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Review Article

Epidemiology of Diarrheagenic *Escherichia coli*: A Mini Review

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Abstract: Diarrheal diseases are a significant public health challenge, leading to high numbers of morbidity and mortality globally. Diarrheagenic *Escherichia coli* (DEC) strains exhibit a complex spectrum, ranging from benign gut inhabitants to severe pathogens causing intestinal and extraintestinal diseases. This review focuses on elucidating DEC epidemiology, emphasizing research conducted worldwide. A comprehensive review searched for relevant studies on DEC's impact, using keywords like "diarrheagenic *Escherichia coli*," "DEC pathotypes," and "epidemiology" in databases like PubMed. Inclusion criteria covered 67 studies on virulence, pathogenesis, detection, and geographic diversity. Studies globally indicate variable prevalence rates for DEC. Enteropathogenic *E. coli* is prominent in Bangladesh (17.2% prevalence), relying on intimin, Bundle-forming pilus, and the locus of enterocyte effacement (LEE) pathogenicity island. Enterohemorrhagic *E. coli*, prevalent in the US and Europe (up to 1.5% outbreak rates in the US), utilizes Shiga toxin and the LEE pathogenicity island. Enteroaggregative *E. coli*, notably in Africa (Kenya, 13.5% prevalence), employs multilocus enzyme electrophoresis analysis, Escherichia coli heat-stable enterotoxin 1 (EAST-1), adherence mechanisms, and biofilm formation. Enterotoxigenic *E. coli* is highly prevalent in South Asia and Sub-Saharan Africa (Bangladesh, 6% prevalence), producing colonization factors and enterotoxins. Enteroinvasive *E. coli* is common in Asian developing countries like Bangladesh, relying on invasion genes and a large plasmid. Conversely, Europe exhibits notably low prevalence rates, with Enterohemorrhagic *E. coli* prevalence falling below 1%, especially in the UK. This review underscores the global prevalence of DEC, emphasizing the need for a global approach to disease management. Understanding the distinct virulence factors and pathogenesis of various DEC pathotypes is crucial for developing targeted interventions.

1. Introduction

The genus *Escherichia* is composed of facultative anaerobe, Gram-negative bacteria that are members of the *Enterobacteriaceae* family [1]. This species of the family, *Escherichia coli (E. coli)*, is a widely dispersed facultative anaerobe primarily found in the large intestine of warm-blooded mammals like humans. Certain pathogenic strains of *E. coli* can cause intestinal disorder and many other extraintestinal infections in immunocompromised and even in healthy individuals, however, the majority of these strains colonize in the colon and rarely cause illness in healthy individuals [2]. Diarrheal illnesses are a serious public health concern because they significantly increase morbidity and mortality, especially in newborns and early children. Diarrheal diseases disproportionately impact low- and middle-income nations in Asia, Africa, and Latin America. These countries are generally plagued by poor

environmental conditions, including non-proper water supplies, poor hygiene and sanitation, and restricted access to education. These situations frequently result in catastrophic outcomes [3].

Among the various causes of diarrhea, certain strains of *E. coli* play a crucial role and are implicated as significant etiological agents. These *E. coli* strains have evolved through horizontal gene transfer to acquire specific traits that facilitate their survival within the host, leading to the formation of distinct pathotypes known as diarrheagenic *E. coli* (DEC) [2]. Different host colonization, virulence mechanisms, clinical symptoms, and outcomes are displayed by the DEC pathotypes, which include enterohemorrhagic *(Shiga toxin-producing) E. coli* (EHEC/STEC), enteropathogenic *E. coli* (EPEC), enteroaggregative *E. coli* (EAEC), enteroinvasive *E. coli* (EIEC), and enterotoxigenic *E. coli* (ETEC) [4].

The diversity of the *E. coli* genome makes it difficult to categorize some isolates as belonging to a particular pathotype, even though DEC pathotypes have been classified. This is because some strains exhibit traits from numerous pathotypes, which may make them more virulent

[5]. Furthermore, *diffusely adherent E. Coli* (DAEC), a less well-defined pathotype, distinguished by its ability to adhere to epithelial cells, has been discovered. Given the difficulties in identifying and classifying DAEC, more epidemiological research is necessary to properly comprehend its relevance as a unique pathotype. Furthermore, some *E. coli* strains categorized as adherent invasive *E. coli* (AIEC) have been linked to Crohn's disease, an inflammatory bowel condition with a complex etiology that includes genetic, microbiome, environmental, and enteric pathogens [6].

Diarrheal episodes resulting from infections with DEC represent a significant public health concern in both children and adults in developing nations, primarily due to their impact on the morbidity and mortality rates of children under the age of five [7]. The objective of this review is to compile data regarding the current definitions of the bacteria, serotypes, virulence, mechanisms of virulence, epidemiology, and diagnostic methods pertaining to the principal DEC pathotypes.

2. Pathogenic Strains of *E. coli* that Causes Diarrhea: Enteropthogenic *E. coli*

The EPEC, introduced by Neter *et al.* in 1995 [8], delineates a group of *E. coli* variants initially linked to outbreaks of infantile diarrhea in the mid-20th century. EPEC strains are distinguished by their capacity to induce diarrhea and trigger attaching and effacing (AE) lesions on the epithelial cells of intestine, while notably lacking the synthesis of Shiga toxins or enterotoxins [6]. Based on genetic and pathogenicity characteristics, these strains have been categorized onto two groups: atypical EPEC (aEPEC) and typical EPEC (tEPEC) [9]. The EPEC adherence factor (EAF) plasmid, which codes for the bundle-forming pilus (BFP), is present in tEPEC strains but absent in aEPEC strains. tEPEC strain serotyping yields a variety of traditional serotypes, including O86, O55, O111, O114, O119, O142, and O127, which are frequently associated with particular H antigens. Using allelic variations in housekeeping genes as a basis for multilocus enzyme electrophoresis analysis (MLEE), subtyping of tEPEC strains further divides them into two main groups, known as EPEC1 and EPEC2. Type III secretion system (T3SS) effectors and thorough genomic research reveal that tEPEC strains belong to three main lineages: EPEC1, EPEC2, and EPEC4. These lineages most likely separately acquired the EAF plasmid and the locus of enterocyte effacement (LEE) region [10]. Conversely, aEPEC strains showcase a wider spectrum of serotypic diversity, encompassing both classical and non-classical serotypes, with over 20% of strains being O non-typeable and numerous non-motile and H non-typeable strains [11]. Notably, a considerable proportion of aEPEC strains exhibit genetic similarities with tEPEC strains, hinting at a potential evolutionary link wherein aEPEC may have derived from tEPEC strains losing the EAF plasmid either within the host during infection or in normal time or in the environment [3]

2.1. Virulence Factors, Mechanisms, and Pathogenesis

Subsequent research endeavors have endeavored to delineate this principal pathogenic pathway, which is prevalent in both atypical and conventional strains of EPEC. There are four stages to the interaction between EPEC and host cells [12].

Typical EPEC strains adhere to various cell lines, forming localized adherence (LA) patterns, observed both in vitro and in tissue biopsies. Bundle-forming pilus (BFP) facilitates LA and plays roles in antigenicity, autoaggregation, and biofilm formation. BFP expression requires an operon located on the

pEAF plasmid. EPEC strains form tight auto aggregates and biofilms on abiotic surfaces, crucial for colonization and persistence [13]. The LEE pathogenicity island mediates the intimate adhesion and effacement of intestinal epithelial-cell microvilli in AE lesions, which are crucial for pathogenesis. The *eae* gene encodes intimin, which is necessary for pedestal formation and intimate adhesion. Bacterial pathogenicity is increased by effector genes encoded with non-LEE (Nle) that interfere with host cell functions [14]. Intracellular tEPEC have been observed, indicating diverse infection mechanisms. Typical EPEC strains encode LifA, efa1, and toxB, contributing to adherence and colonization. Some tEPEC strains possess additional fimbriae or pili, aiding adherence and colonization [15]. EspC is one of the autotransporter (AT) proteins that supports cytotoxicity, biofilm development, and adhesion. A three-stage model of tEPEC adhesion and pathogenesis has been proposed [16, 17]

aEPEC lack pEAF and do not generate BFP but exhibit diverse adherence patterns. Intimin subtypes vary among aEPEC strains. Flagella and other adhesins contribute to aEPEC colonization. Some aEPEC strains adhere to abiotic surfaces, with curli and T1P mediating binding. Certain aEPEC strains have the LEE region with a genomic structure resembling that of tEPEC, but with different effector proteins. Nle effectors play diverse roles in host damage and disease causation [18]. Although invasion of epithelial cells is described in some aEPEC strains.

2.2. Epidemiology

While the prevalence of EPEC strains in infectious diarrhea has decreased in the last few decades, especially in developed nations, EPEC strains are a reason for a large number of infantile watery diarrhea cases, which can result in outbreaks and sporadic cases with high rates of morbidity and mortality [19]. Due to variations in age groups, inhabitants, diagnostic techniques, socioeconomic level, and geographic locations, the reported prevalence of EPEC infections varies widely. EPEC is particularly prevalent in developing countries, with Bangladesh having a prevalence rate of approximately 17.2% among children with diarrhea [20]. Over the previous few decades, there has been a shift in the epidemiology of diarrhea caused by EPEC. EPEC strains were long linked to diarrhea in infants under the age of one, particularly in those under six months [21]. More subsequent research, however, has not discovered the same robust correlation. Thirty-eight percent of the EPEC strains in Brazil between 1998 and 1999 were discovered to be unusual, while ninety-two percent were between 2001 and 2002 [22]. In certain developing nations, such as parts of Asia and Africa, typical EPEC strains are still most commonly linked to diarrhea [23]. The oral-fecal route is the route by which EPEC is spread; contaminated surfaces, fluids, and carriers without symptoms are important sources of infection. Symptomatic and asymptomatic humans are the main known reservoirs for common EPEC strains. Animals are rarely used to isolate these strains, however, they are often used to isolate unusual strains. Though there are currently no vaccinations to prevent EPEC infections, a lot of research is being done in this important area [24]. Due to its crucial involvement in pathogenesis, EspB is a major protein that is being examined for the development of an EPEC vaccine. There are three variations of the EspB protein (α, β, and γ), which makes developing a vaccine difficult. The idea is to use a hybrid recombinant protein that combines the three variations as an antigen in vaccinations to boost the production of antibodies. Furthermore, it has been demonstrated that a synthetic peptide that binds to EspB can decrease EPEC adhesion to cells by as much as 40% in vitro. The translocator protein EspA is the focus of further vaccination candidates. These peptide-based tactics might work, but they would not be as useful against strains that are LEE-positive [23].

2.3. Detection and Diagnosis of EPEC

Detection and diagnosis of EPEC involve DNA probes (hybridization) or Polymerase chain reaction PCR tests targeting virulence genes eae and stx. Differentiating typical from atypical strains may require further testing for the bfpA gene or EAF plasmid. Virulence proteins like intimin and EspB are diagnostic targets using methods like immunoblotting and latex agglutination [25].

3. Enterohemorrhagic (Shiga Toxin producing) E. coli (EHE/STEC)

EHEC/STEC are foodborne pathogens known for Shiga toxin production, causing illnesses from mild diarrhea to severe conditions like hemolytic uremic syndrome and hemorrhagic colitis. Children are particularly vulnerable. *E. coli* O157:H7 and other serotypes (e.g., O26, O45, O103) are common. New strains like O104:H4 have emerged recently [26].

3.1. Virulence Factors, Mechanisms, and Pathogenesis

EHEC/STEC isolates produce Shiga toxin (Stx), a cytotoxin family with an AB5 subunit structure, inhibiting protein synthesis and causing proinflammatory and pro-apoptotic responses. Stx1 and Stx2 families, including variants like Stx2a, Stx2c, and Stx2d, are linked to severe diseases such as hemolytic uremic syndrome and hemorrhagic colitis. EHEC/STEC adherence to epithelial cells of intestine, often facilitated by the LEE pathogenicity island, is crucial for pathogenesis. Additionally, some LEE-negative strains cause serious infections. EHEC/STEC pathogenesis also involves biofilm formation and signaling systems like autoinducer-3 (AI-3)/epinephrine/norepinephrine [27, 28].

3.2. Epidemiology

There is a lack of knowledge on the immunological response against Stx, and the incidence of Hemolytic Uremic syndrome (HUS) cases differs worldwide. Recent studies examined the frequency of anti-Stx2-antibodies in the sera of children with HUS diagnoses and healthy children in an effort to close this gap. The results demonstrated that, in spite of the low incidence of HUS cases, a greater proportion of HUS patients than controls had antibodies against Stx2, indicating the circulation of STEC strains [29]. O157:H7 is one of the serotypes linked to infections in humans that is known to cause severe cases. Hospitalized patients, including those suffering from HUS, have been found to harbor O157:H7 strains following epidemiological investigations of diarrheal epidemics in different countries. EHEC is notably prevalent in the United States, with certain outbreaks showing prevalence rates of up to 1.5% [30]. Furthermore, ambulatory patients have EHEC/STEC strains from other notable non-O157 groups such as O26, O111, O103, and O145. Additionally, uncommon serogroups were found, mainly linked to severe diarrhea [31]. Remarkably, most of the patients infected with STEC were female, and most of them were young children. EHEC/STEC is widely distributed among many animal species, which emphasizes its zoonotic character.

These infections have been found in studies to be present in the feces of sheep, pigs, cattle, dairy buffaloes, fish, birds, and other animals, suggesting that they may spread from animals to people. From animal excrement, certain pertinent serotypes connected to diseases in humans have been found [32]. Furthermore, the high frequency of specific EHEC/STEC strains found in cattle hides intended for slaughter emphasizes the significance of measures pertaining to animal care and food safety during the entire production and processing cycle. Because EHEC/STEC may live in soil, manure, pastures, and water, their presence in the environment presents a danger of transmission. Recent research highlighted the potential concern posed by untreated water sources as a reservoir for pathogenic strains by describing the isolation of STEC [33]. Public health concerns are also raised by the discovery of STEC in organic fertilizer sourced from chickens in agricultural fields. Although there is currently a dearth of information regarding the detection of EHEC/STEC in foods worldwide, new research has found specific serotypes in ground beef and chilled raw kibbeh from retail outlets. EHEC/STEC has not been found in some dairy products or meat tests, though. Sensitive techniques must be used in laboratories in order to evaluate the danger of foodborne transmission [34].

3.3. Detection and Diagnosis

Identifying Shiga toxin-producing *E. coli* in food or stools involves selective enrichment and cytotoxicity evaluation. Multiplex PCR and various assays target stx genes for STEC screening. Detecting of serogroup O157 by serological tests is crucial for diagnosis. Serum antibody reacts with the lipopolysaccharide portion of lipoprotein antigen and it can be detected through serological tests such as

ELISA. Commercial tests are costly for developing countries, leading to affordable immunoassays development. Monoclonal antibodies show promise for efficient, cost-effective detection [35].

4. Enteroaggregative *E. coli*

EAEC is characterized by the AA pattern on epithelial cells, defined in 1987 as stacked-brick adherent bacteria [36]. This pattern, while diagnostic for EAEC, can appear in other pathotypes. EAEC typically causes watery diarrhea, sometimes with mucus or blood, and abdominal symptoms. Genetic variations, especially in IL-8 and immune protein genes, affect susceptibility. EAEC strains vary in serotypes and virulence factors, with specific factors driving diarrhea [37, 38].

4.1. Virulence Factors, Mechanisms, and Pathogenesis

EAEC infection progresses through stages (Figure 1): bacterial adherence to mucous membranes, biofilm formation, and triggering inflammatory reactions with toxin release [39]. Research, particularly on EAEC strain 042, has shown its role in human diarrhea. EAEC has diverse virulence factors, including plasmid-borne adhesins and toxins like EAST-1 and Pet [40]. Strains are categorized as typical or atypical based on the presence and absence of aggR, a virulence regulator gene [41].

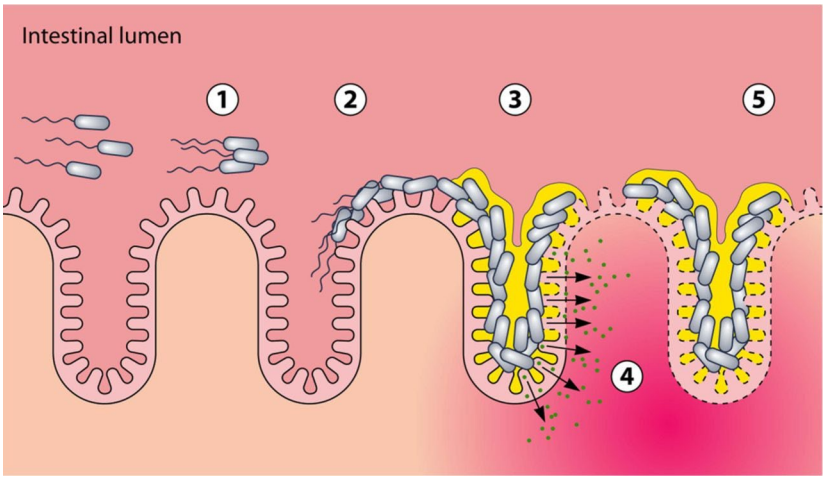

Figure 1: Steps of intestinal infection by EAEC. In the context of contracting various EAEC strains, scientists have delineated multiple stages in the progression of the illness: initially, the bacteria attach to the mucosal surfaces, followed by the formation of biofilms, and ultimately, the initiation of an inflammatory response along with the release of toxins [39].

4.2. Epidemiology

EAEC, an emerging pathogen, leads acute and continuous diarrhea worldwide, notably impacting children under 5 in developing countries. Epidemiological studies associate EAEC with diarrhea in both developed and developing nations, including cases among HIV-infected patients and adult travelers [42]. It has significant prevalence in Kenya, where it affects children in high rate with diarrhea [43]. Although data on EAEC epidemiology vary due to detection methods and geographical differences, it consistently emerges as a significant enteropathogen, affecting children and adults. Foodborne outbreaks of EAEC-induced diarrhea have been recorded globally, including incidents in Japan and Mexico [44].

EAEC is frequently implicated in persistent diarrhea in children, linked to malnutrition and developmental delays. Even asymptomatic EAEC carriers, particularly in low-income countries, may experience growth impairment [45]. The fecal-oral route is the mode of transmission, wherein contaminated food and water are the main carriers. Uropathogenic strains of EAEC that are resistant to several antibiotics and have uropathogenic features have been identified as a reason for urinary tract infections (UTIs) in recent years. Notably, EAEC O78 caused a community-acquired UTI outbreak in Denmark, marking its first involvement in extraintestinal disease outbreaks [39].

3.3. Detection and Diagnosis

Among DEC strains, EAEC is challenging to classify due to its heterogeneous nature. Its defining feature is the aggregative adherence (AA) pattern, resembling a stacked-brick formation [46]. The standard identification of EAEC involves culturing *E. coli* and infecting HEp-2 cells to observe the AA pattern, which is resource-intensive. Various detection methods include immunoblotting assays and PCR-based protocols targeting specific genes like aggR, aatA, and aaiA. Multiplex PCR assays enhance EAEC detection sensitivity and specificity, crucial given EAEC's association with both sporadic and outbreak-related diarrheal illnesses [47].

5. Enterotoxigenic *E. coli*

Enterotoxins are produced in the intestines by ETEC and induce diarrhea. It is frequently transmitted by the use of tainted food or water, and is a major reason for traveler's diarrhea and pediatric diarrhea in underdeveloped nations. Phenotypic characteristics such as varying flagellin and lipopolysaccharide (LPS) composition, as well as distinct CFs and toxin types, were the first indicators of ETEC's diversity. The process of serological typing of ETEC strains has been dependent on flagellar (H) and somatic LPS (O) antigens, as well as outer membrane proteins [48]. Genetically distinct ETEC strains, often found in asymptomatic individuals, exhibit high antigenic variability regarding virulence traits and serotypes, likely due to recent acquisition of virulence-associated genes under selective pressure [49].

5.1. Virulence Factors, Mechanisms, and Pathogenesis

ETEC strains produce colonization factors (CFs) and LT or ST enterotoxins, causing diarrhea in children and travelers in developing nations. ETEC affects livestock, posing economic challenges. Identified by diverse CFs and toxins, ETEC's genetic diversity includes over 100 somatic serogroups and 34 flagellar types [50].

5.2. Epidemiology

Every year, illnesses brought on by various ETEC strains account for over 200 million instances of diarrhea worldwide, with over 75,000 deaths from these infections, which mostly affect newborns and young children living in tropical regions with poor sanitation [51]. ETEC is prevalent in Bangladesh, with a rate of around 6% among children with diarrhea [52]. Across different periods, epidemiological data have shown ETEC-induced diarrhea in Nicaragua Peru, Egypt, Argentina, India and ranging from 3.5% to 20.45% in Brazil [53].

5.3. Detection and Diagnosis

ETEC diagnosis relies on detecting enterotoxins LT and/or ST, expressed by ETEC strains. PCR assays target virulence genes like clyA, eatA, and tia. Traditional methods used supernatants from *E. coli* colonies, while modern immunoassays (ELISA, latex agglutination) detect toxins. Optimizing toxin release enhances diagnostic sensitivity [54].

6. Enteroinvasive *E. coli*

The EIEC is responsible for dysentery in humans, particularly prevalent in developing nations. It invades human colon cells, resulting in a *Shigella* sp.-like infection [55]. EIEC was initially discussed by EWING and GRAWATTI in 1947 [56]. With the exception of the O124 serogroup, it displayed traits such as late lactose fermentation, lysine decarboxylase negative, and general non-motility. The categorization of 97 EIEC samples into unique bioserotypes was validated by additional investigation. The big (77 kDa) flagellin protein produced by the nonmotile EIEC serotypes is noteworthy since it allows swimming in modified motility agar (0.2%). Study of the fliC gene revealed six molecular profiles among 11 different EIEC serotypes, with major serotypes exhibiting low fliC diversity and forming two distinct clusters, means flagellin gene sourced from different origins and indicating the presence of common clones within serotypes [57].

6.1. Virulence Factors, Mechanisms, and Pathogenesis

Diarrhea caused by EIEC and *Shigella* results from bacterial invasion of enterocytes, facilitated by adherence to the large intestine mucosa and subsequent endocytosis. EIEC's colonization and survival depend on a large plasmid, similar to *Shigella*'s, containing genes crucial for invasion, escape, and immune response modulation. Despite their similarities, EIEC requires a higher infectious dose and typically induces milder, self-limiting disease compared to [58]. The pathogenic difference is attributed to factors such as reduced intracellular proliferation and less potent proinflammatory responses induced by EIEC. Moreover, EIEC's ability to acquire iron and its interaction with M cells in the intestinal mucosa contribute to its pathogenesis. EIEC targets M cells for entry into deeper tissues, followed by invasion of enterocytes from the basolateral side. These processes involve complex interactions between bacterial virulence factors and host immune responses [59].

Studies suggest that EIEC may show an intermediate stage between *E. coli* and fully developed *Shigella* strains, sharing common ancestry but retaining some *E. coli* properties lost in *Shigella*. Genetic analyses reveal polymorphisms in invasion-related genes among different EIEC serotypes, but no changes that explain variations in pathogenicity compared to *Shigella*. In experimental models, EIEC exhibits comparable initial invasion capacity to *Shigella* but demonstrates lower expression of virulence genes and reduced intracellular proliferation. EIEC-infected macrophages produce higher levels of anti-inflammatory cytokines compared to *Shigella*-infected cells, contributing to the milder inflammatory response observed in EIEC-induced disease. In conclusion, while EIEC and *Shigella* share mechanisms of invasion and pathogenesis, differences in their virulence profiles and host responses account for variations in disease severity. Understanding these distinctions is crucial for developing targeted interventions against these enteric pathogens [60].

6.2. Epidemiology

With no known animal reservoirs and oral-fecal transmission being the predominant mode of infection, humans seem to be the main source of EIEC infections. These illnesses are more prevalent in low-income nations with lax sanitation regulations [61]. The incidence of EIEC varies among different regions and countries. Discrepancies in reported incidence rates may arise due to challenges in differentiating between EIEC and *Shigella*. In certain Latin American and Asian countries, EIEC has been known as a common cause of diarrhea in asymptomatic carriers. In industrialized nations, EIEC infections are often related to traveling, occurring in individuals returning from high-incidence regions [62]. EIEC has a high prevalence in children with diarrhea in Bangladesh [20]

EIEC can cause sporadic infections and outbreaks, sometimes occurring in large numbers of cases. Notable outbreaks include a 1970s incident in the United States linked to contamination of cheese with an O124 *E. coli* strain, and a 2012 outbreak in Italy involving over 100 cases of severe bloody diarrhea associated with an emerging EIEC. Other outbreaks have been linked to food contamination and sources of water, often through secondary contamination by human carriers [63]. In recent years, several outbreaks of gastrointestinal illness in Europe have been associated with EIEC, including cases traced back to contaminated salad vegetables. The emergence of new EIEC serotypes, such as O96:H19, has been observed, potentially due to the acquisition of invasive plasmids by certain *E. coli* strains [64].

6.3. Detection and Diagnosis

EIEC samples usually grow efficiently on common culture media, such as MacConkey agar, Eosin methylene blue, XLD agar, and HE agar, which are used for *Enterobacteriaceae* isolation. Identification of *E. coli* species often involves conventional biochemical tests, including indole production, glucose, sucrose, and lactose fermentation, gas production, citrate utilization, motility, and decarboxylation of lysine, arginine, and ornithine [65]. Slow lactose fermentation in EIEC strains, taking up to 72 hours, can complicate differentiation from *Shigella*. Serotyping may be necessary for differentiation, especially if some S. flexneri serotypes produce indole. Characterization of EIEC requires the detection of plasmid virulence genes. PCR investigation of the ipaH gene, which exists in both EIEC and *Shigella*, is recommended, along with studies on other DNA sequences like the ial gene. The iudA and lacY genes are

able to distinguish EIEC from *S. flexneri* [66]. A stool test that depends on apyrase activity has been proposed for rapid EIEC detection, offering a simple, cost-effective method suitable for routine laboratory use [67].

7. Conclusions

The diverse nature of *E. coli* strains, ranging from harmless gut inhabitants to potent pathogens causing both intestinal and extraintestinal diseases, presents significant classification challenges, especially with the emergence of hybrid pathotypes that combine virulence traits from multiple types. The analysis of 64 studies reveals that while all these strains cause diarrhea, each exhibits different colonization patterns and mechanisms for damaging the host. The diverse pathogenic mechanisms and virulence factors of various DEC pathotypes, including EPEC, EHEC, EAEC, ETEC, and EIEC. Further, studies have shown that DEC is not confined to a specific location or country, confirming its global presence. The prevalence of DEC varies significantly worldwide. EPEC, ETEC and EIEC are particularly prevalent in developing countries like Bangladesh; moreover, EHEC is most prevalent in the United States and Europe, with outbreaks in the U.S.; additionally, EAEC is prevalent in Africa, especially Kenya. Conversely, the lowest prevalence rates for these pathotypes are observed in Europe. For example, EHEC has one of the lowest prevalence rates in Europe, specifically in the UK, with a rate below 1%.

With regard to the detection methods, the advancements in whole-genome sequencing offer promising avenues for improving epidemiological surveillance and outbreak investigations. Comprehensive genetic data from sequencing facilitate precise typing and tracking of *E. coli* strains, enhancing our ability to identify sources of infection and monitor pathogen spread. However, despite these technological advancements, there remains a gap in understanding the full spectrum of genetic factors influencing *E. coli* pathogenicity. Further exploration of novel genes and their roles in *E. coli*-host interactions is essential for refining epidemiological strategies and effectively combating *E. coli*-related diseases.

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