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Bacterial diarrhea among infants in developing countries: An overview of diarrheagenic *Escherichia coli* (DEC)

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Abstract

Many cases of diarrhea are due to an infection in the gastrointestinal tract caused by microorganisms such as bacteria, viruses and parasites. This may be present alone or can be together with different symptoms, such as vomiting, abdominal pain, nausea and weight loss. There is an estimate of 2 billion cases of diarrhea disease globally that happens yearly. Also, approximately 1.9 million children globally below the age of 5 years die from diarrhea every year mostly in the developing countries making it the second leading cause of mortality in children of this age group. Recurring and regular diarrhea can affect growth of children and cognitive development and increase their vulnerability to different communicable diseases. About 89% of diarrhea related deaths are caused by insufficient hygiene, bad water, and inadequate sanitation. Major cause of diarrhea in children is Diarrheagenic *Escherichia coli* (DEC) which is acquired through water and food that is contaminated. There are 6 main pathotypes:, diffusely adherent *E. coli* (DAEC), enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), shiga toxin–producing *E. coli* (STEC), enteroinvasive *E. coli* (EIEC), and enteroaggregative *E. coli* (EAEC). Adherent invasive *E. coli* (AIEC) is is the new pathotype that has been recently reported. Biochemical tests, culture and modern methods like Polymerase Chain Reaction are the conventional techniques carried out in the identification of *E. coli* species. Preventive measures and treatment includes proper sanitation, improved hygeine, access to safe drinking-water, exclusive breastfeeding of the babies for the first 6 months of life, proper rehydration with oral rehydration salts (ORS) or intravenous fluids in case of shock, early hospitalization for children who are extremely malnourished, zinc supplementation, and in some circumstances, the use of antibiotics which should be implemented to reduce the burden of diarrhea among children.

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1.0 Introduction

The excretion of liquid or loose stools several times in a day (or frequent passage than the normal for an individual) is referred to as diarrhea. The symptom is common to gastrointestinal infection resulting from the intake of many parasite or viruses, bacteria that can be transmitted through the means of food, water, utensils, hands and flies. The three main clinical syndrome of diarrhea include; 1) acute watery diarrhea which lasts for less than 2 weeks; 2) bloody diarrhea and 3) Persistent diarrhea which lasts for at least 2 weeks. Diarrhea leads to loss of electrolyte, dehydration, shock and sometimes death (WHO, 2017).

Young children in impoverished nations are severely impacted by the burden of diarrheal disease because of its high incidence rates brought on by insufficient access to clean water, inadequate sanitation, inadequate nursing, and deficiencies in zinc and vitamin A. Due to a lack of access to prompt

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intervention and high-quality healthcare, vulnerable children in underdeveloped and underprivileged areas also experience greater fatality rates than children in industrialized nations (Peter and Umar, 2018).

Globally, diarrheal illnesses are a public health issue that significantly increase infant and child morbidity and mortality, particularly in poorer nations (Okeke *et al*., 2000). Diarrhea is a major cause of death among children accounting for about 8% of all the deaths among children below 5 years old world-wide in 2017. This translates to over 1,300 young children dying each day, or about 480,000 children a year, despite the availability of a simple treatment solution (UNICEF, 2020).

1.1 General Characteristic of *Escherichia coli*

The first description of *Escherichia coli* (*E. coli*) was made by Theodor von Escherich in 1885 (Escherich, 1988). Gram-negative, rod-shaped, non-spore-forming, motile bacteria belonging to the *Escherichia coli* species range in size from 2 micrometers in length to 0.6 micrometers in diameter and have a cell volume of 0.6 to 0.7 micrometers (Darnton *et al.,* 2007). They are oxidase-negative facultative anaerobes with an optimal growth PH of 6.0-7.0 and temperature of 37^0C. They can ferment glucose, lactose, and sucrose. However, certain laboratory strains can proliferate at a temperature of 49^0C (Fotadar *et al.,* 2005). *E. coli* is a commensal bacterium that is classified as a member of the Enterobacteriaceae family and is found in the intestinal microflora of mammals, including humans (Tenaillon *et al*., 2010). However, the development of the intestinal *E. coli* flora is a more complicated process that is influenced by microbial and host interactions as well as by internal and external factors that can significantly affect the prevalence and density of *E. coli*, such as delivery method, feeding practices, lifestyle, environment, and immunological status (Adlerberth, 2008; Adlerberth and Wold, 2009; Penders *et al.,* 2006).

1.2 Acquisition of *Escherichia coli*

The digestive system of a newborn is thought to be sterile at birth. However, its colonization begins as soon as the baby is exposed to a microflora, which occurs after the fetal membranes rupture. Within a few hours after birth, *E. coli* and other enterobacterial species are among the first to colonize the infant's intestine (Fanaro *et al.,* 2003). *E. coli* and the host continue to benefit from each other for decades (Kaper *et al.,* 2004). The first strains of *E. coli* that colonized the newborn's intestine may have come from the mother's feces during delivery (vertical transfer) or may have been spread from infant to infant by nursing personnel (horizontal transfer) (Fanaro *et al.,* 2003). The consumption of contaminated food and water is a further exposure pathway (Duriez *et al.,* 2001; Hammerum and Heuer, 2009). According to several research conducted in affluent nations, *E. coli* strains were present in 42–49 percent of newborn newborns, with a mean of 1.6–2.1 strains by day three of life (Nowrouzian *et al.,* 2003). This flora was found to be stable and demonstrating an environment in modern civilization in developed countries largely free of harmful fecal bacteria. It is interesting to note that the equivalent carriage rate among babies was only 61–64 percent at 3-6 months of age. Since 8.5% of *E. coli* strains were discovered per child over the course of a year in a sample of babies that was comparable, this should be compared to the quick and large turnover of strains in poor nations (Adlerberth and Wold, 2009). Resident *E. coli* strains are more likely to belong to distinct or particular pathogenic clonal groups and also have an increased capacity to adhere to colon epithelial cells (Kaper *et al.,* 2004; Müller *et al.,* 2007).

2.0 Acute Infectious Diarrhea (AID)

The condition known as AID primarily affects children under the age of five, while it can also affect adults. According to numerous researchers, it is and has been a major cause of mortality and morbidity for decades globally (UNICEF, 2012). In underdeveloped nations where it is the second-leading cause of death after pneumonia, diarrhea continues to be a serious public health problem (UNICEF/WHO, 2009; UNICEF, 2012). Around the world, 780 million people lack access to clean drinking water, and 2.5 billion people lack better sanitation (WHO, 2017). According to UNICEF's most recent figures (2020), diarrhea is directly responsible for 8% of all under-five-year-old deaths worldwide. Africa and South East Asia account for about 78% of the deaths of these children, the majority of whom are from underdeveloped nations (Farthing, 2012). The biggest problem with developing countries is hunger with most of their citizens not being able to access a meal per day hence the countries major priority is food security. This has caused the majority of these nations to concentrate on ways to feed their citizens. Even though these countries list health as one of their top five concerns, they are unable to give it the attention it requires because they lack the resources and therefore rely on loans and grants from richer nations. This circumstance has resulted in less money being donated by rich nations to issues relating to health, which has led to the high prevalence of diseases in these nations—including diarrhea—at the moment. Children under the age of five from developing regions experience an average of 3 episodes of diarrhea each year, with the peak occurring at about 3.2 years (Gupta, 2014). The highest incidence (4.8 episodes) occurs within the first year of a child's life and gradually declines to 1.4 episodes per year by the time the child is four years old (Kosek *et al.*, 2003). These incidents weaken the children's bodies' nutritional state, which inhibits growth and development and contributes to the underlying malnutrition which leads to diarrhea and vice versa (Bryce *et al*., 2003; WHO, 2017).

Worldwide, diarrhea occurs as a result of connected factors. People who are exposed to unsanitary living circumstances, incorrect waste disposal, a lack of potable drinking water, and inadequate drainage systems, among other things, are more prone to diarrhea than people who live in healthy environments. About 30 million people in Nigeria still practice open defecation and utilize outdated sanitation facilities, which raises the risk of developing diarrheal infections (67 percent of whom are concentrated in the country's northern region) (Peter and Umar, 2018). Since better sanitation and even sewer connections might not involve comprehensive safe treatment of human waste, research have indicated that diarrheal deaths owing to poor sanitation are more common. Wider population exposure to untreated sewage and feces is anticipated to significantly increase the risk of disease, particularly diarrheal diseases in children under the age of five. Lethality of severe AID decreased from 4.6 million in 1982 to an estimate of fewer than 0.6 million in 2014, among other things, due to improvements in sanitation, nutrition, education, and early availability to oral rehydration therapy (UNICEF, 2014).

Severe AID in children is linked to a number of well-known microorganisms, including bacteria, viruses, and parasites (Al-Gallas *et al.*, 2007; Dupont, 2009; O'Ryan *et al.*, 2010; UNICEF, 2014). There is a dearth of etiological information that tries to identify every factor that contributes to severe AID in young children. Despite the fact that a number of studies from various nations have indicated that DEC pathotypes are the primary bacterial cause of AID in infants from underdeveloped nations, the frequency of these infections vary with geographic region and depend on the socio-economic sanitary conditions attained, according to research by Black *et al.* (2010) and O'Ryan *et al.* (2010). These ailments account for between 30 and 40 percent of cases (Black *et al.*, 2010).

2.1 Causes of diarrhea

When fluid from the bowel contents cannot be absorbed or when too much fluid is produced into the bowel, it can cause diarrhea and watery stools. Infections, malnutrition, and other factors, such as inadequate personal hygiene, are frequent causes of diarrhea. Diarrhea is the symptom of infections caused by microorganisms like bacteria, viruses and parasites, most of which are commonly spread by water contaminated with feaces. Infection is more frequent when there is inadequate hygiene and sanitation and lack of safe water for drinking. *Salmonella*, *Shigella*, *Campylobacter*, and different strains of *Escherichia coli* are just a few of the organisms that can cause bacterial diarrhea (WHO, 2017). Children mortality caused by diarrhea is usually as a result of underlying malnutrition, which exposes them to diarrhea. Malnutrition worsens by each diarrheal episode. Diarrhea is a leading cause of malnutrition in children under five years old (WHO, 2017).

Poor personal cleanliness makes it easier for diarrheal illness to spread from person to person. Septic tanks, latrines, and other water sources that are contaminated by human waste are of particular concern. Microorganisms that can cause diarrhea are also present in animal feaces. Food is also a major cause of diarrhea when it is prepared or stored in an unhygienic conditions. During irrigation, polluted water may contaminate food. Fish and seafood from polluted water may contribute to the disease (WHO, 2017).

2.2 Emerging Pathogen with Potential to Spread Virulence

Despite being classified as commensals and a natural component of the intestinal microbiota of warm-blooded animals and humans, supporting a healthy intestinal ecology, *E. coli* strains can nonetheless cause diseases in some situations (Kaper *et al.*, 2004). *E. coli* related illnesses can result from either specific or non-specific infections. When the normally harmless, commensal *E. coli* strain becomes hazardous due to the host immune system being impaired, such as in aged, pre-term babies, malnourished, and immuno-compromised people, non-specific infections may occur (Kaper *et al.*, 2004). Some subsets of *E. coli* strains, which make up a versatile and diverse group of microorganisms with a number of highly adapted clones, are the cause of specific infections. These strains have developed specific virulence characteristics that give them the capacity to adapt to new surroundings and the ability to infect healthy people with a variety of infections (Kaper *et al.*, 2004).

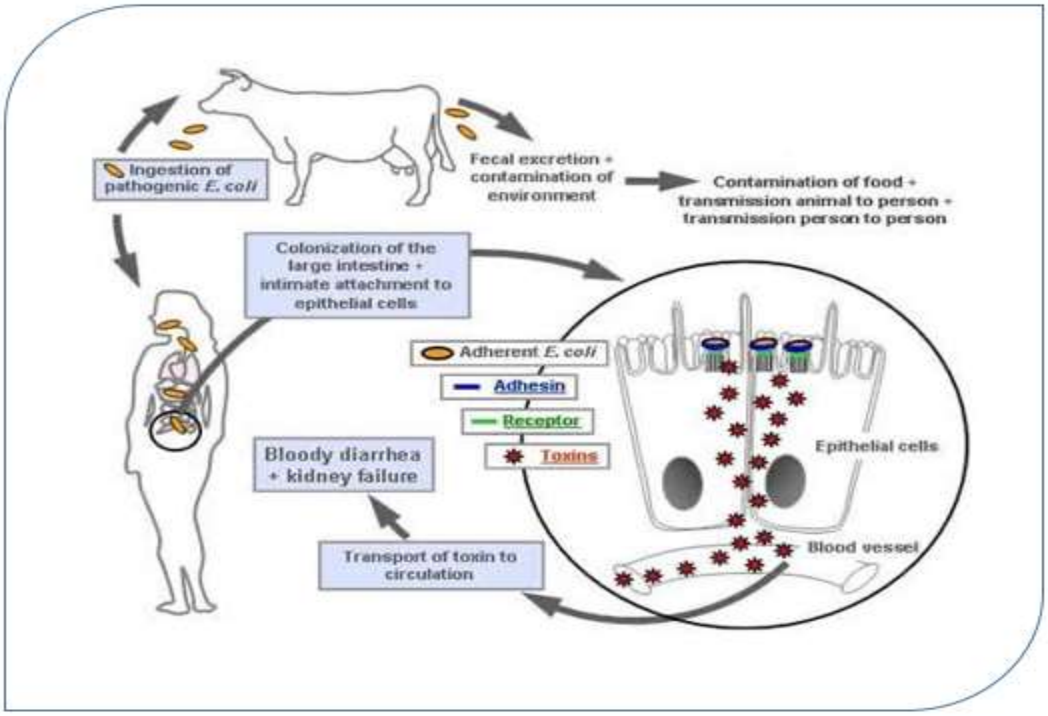

Figure 1. Mechanism of Invasion of diarrheagenic *E. coli* in Host (John, 2004).

2.3 Diarrheagenic *Escherichia coli* (DEC)

Diarrheal diseases are a leading cause of morbidity and mortality in newborns and young children which is a serious public health issue (WHO, 2012). Poor living conditions (inadequate water supplies, poor environmental hygiene and sanitation, and inadequate education) are the main causes of diarrheal infections occurring more frequently and fatally in low- and middle-income nations in Africa, Asia, and Latin America (Croxen *et al.,* 2013). One of the most significant etiological agents of diarrhea are *E. coli* strains, which have evolved by acquiring a particular set of traits that have effectively persisted in the host through horizontal gene transfer (Croxen *et al.,* 2013;). The group of acquired virulence determinants, a determinant of the currently recognized *E. coli* pathotypes generally known as diarrheagenic *E. coli* (DEC), led to the discovery of specific combinations. The pathotypes of diarrheagenic *E. coli* are classified as enteroaggregative *E. coli* (EAEC), enterohemorrhagic (Shiga toxin-producing) *E. coli* (EHEC/STEC), enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), and enteroinvasive *E. coli* (EIEC). They differ in terms of their preferred host colonization sites, harmfulness mechanisms, and the ensuing clinical symptoms and consequences.

Each of these pathotypes consists of a collection of clones that have unique virulence traits in common. However, it should be noted that the *E. coli* genome's plasticity has made it difficult to classify some isolates as a specific pathotype because some of these isolates combine the key virulence traits of various pathotypes and are therefore thought to be potentially more virulent hybrid pathogenic strains (Croxen *et al.,* 2013). A less well-known pathotype known as the diffusely-adherent *E. coli* (DAEC) pathotype, which consists of strains that adhere to epithelial cells in an irregularly dispersed way, has been reported. The categorization of DAEC as a new DEC pathotype requires further epidemiological investigations, which have been delayed by the challenges in its identification and classification, despite their classification as a group different from the other pathotypes (Croxen *et al.,* 2013). Additionally, some *E. coli* strains that belong to the adherent invasive *E. coli* (AIEC) pathotype contain one of the possible agent of Crohn's disease (CD). It is believed that a combination of variables, including genetics, the intestinal microbiota, environmental factors, and enteric infections are the causes of CD, an inflammatory bowel disease (IBD) (Rolhion and Michaud, 2007; Cieza *et al.,* 2012). Diarrheal episodes caused by DEC infections are a significant public health concern among children and adults in poor countries because of their correlation with the prevalence of illnesses and the mortality rate of children under the age of five.

3.0 Detection of Diarrheagenic *E. coli*

Detection of diarrheagenic *E. coli* can be carried out using cultural, enzymatic, serology and molecular techniques which is the most advanced method of detection. The genome of pathogenic *E. coli* has been extensively studied using whole-genome sequencing which is a molecular technique. This technique has provided information which is useful in disease management, epidemiology, outbreak investigations, and monitoring pathogen spread (Croxen *et al.,* 2013).

3.1 Sample collection

Mammal gastrointestinal tracts are the primary habitat of *E. coli*, which is released into the environment through excrement. For the purpose of isolating diarrheagenic *E. coli*, the feces of children with diarrhea can be collected. It is advisable to process the fecal samples for *E. coli* isolation as soon as possible after collection, usually within 24 hours. This involves the inoculation into enrichment or inoculation into solid culture media..

3.2 Cultural method of detection of Diarrheagenic *E. coli*

The ability to ferment lactose gives an option to use MacConkey agar to discriminate *E. coli* from other nonlactose fermenting coliforms from fecal samples. Sample suspension (for solid samples) is made at any concentration, for example, 5% in normal saline or phosphate buffer solution and inoculated onto MacConkey agar followed by 18–24 hours incubation at 37°C. Pink, round medium-sized colonies are picked as *E. coli* suspect colonies (Lupindu, 2017).

E.coli isolates can be confirmed using biochemical, enzymatic, or molecular techniques. The choice of approach is influenced by a variety of factors, including resource accessibility. The methods for confirmation includes biochemical techniques such as IMViC, enzymatic methods like the use of brilliance *E. coli* agar, and molecular methods.

3.2.1 Biochemical method (IMViC Test)

IMViC tests, a conventional technique, can be used to biochemically confirm *E. coli* isolates. These are four sets of tests are used to distinguish between members of the *Enterobacteriaceae* family. IMViC is an abbreviation that stands for the Indole, Methyl red, Voges-Proskauer, and Citrate utilization tests (Lupindu, 2017).

Using the enzyme tryptophanase, the indole test measures the bacteria's capacity to synthesize indole from the amino acid tryptophan. The indole in Kovac's reagent combines with the aldehyde to produce a red or pink ring at the tube's top. Indole-positive bacteria include *E. coli*. A bacterium's capacity to create acid through the fermentation of glucose is identified using the methyl red test. At a pH of less than or equal to 4.4, methyl red, a pH indicator, maintains its red color. The color of MR-negative bacteria turns yellow. The bacteria *E. coli* are MR positive. Acetoin can be found in the media containing bacteria using the Voges-Proskauer test. When sodium hydroxide and air are present, acetoin is converted to diacetyl. When dialdetyl and guanidine react in the presence of alpha-naphthol, a red color results. *E. coli* is VP negative with no color change.

The ability of the bacteria to utilize citrate as its only source of carbon and energy is determined by the citrate utilization test. Bromthymol blue is a pH indicator found in citrate agar media. At an alkaline pH, the agar media turns from green to blue. Due to the activity of the enzyme citritase, citrate in the medium degrades to oxaloacetate and acetate. Pyruvate and CO2 are produced after further breakdown of oxaloacetate. Production of Na_2CO_3 from sodium citrate changes the media into alkaline pH, and hence color change from green to blue with *E. coli* being citrate negative (Lupindu, 2017).

3.2.2 Enzymatic method

E. coli isolates can be confirmed using strict selective media that look out for certain enzymatic activity in *E. coli*. Using brilliance *E. coli* agar, for instance, one can test for the presence and activity of the -glucuronidase enzyme. On Brilliance *E. coli* agar, the *E. coli*-specific beta-glucuronidase enzyme breaks down the glucuronide substrate, resulting in purple colonies. While most *E. coli* have both ß-galactosidase and ß-glucuronidase, non-E. coliforms only have ß-galactosidase, which allows them to digest lactose. However, *E. coli* O157 are glucuronidase negative; hence, these media are not appropriate for initial screening of *E. coli* population but can be used to differentiate *E. coli* O157 from confirmed *E. coli* population (Lupindu, 2017).

3.2.3 Characterization of Diarrheagenic E. coli Isolates

Detection of bacterium isolates from various sources and typing of isolates of the same species are both included in characterization. Depending on the attribute being investigated, *E. coli* can be characterized in several ways. The approaches might be classified as serology, molecular, or cytopathic tests. Numerous methods, including the polymerase chain reaction (PCR), DNA hybridization, and pulsed-field gel electrophoresis (PFGE), to name a few, are used in molecular characterization.

i. Serotyping

Agglutination assays and the use of specific antisera can be used to detect the presence of antigenic components that characterize a particular *E. coli* strain, such as somatic antigen O, capsular antigen K, and flagella antigen H. The somatic and flagella antigens are either tested against pools of antisera first, and then against each of the unique antisera from the positive pools, or they are tested against each individual antiserum. In the nomenclature of O and H antigens, the number of positive antisera is utilized, for instance, *E. coli* O113:H21, O142:H34, and O157:H7. There are more than 180 O somatic antigens and more than 50 H-flagella antigens that are known and used as reference in *E. coli* serotyping (Lupindu, 2017).

ii. Polymerase chain reaction (PCR)

Through the use of polymerase chain reaction, different virulence genes that code for various virulence factors are targeted in order to characterize different *E. coli* strains. Verocytotoxin1, verocytotoxin 2, intimin, heat-stable enterotoxin, human variant, heat-stable enterotoxin, porcine variation, heat labile enterotoxin, and invasive plasmid antigen are examples of common virulence factors for intestine pathogenic *Escherichia coli* (IPEC). These virulence genes can be detected using multiplex DEC PCR kit as described by Persson *et al.* (2007).

DNA hybridization can also be used to detect virulence components and determine how closely related different *E. coli* strains are genetically. A single strand of DNA anneals to a complementary single-stranded DNA fragment (probe) in this phenomena to create a hybrid. The probe's labeling allows detection of the synthesis of a hybrid molecule, which demonstrates the presence of the complementary (target) nucleic acid strand. Apart from detection of conventional virulence genes, DNA hybridization can be used as a complementary to PCR to check for additional virulence factors (Lupindu *et al.*, 2014). In order to distinguish between isolates that are closely related to one another, additional virulence factors might be analyzed via hybridization.

iii. DNA sequencing

This involves determining the exact sequence of bases in the nucleotides that make up a particular DNA section. DNA sequencing helps in the comparison of genetic make-up from various sources, such as in the evaluation of the association of various disease outbreaks, in addition to characterizing genetic material for the aim of identifying an *E. coli* strain. Typically, electrophoresis is used in sequencing to separate DNA fragments into bands. The introduction of an electric and segregation of molecules based on size, tiny molecules travel through the gel more quickly. Fluorescence dyes are used to tag bases during sequencing, and each base type produces a different color, such as blue for thymine, green for cytosine, red for adenine, and yellow for guanine. DNA molecules will frequently be copied. Elongation of the chain terminates when one of the modified bases is absorbed into the DNA molecule, and all DNA fragments in that batch will have an ending with that specific modified base. The artificial base at the end of the subsequent batch of DNA copies will be different, and so on. As a result, each DNA batches will have different T, A, G, and C bases at the end, each with a distinct color. Therefore, a color pattern of the final (modified) base will be used to determine the base sequence in the assembled DNA material. The data is used for interpretation after being saved in computer memory.

The characterization of genetic material by sequencing is superior to previous techniques. Using a clonal relationship between isolates from PFGE fingerprinting as an example, whole genome sequencing can identify false positive and false negative results (Salipante *et al.*, 2015). The method for sequencing DNA is the same regardless of how the genome is approached as a whole. Kwong *et al*. (2015) described comprehensive guidelines and techniques for sequencing.

4.0 Treatment and Prevention of Diarrheal infection

4.1 Treatment of Diarrheal Infection

Maintaining hydration, treating the underlying causes, and alleviating diarrheal symptoms are the objectives of treatment. While the WHO's control of diarrheal deaths (CDD) programme and other organizations (UNICEF, USAID) have prioritized the prevention of diarrheal deaths, rather than the prevention of cases, and focused on promoting oral rehydration therapy (ORT), rehydration and its correction of any electrolyte imbalance are crucial in the treatment of diarrhea. According to estimates, inadequate personal, household, and community hygiene practices and poor sanitary conditions account for 90% of the burden of pediatric diarrheal illness (Peter and Umar, 2018). Re-hydration with oral re-hydration salts (ORS) solution. ORS is the mixture of clean water, salt and sugar. Treatment with ORS is cheap. ORS replaces the water and electrolytes lost in the faeces by being absorbed in the small intestine. Also, Zinc supplements are linked to a 30% reduction in stool volume and a 25% reduction in the duration of diarrheal episode. Re-hydration can also be done with an intravenous fluids in case of shock or severe dehydration. By continuously providing nutrient-rich foods, which includse breast milk, during an episode and by providing a nutritious diet, such as exclusive breastfeeding for the children for at least six months when they are healthy, the vicious cycle of malnutrition and diarrhea can be broken. Seeing a doctor, especially for the treatment of chronic diarrhea, blood in the stool, or if there are indications of dehydration is recommended (WHO, 2017).

4.1.1 Oral rehydration therapy (ORT): The ORT, which is a prime example of the technological transfer from underdeveloped to industrialized nations, is the greatest medical invention of the 20th century. According to the instructions, ORT solutions are made by combining clean/pure water with appropriate amounts of sodium, glucose, potassium, chloride, and alkali (bicarbonate or citrate). Oral rehydration therapy (ORT) is effective for treating all forms of dehydration using the WHO formula. Due to its exceptional efficacy in treating acute, chronic, and watery diarrhea, it has significantly decreased the death rate of children from diarrheal disease. Although ORS-WHO (oral rehydration salts) might be thought of as a general and all-purpose solution, it is important to have a standard formula that can be prescribed and promoted internationally (Peter and Umar, 2018).

A very safe treatment instrument is ORS. ORS has been administered in excess of two billion units without any major issues. It is not advisable to treat children with acute diarrhea with symptomatic antidiarrheal medications. Even though the intravenous method is always advised in the presence of shock, ORT given via mouth or nasogastric tube has proven to be beneficial in treating chronic dehydration brought on by diarrhea. W.H.O. currently advises a salt level of 75mmol/L for single oral rehydration solution (ORS) (Peter and Umar, 2018).

4.1.2 Homemade Fluids: A set of suitable homemade fluids is also useful in preventing dehydration if ORS are not accessible to treat diarrhea. What is considered an acceptable homemade fluid varies across nations, and these policies aren't usually well defined. For instance, in Nigeria, a solution of salt and sugar is generally considered to be an acceptable homemade fluid. Even though they are less effective at treating children who are already dehydrated, other fluids will help avoid dehydration in children with diarrhea. A homemade fluid is always created at home using readily available, inexpensive solutes (salt and sugar). Oral treatments based on cereal and homemade fluids have been shown to be successful in preventing diarrheal dehydration (Peter and Umar, 2018).

4.1.3 Zinc Treatment: For overall health, development, and growth, zinc is essential. The immune system's function is also supported. Zinc insufficiency is common in the developing world and has been linked to greater incidence of infectious disorders, especially diarrhea, and fatalities from these illnesses, despite the fact that it is abundant in protein-rich and other food sources. In order to restore the body's reserves and aid children in recovering from illness and maintaining their health later, zinc supplementation is essential as part of the course of treatment. It is clear that many of the affected children with diarrhea show deficiency in essential vitamins and trace elements required by the body system, which is relevant to reducing the burden of diarrhea in the world. The relationship between poor feeding and diarrheal illnesses has been correlated over time (Winch, 2009).

Zinc plays a significant role in the healing of injured skin while vitamin A helps to maintain the epithelial cross-linkage. It also helps children under the age of five by boosting their immunity. The incidence, frequency, and persistence of diarrheal diseases are demonstrated to be lower in children who receive zinc supplementation early. Zinc also seems to boost ORS uptake and prevent inappropriate drug use with antibiotics and anti-diarrhea drugs. Children who took zinc supplements seemed to heal more rapidly, had greater energy and appetites, and were less unwell than other kids in their neighborhoods (Walker *et al.*, 2012).

4.2 Prevention and Control of Diarrheal Infection

Ingestion of pathogens, primarily through faecal-oral pathways, results in diarrheal illness. Social, cultural, and economic constraints significantly impede preventive measures. It has been demonstrated, however, that proper water, hygiene, and sanitation interventions can reduce diarrhea incidence by 26% and mortality by 65%. Access to safe drinking-water, encouragement of early and exclusive breastfeeding for the first six months of life, vitamin A supplementation, good personal and food hygiene, hand washing with soap and health education about how infections spread can serve as a community-wide cleanliness measure. The health of children across the nation may be improved if these preventive actions are implemented in a coordinated manner, which could have a greater overall influence on the population (WHO, 2017). New aspects of this approach include rotavirus vaccination, which was recently recommended for global introduction into routine schedules for immunization procedures, this helps to ensure that viral diarrhea are not mis-diagnosed for bacterial diarrhea (WHO, 2017).

5.0 Conclusion

Despite recent advances in understanding the genetic background and the pathogenicity of various DEC pathotype strains, many additional genes encoding unidentified functions remain undefined to enhance our comprehension of how these pathogens interact with their hosts. The World Health Organization (WHO) projects that 5 million deaths in children under the age of five will still occur by 2025, with 97 percent of these deaths occurring in developing countries primarily in Africa and some regions of Asia, with diarrhea accounting for a significant portion of the burden. These estimates of diarrheal disease are sensitive to the main assumptions made above. Adherence to preventive measures should be practiced in other to curb diarrhea diseases among children under five years old with all countries aiming to reduce neonatal mortality.

List of Abbreviations

AID - Acute Infectious diarrhea
AIEC - Adherent invasive *Escherichia coli*
CD - Crohn's Disease
DAEC - Diffusely Adherent *Escherichia coli*
DEC - Diarrheagenic *Escherichia coli*
DNA - Deoxyribonucleic Acid
EAEC - Enteroaggregative *Escherichia coli*
EHEC - Enterohaemorrhagic *Escherichia coli*
EIEC - Enteroinvasive *Escherichia coli*
EPEC - Enteropathogenic *Escherichia coli*
ETEC - Enterotoxigenic *Escherichia coli*
IBD - Inflammatory Bowel Disease
IPEC - Intestinal Pathogenic *Escherichia coli*
ORS - Oral Rehydration Salts
PCR - Polymerase Chain Reaction
PFGE - Pulsed-field Gel Electrophoresis
STEC - Shiga toxin–producing *Escherichia coli*
UNICEF - United Nation Children Fund
WHO- World Health Organisation

Declarations

Ethics approval and consent to participate

Not Applicable

Consent for publication

All authors have read and consented to the submission of the manuscript.

Availability of data and material

Not Applicable.

Competing interests

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