4,79,80].

Despite these similarities, important differences remain regarding surveillance strategies and diagnostic capacities. In countries with well-established surveillance programs, molecular approaches such as multiplex RT-PCR, sequencing, and phylogenetic analyses are routinely used to detect, characterize, and monitor circulating enteropathogens. In contrast, the available Moroccan data are still derived predominantly from isolated cross-sectional studies using conventional diagnostic methods, limiting our understanding of the genetic diversity, evolution, and epidemiological dynamics of circulating pathogens.

Furthermore, while international research is increasingly adopting a One Health perspective integrating animal, human, and environmental health, this approach remains insufficiently explored in Morocco despite the recognized zoonotic potential of several enteric pathogens. Strengthening nationwide epidemiological surveillance, expanding molecular characterization of circulating strains, and promoting multidisciplinary One Health research should therefore constitute key priorities for improving the understanding and control of neonatal calf diarrhea in Morocco.

Current knowledge gaps and future perspectives

Studies conducted in Morocco have considerably improved the understanding of neonatal calf diarrhea by confirming the major role of bovine rotavirus, bovine coronavirus, *Escherichia coli* F5 (K99), and *Cryptosporidium parvum*, as well as the importance of mixed infections and herd management-related factors. Nevertheless, several knowledge gaps remain and still limit a comprehensive understanding of the epidemiology of this disease at the national level.

The available data are based mainly on cross-sectional studies conducted in specific regions of the country, without a structured national surveillance program. The development of multicenter studies covering the main cattle-producing regions would provide more representative data on the prevalence, geographical distribution, and associated risk factors of neonatal calf diarrhea.

The heterogeneity of the diagnostic approaches used across different studies also constitutes an obstacle to the comparison of results. The adoption of harmonized methods and the use of modern molecular tools, such as multiplex RT-PCR, high-throughput sequencing, and phylogenetic analyses, would contribute to improving detection and characterization of circulating pathogens.

Knowledge regarding the genetic diversity of enteropathogenic agents remains limited, particularly for bovine coronavirus and *Escherichia coli* involved in neonatal calf diarrhea. Although several Rotavirus A genotypes have been identified in Morocco, data on the genetic variability of BCoV, recombination events, and the emergence of new variants remain insufficient. Likewise, information on the molecular characterization of pathogenic *E. coli* strains, particularly regarding the distribution of virulence factors, adhesive fimbriae, and antimicrobial resistance profiles, remains fragmentary. Strengthening molecular surveillance therefore appears essential for monitoring the evolution of circulating strains, improving our understanding of their pathogenic potential, and evaluating the effectiveness of vaccination strategies and control measures implemented in cattle farms.

Furthermore, several emerging enteric pathogens described in other countries, including bovine noroviruses, neboviruses, astroviruses, kobuviruses, and bovine toroviruses, remain unexplored in the Moroccan context [32,81]. More broadly, the epidemiological importance of several bacterial, viral, and parasitic enteropathogens commonly reported in neonatal calf diarrhea worldwide remains unknown in Morocco owing to the absence of dedicated epidemiological investigations. Similarly, no studies have investigated group B and group C rotaviruses in cattle in Morocco. Although these viruses, while only rarely detected, have been associated with episodes of diarrhea in cattle in several regions of the world [35,82], no data are available on their circulation, genetic diversity, or contribution to enteric disease in calves in Morocco. In addition, further investigations are needed to better characterize mixed infections, antimicrobial resistance patterns, and the zoonotic potential of certain enteric pathogens.

Finally, increasing evidence of interspecies viral transmission and the zoonotic potential of certain enteric pathogens highlights the importance of adopting an integrated One Health approach. The development of collaborations involving animal health, human health, and environmental surveillance could contribute to a better understanding of transmission dynamics.

Conclusion

At the same time, strengthening molecular investigations appears essential to better characterize the genetic diversity of circulating strains, detect the possible emergence of new variants, and improve the understanding of transmission dynamics. Such data are also essential for evaluating the suitability of the vaccination strategies currently in use and guiding the development of more effective preventive measures.

Finally, considering the zoonotic potential of certain enteric pathogens and the close interactions among animals, humans, and the environment, the adoption of an integrated One Health approach should constitute a major component of future research and surveillance programs dedicated to neonatal calf diarrhea in Morocco.

Overall, this review highlights that, despite the major importance of neonatal calf diarrhea for Moroccan cattle industry, the current knowledge remains fragmented and largely based on studies conducted several decades ago. By critically compiling the available national evidence, this review emphasizes the urgent need for updated epidemiological and molecular investigations to better characterize the current situation of neonatal calf diarrhea in Morocco and support evidence-based prevention and control strategies.

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