**Pathogenesis of Escherichia coli: A clinical findings**

**ABSTRACT.**

Introduction/Background.

Theodore Escherich, a German doctor, found E. coli for first time while studying the gut flora of newborns. Bacterium coli commune (Escherich 1885) was named after him in 1885, and its virulence in extra intestinal illnesses is established by him (1894 Escherich). Until 1919 the term Bacterium coli was commonly used. Then after the formation of the genus escheria , Castellani and Chalmers called the type species E. coli (Chalmers & Castellani 1919).

Escherichia coli is the member of Enterobacteriaceae family and is a gram-negative facultatively anaerobic rod (with both a fermentative and respiratory metabolism) that lack oxidase production. One single rod cell of Escherichia coli cell is generally 1.1–1.5 m broad by 2–6 m long. They maybe motile or nonmotile, producing lateral flagella as opposed to polar flagella when motile. Many strains expand fimbriae or pili, which might be proteinaceous appendages (or structures or fibres ) that extend outwardly from the bacterial cell and assist in bacterial mobile adhesion or adherence to other host cells or tissues.

Shigella spp. are closely related to Escherichia coli, albeit Shigella is less biochemically active than most E. coli strains. Although genetic relatedness allows Shigella and E. coli to be classified as a single genus, the two have typically been kept apart to avoid medical diagnostic confusion.

E. coli are found in the nature, edibles, water and intestines of many living organisms E. coli is a totally giant and numerous organization. Most of the E. coli traces are secure, some can purpose contamination. Some E. coli strains are chargeable for causing diarrhoea, and lots of other lines motive urinary tract infections, pneumonia, and lots of different diverse different infections and diseases.

Key words: E.coli, microbiology, metabolic, organism ,prokaryotic, eukaryotic, diarrhoea.

**Introduction.**

In the stomachs of homo sapiens and creatures with warm blood characteristics, the bacterium Escherichia coli (E. coli) is common. The broad majority of E. coli strains are completely safe to consume. Few, such as Shiga toxin-producing E. coli (STEC), can, nevertheless, cause significant foodborne illness. Humans become infected by consuming tainted foods such as uncooked ground beef, unpasteurized milk, and tainted fresh vegetables and sprouts.

Micro organism which are oxidase-terrible, gram-terrible, rod-fashioned, motile through peritrichous flagella, and non -spore generating belong to this genus. they are anaerobic, which means they produce fuel from complex sugars. these are methyl red high-quality and Voges–Proskauer poor. several lines create polysaccharide drugs or microcapsules. these are o-nitrophenyl-b-D-galactopyranocide superb & those generate indole, are unable to hydrolyze urea, and are incapable of growing in Mller's KCN broth. No hydrogen disulfide is formed, phenylalanine isn't deaminated, gelatin isn't liquefied, and gluconate is not oxidised on triple sugar iron (TSI) or Kligler's iron agar (KIA).Although most bacteria decarboxylate lysine and utilise sodium acetate, Simmons' citrate agar does not support their growth. Other Escherichia species include Escherichia blattae, Escherichia fergusonii, Escherichia hermannii, and Escherichia vulneris. The sixth species is Escherichia albertii. [1]

**Pathogenic Escherichia coli.**

E. coli strains can cause septicemia, pneumonia, meningitis, bladder and kidney infections, hemolytic–uremic syndrome (HUS), diarrhoea, and dysentery, to name a few. On the other hand, different strains with diverse combinations of virulence genes cause varied signs and symptoms. Despite their diverse toxicity, the vast species of E. coli strains found in the colon must be classified as non-virulent.

Various highly adaptive E. coli clones have begun showing unique virulence characteristics, making them able to survive in novel surroundings and lead to a vast spectrum of illnesses. These virulence features are usually stored on genetic elements that may be used to create new virulence factor combinations in new strains, or on genetic elements that were formerly mobile but have since evolved to be 'locked' into the genome. The combinations of most potent virulence factors only have lived past to be called unique E. coli 'PATHOTYPES' allowing them to affect healthy individuals. Enteric/diarrhea, urinary tract infections (UTIs), and

sepsis/meningitis are three of the most common illnesses. The six forms of intestinal pathogens include enteropathogenic E. coli (EPEC), enterohaemorrhagic E. coli (EHEC), enterotoxigenic E. coli (ETEC), enteroaggregative E. coli (EAEC), enteroinvasive E. coli (EIEC), and diffusely adherent E. coli (DAEEC). Uropathogenic E. coli causes UTIs, which are the most common E. coli infections outside of the gut (UPEC). Meningitis-associated E. coli, the serotype that leads to meningitis and sepsis, is proving to be an increasingly prevalent source of extraenteric disorders (MNEC). E. coli pathotypes linked in extraintestinal infections are now known as ExPEC. EPEC, EHEC, and ETEC all employ many of the same pathogens to produce sickness in animals. [2]

**Virulence Factors.**

In E coli two types of virulence factors have been recognized : toxins & surface antigens

**Surface antigens**

• **Antigen**: Endotoxic activity is caused by the somatic lippopolysacharide O antigen . The protection of the organism against phagocytosis and bactericidal actions is mediated by complement. The envelope or K antigens in normal serum defend against phagocytosis and antibacterial agents. Antibodies to the K & O antigens stop these activities from happening . The Kl envelope antigen is carried by the E. coli that causes septicemia & infant meningitis , The group B antigen of meningococci is comparable with it .

In early attachment and colonization crucial role is played by Fimbriae.

Due to the discovery of Colonisation factor antigens (CFA) in the enterotoxigenic escherechia which is the cause of diarrhea in males & females . During a urinary tract infection, fimbriae are also required for the organism's adherence. [2]

Human erythrocytes and uroepithelial cells have P blood group material that binds solely to P fimbria, as shown in uropathogenic strains.

**Toxins:** E.coli develops two types of exotoxins: enterotoxins & hemolysins

• Despite the fact that virulent strains manufacture them more frequently than avirulent strains, a function in pathogenesis is not seen to be played by hemolysis.

• In uropathogenic E.coli, CNF l (cytotoxic necrotizing factor-1) and siderophores are important components of adhesion & biofilm formation . • In the development of diarrhea Enterotoxins are involved . E.coli enterotoxins detected are of three types , (ST) heat stable toxin , (VT) verotoxin & heat (LT)labile toxin , are together given the terminology " Shiga-like toxin (SLT)".

• E. coli LT (heat-labile toxin) (De and colleagues found it in samples from adult diarrhea patients in Calcutta in 1956) . In terms of antigenic features, structure & mode of action E.coli is comparable to cholera toxin[3] . Each unit consists of a polypeptide subunit complex with five B subunits (B for binding) & one active subunit A. Subunit B of the toxin binds to the GMl ganglioside receptor present on the epithelial cells of the intestine , causing subunit A to divide into two fragments, Al & A2 . The Al fragment leads to activation of the adenyl cyclase present in the enterocytes, which produces cyclic adenosine 5' monophosphate (cAMP), which increases water and electrolyte outflow into the bloodstream.[3]

The heat-stable toxin (ST) of E. coli was discovered in 1970 and is composed up of antigenic polypeptides with a low molecular weight. STB and STA (or ST I, which is methanol soluble) are two forms of ST (or ST II, insoluble in methanol).[4]

In the stomach, STA activates cyclic guanosine monophosphate (cGMP). Within the duration of intragastric treatment of four hours , it causes fluid buildup in the intestines of newborn mice. A baby mouse is a frequent tool for demonstrating STA.[4]

ST B causes accumulation of fluid in young piglets (age : upto about nine weeks), but this is not seen in the baby mice. Although there is uncertainity in the mechanism of action , it excludes cAMP or cGMP. On plasmids, ST genes can be found with other genes such as drug resistance genes and LT genes. On the other hand, the genes STA & STB are not there on the exactly identical plasmid. [4]

• Verocytotoxin, commonly termed as verotoxin, which is a cytotoxic substance produced by E. coli that is affecting the Vero cells (i.e. the cell line created from kidney cells of Afrin green monkey). Because of its physical, antigenic, and biological similarities to Shigella dysenteriae type 1 toxin, it's also recognize as Shiga-like toxin (SLT). It acts by the inhibition of the creation of proteins. VT, like Shiga toxin, causes enterotoxicity in rabbit ileal loops in addition to

producing toxicity in Vero and HeLa cells. Both A and B subunits are present in VT. The genes in question are seen to be phage-encoded. VT 2 has been discovered as an antigenically distinct VT that, unlike VT 1 and Shiga antitoxin does not neutralize it.[5]

**Clinical Infections caused.**

E.coli gives rise to four distinct types of infections in the host:

• Urinary tract infection

• Diarrhea

• Septicemia, neonatal sepsis & neonatal meningitis

• Pyogenic infections [5]

The great majority of spontaneously acquired infections of the urinary tract are caused by E.coli and other coliforms (UTI). E.coli serotypes that are typically prevalent in a person's gut, such as O groups 1, 2, 4, 6, 7, and so on, cause community-acquired UTI (Case 1). Bacteria such as Pseudomonas and Proteus are more common in samples acquired following instrumentation in hospitals.[6]

Infection can be induced by urinary obstruction caused by prostatic hypertrophy, calculi, or pregnancy. Asymptomatic bacteriuria has been reported in 5-7 percent of pregnant women, which, if left untreated, can lead to infections which will appear with diverse symptoms later in pregnancy, pyelonephritis & hypertension.[6]

While 'ascending infections' induced by gut flora can cause lower urinary tract infections, pyelonephritis is most commonly caused by hematogenous spread. Most cystitis isolates lack K antigens, but bacteria that express K antigens are more likely to cause pyelonephritis. In general, E.coli that are P pili positive are uropathogenic.[6]

**Adhesion/Colonization.**

Adhesion factors in pathogenic E. coli strains leads to the colonization of the bacteria them where it doesn't normally survive, examples the jejunum, duodenum and ileum and the urethra. The commonest morphological structures created by adhesins are fimbriae (also called pili) or

fibrillae, which may be classified into various categories. Fimbriae are non-flagella rod-like structures having a diameter of 5–10 nm. Fibrillae can be long and wiry or curly & springy, with a diameter of 2–4 nm. Afa adhesins, which are described as afimbrial adhesins but appear to contain a thin fibrillar part which is not so easy to visualize, are formed by several diarrhoeagenic and uropathogenic E. coli strains. Supramolecular proteins, outer-membrane proteins . If the bacteria comes into touch with the correct receptor, even surface characteristics which are there on commensal E. coli strains can trigger signalling cascades. TLR4 binds to E. coli LPS and other Gram-negative bacteria's LPS, initiating a strong cytokine cascade that can initiate septic shock and death. Flagellin, the main component of flagella, can bind to TLR5, causing interleukin-8 production and an inflammatory reaction.[7]

**Pathotypes and Pathogenesis/Diarrheagenic E.coli.**

- Enteropathogenic E.coli
- Enterotoxigenic E.coli
- Enteroinvasive E.coli
- Enterohemorrhagic E.coli
- Enteroaggregative E.coli
- Diffusely adherent E.coli **(DAEC)**[8]

EPEC: These bacteria have been related to diarrhoea in babies and children, largely as a result of institutional outbreaks, but they can also cause sporadic diarrhoea in children and adults.

The presence of O antigens distinguishes EPEC. Colonies produced on cultivating with polyvalent & monovalent EPEC-O antisera can be detected via slide agglutination . EPEC are neither invasive nor create enterotoxins. The plasmid-encoded protein EPEC adherence factor (EAF) has been related with attachment in infantile enteritis. One more approach is adhesion to the enterocyte membrane. Such action is controlled by the chromosomally coded enterocyte effacement locus (L). [8]

Diarrhea induced by **enterotoxigenic E.coli (ETEC)** falls into two categories.

• Affects persons of all ages and is endemic to tropical poor nations. It can range in severity from more than light watery diarrhoea to a serious cholera-like infection.

• 'Traveller's diarrhea', which occurs when individuals go from nonendemic areas to endemic areas.

It adheres to the intestinal mucosa primarily through fimbriae known as colonisation factor antigens, which come in a variety of forms (CFA I, II, III, IV). ETEC generates LT, ST, or both types of enterotoxins (described under virulence factors).

Enterotoxins must be present in E.coli isolates for ETEC diarrhoea to be diagnosed.

Similar to enteroinvasive E.coli, the 'Alkalescens-Dispar Group' (EIEC). Because they can infiltrate interstitial epithelial cells in vivo, they're dubbed enteroinvasive E.coli, which is related to shigellosis. Such capacity to infiltrate cells is defined by a huge plasmid, and its identification maybe employed as a laboratory test.[8]

Enterohemorrhagic E.coli produces two strong toxins: verocytotoxin (VT) & Shiga-like toxin (SLT) (EHEC). These may cause diarrhoea in infants and the elderly, with symptoms ranging from a bit more than light diarrhoea to serious hemorrhagic colitis and hemorrhagic uremic syndrome (HUS). The main focus is endothelial cells which have rich blood supply. This might relate to the cause of HUS, which is characterised by capillary microangiopathy, which is a prevalent kidney illness. EHEC diarrhoea and its consequences are linked to E.coli serotype 0157: H7. 026: Hl is also included in this group.[9]

The presence of VT in faeces or culture isolates can be used to diagnose VTEC diarrhoea in the lab. Responsiveness can be greatly enhanced by normal and traditional or RTPCR using specific DNA probes for the VT I and VT 2 genes. On Vero or HeLa cells, the cytotoxic effects of VT may be determined. Other VTEC bacteria, unlike most E.coli strains, belong to serotype 0157:H7, which cannot digest sorbitol. As a consequence, testing for 0: 15 7 VTEC using sorbitol MacConkey medium is useful.[9]

Because they aggregate in a stacked brick structure on HEp-2 cells or glass, these strains are known as enteroaggregative E.coli (EAEC). Chronic diarrhoea has been associated to them, especially in underdeveloped nations. Although the most are 0-untypable, there are a handful that are H-typable.[9]

**Diffusely adherent E.coli (DAEC):** These are not very well known as pathogens.

Pyogenic infections: E.coli is the mostly causes intestinal leakage-related diseases such peritonitis and abscesses. They can even lead to pyogenic infections in the perianal region. One of the most prevalent causes of neonatal meningitis is bacteria.[10]

Life-threatening infections such as "systemic inflammatory response syndrome" (SIRS) & septic shock can be caused when E.coli enters the circulation . Since E.coli usually demonstrates multiple drug resistance, antibiotic sensitivity testing of strains is critical in therapy.[11]

**PREVENTION.**

Despite the numerous safeguards in place, people can become infected by eating tainted food, particularly raw or undercooked meals. There are, however, some easy steps that may be taken to limit the chance of being unwell as a result of possibly contaminated food, animals, or another sick person. By adopting proper food handling and hand hygiene habits, consumers may frequently lower their risk of being unwell at home.[12]

Personal hand hygiene is important. Hands should be cleaned thoroughly with soap, rinsed thoroughly, and dried with a disposable kitchen towel or a textile towel (to be laundered at 60°C on a regular basis) after managing raw vegies, roots, or meat, after contact with farm or after coming in contact with farm animals, after coming in any proximity of faeces from household pets, after going to the toilet or changing nappies (diapers) or before preparing, serving or eating food.[13]

Food handling:

- Anyone suffering from diarrhoea or vomiting should avoid handling food.
- Meat should be properly cooked, even minced meat.
- All fruits with skin should be peeled and cleaned thoroughly under running water.
- All veggies, especially those that will not be prepared before eating, should be thoroughly cleaned under running water.
- All root veggies should be peeled and rinsed under running water.

- Cooking vegetables and meat thoroughly kills disorder-causing germs and other organisms.
- Cross contamination, or the transmission of bacteria from raw to ready-to-eat or cooked food, may be avoided by using different cutting boards for raw and cooked meat or fresh vegetables, and washing the cutting board with soap between handling raw and ready-to-eat fruits and vegies.[14]

Most important step in prevention from E.coli infection is personal hygiene and the natural and surrounding hygiene. If this is taken care off, E.coli infections will be very less in occurrences.[14]

**TREATMENT.**

There are currently no medicines that can treat E. coli infection, reduce manifestations, or avoid after effects. Treatment for the vast number of people entails:

Drink plenty of water to avoid dehydration and weariness.

Avoid anti-diarrheal medications since they slow down one's digestive system and inhibit one's body from eliminating toxins. Antibiotics aren't normally recommended since they might increase the chances of significant problems and don't seem to effectively neutralize the infection.[15]

One will be admitted to the hospital if they have a significant E. coli infection that has resulted in a life-threatening kind of kidney failure (hemolytic uremic syndrome). IV fluids, blood transfusions, and renal dialysis are all part of the treatment.[16]

Without medical treatment, most healthy persons may recover completely from a STEC infection in approximately a week.[17] However, if a person has diarrhoea that lasts more than three days and is accompanied by a high temperature, bloody stools, or severe vomiting that causes dehydration, he or she should seek medical attention.[18-23]

**Conclusion.**

The study of the microbe E. coli has been done extensively in various ways . In studies of cytoskeleton, proliferation and metabolic activity it has been used as a model organism in general microbiology. It eventually became a common method for cloning genomes from both prokaryotic and eukaryotic cells, as well as transcription factor expression. E. coli is highly desirable as a regulate creature in antibiotic and decontamination effectiveness testing, as well as a faecal infection indicator organism in edibles, water, and the nature. It is an essential component of the gut microbial ecology in warm blooded organisms and homo sapiens. It is also known that, certain bacteria are antibiotic-resistant.

**References.**


1. Ahmed, R., Bopp, C., et al. 1987. Phage-typing scheme for Escherichia coli O157:H7. J Infect Dis, 155, 806-9.
2. Albert, M.J., Ansaruzzaman, M., et al. 1991. An ELISA for the detection of localized adherent classic enteropathogenic Escherichia coli serogroups. J Infect Dis, 164, 986-9.
3. Albert, M.J., Qadri, F., Haque, A. and Bhuiyan, N.A. 1993. Bacterial clump formation at the surface of liquid culture as a rapid test for identification of enteroaggregative E. coli. J Clin Microbiol, 31, 1397-9.
4. Allison, L. 2002. HUS due to a sorbitol-fermenting verotoxigenic E. coli O157 in Scotland. Eurosurv Wkly, 6, 2-3.
5. Andersson, P., Engberg, I., et al. 1991. Persistence of Escherichia coli bacteriuria is not determined by bacterial adherence. Infect Immun, 59, 2915-21.
6. Baqui, A.H., Sack, R.B., et al. 1992. Enteropathogens associated with acute and persistent diarrhea in Bangladeshi children, 166, 792-6.
7. Bernier, C., Gounon, P. and Le Bouguenec, C. 2002. Identification of an aggregative adhesion fimbria (AAF) type III-encoding operon in enteroaggregative Escherichia coli as a sensitive probe for detecting the AAF-encoding operon family. Infect Immun, 70, 4302-11.
8. Bilge, S.S., Clausen, C.R., et al. 1989. Molecular characterization of a fimbrial adhesin, F1845, mediating diffuse adherence of diarrheaassociated Escherichia coli to HEP-2 cells. J Bacteriol,171, 4281-9.

9. Bitzan, M., Ludwig, K., et al. 1993. The role of Escherichia coli O157 infections in the classical (enteropathic) haemolytic uraemic 21 Escherichia syndrome, results of a central European, multicentre study. Epidemiol Infect, 110, 183-63.
10. Brenner, D.J., Davis, B.R., et al. 1982a. Atypical biogroups of Escherichia coli found in clinical specimens and description of Escherichia hermannii sp. nov. J Clin Microbio, 15, 703-13.
11. Cravioto, A., Reyes, R.E., et al. 1988. Prospective study of diarrhoeal disease in a cohort of rural Mexican children, incidence and isolated pathogens during the first two years of life. Epidemiol Infect, 101, 123-34.
12. Cravioto, A., Telo, A., et al. 1991. Association of Escherichia coli HEp-2 adherence patterns with type and duration of diarrhoea. Lancet, 337, 262-4.
13. Crichton, P.B. and Old, D.C. 1985. Biotyping of Escherichia coli, methods and applications. In: Sussman, M. (ed.), The virulence of Escherichia coli. London: Academic Press, 315-32.
14. Donnenberg, M.S. and Kaper, K.B. 1992. Enteropathogenic Escherichia coli. Infect Immun, 60, 3953-61.
15. DuPont, H.L., Formal, S.B., et al. 1971. Pathogenesis of Escherichia coli diarrhea. N Engl J Med, 285, 1-9.
16. Gilligan, P.H., Janda, J.M., et al. 1992. Laboratory diagnosis of bacterial diarrhea. Cumitech 12A. Washington, DC: American Society for Microbiology.
17. Griffin, P.M. and Tauxe, R.V. 1991. The epidemiology of infections caused by Escherichia coli O157:H7, other enterohemorrhagic E. coli, and the associated hemolytic uremic syndrome. Epidemiol Rev, 13, 60-98.
18. Nataro, J.P. and Kaper, J.B. 1998. Diarrheagenic Escherichia coli. Clin Microbiol Rev, 11, 142-201.
19. Thakare, Seema H. "Assessment Of Role Of Diet, Life Style & Stress In The Etiopathogenesis Of Constipation In Geriatric Patients." International Journal Of Modern Agriculture 9, No. 3 (2020): 137–41.
20. Chandi, Dhruba Hari, Praful Patil, Smita Damke, Silpi Basak, and Rangaiahagari Ashok. "Bacteriologic Antibiography Outline of Isolates from Blood Culture at Tertiary Center." JOURNAL OF PURE AND APPLIED MICROBIOLOGY 14, no. 4 (December 2020): 2801–6. https://doi.org/10.22207/JPAM.14.4.55.

21. Patil, Praful S., Dhruba Hari Chandi, Smita Damke, Shital Mahajan, R. Ashok, and Silpi Basak. “A Retrospective Study of Clinical and Laboratory Profile of Dengue Fever in Tertiary Care Hospital, Wardha, Maharashtra, India.” JOURNAL OF PURE AND APPLIED MICROBIOLOGY 14, no. 3 (September 2020): 1935–39. https://doi.org/10.22207/JPAM.14.3.32.
22. Toshniwal, Vaishnavi, Gargi Mudey, Aditya Khandekar, Vandana Kubde, and Abhay Mudey. “Gram Positive Bacteria Carriage among Health Care Workers: An Under-Reported Source of Infections?” JOURNAL OF PURE AND APPLIED MICROBIOLOGY 14, no. 4 (December 2020): 2677–82. https://doi.org/10.22207/JPAM.14.4.45.
23. Jain, Jyoti, Shashank Banait, Iadarilang Tiewsoh, and Madhura Choudhari. “Kikuchi’s Disease (Histiocytic Necrotizing Lymphadenitis): A Rare Presentation with Acute Kidney Injury, Peripheral Neuropathy, and Aseptic Meningitis with Cutaneous Involvement.” INDIAN JOURNAL OF PATHOLOGY AND MICROBIOLOGY 61, no. 1 (March 2018): 113–15. https://doi.org/10.4103/IJPM.IJPM_256_17.