REVIEW OF LITERATURE
In 1980, in the developing countries an estimated 5 million children under 5 years of age died as a consequence of diarrhoeal disease. The deaths were an outcome of some 1000 million episodes that occurred among 338 million children in this age group and undoubtedly more frequently in poorer families (WHO, 1983). 3.5 million children still die due to diarrhoeal disease in developing countries (WHO, 1989). The diarrhoeal morbidity rate has been found to be higher in first two years of life. In less than 5 years' age group attack rate of diarrhoeal diseases ranges from 2-3 per child per year in many developing countries (Gordon et al, 1963; Synder and Merson, 1982; Reddiah and Kapoor, 1991). Mata et al in his study in rural Guatemala showed a higher incidence; 7.9 per child per year probably because of much closer follow up.

Most diarrhoeas occurring in general population are of an infectious nature. The recognition of role of certain viruses and bacteria as causes of diarrhoea now makes it possible to identify the causative agent in over 2/3rds of the diarrhoea presenting at treatment centre (WHO, 1980). This dramatic development reverses the situation present 2 decades ago when the aetiology in over 80% of these cases remained unknown.

A wide variety of infectious agents including viruses, bacteria and parasites cause diarrhoea in
susceptible host. Rotavirus, Norwalk agent, Adeno viruses, calci virus, corona virus and astro virus are notable among viruses. Bacteria like Escherichia Coli - Enterotoxigenic E. Coli (E.T.E.C.), Enteropathogenic E. Coli (EPEC), enteroinvasive E. Coli (EIEC), Enterococherent E. Coli (EAEC) and enterohaemorrhagic E. Coli Shigella - non typhoid salmonella, Campylobacter jejuni, Vibrio cholerae. 01 and non 01, Vibrio parahaemolyticus, Aeromonas hydrophila, Plesiomonas shigelloides, Pseudomonas aeruginosa, Klebsiella pneumoniae, Yersinia enterocolitica, Clostridium difficile and C. perfringens, Arizona and Edward. Sicile have been incriminated in the etiology of diarrhoea.

Among parasites, Entamoeba histolytica, Giardia lamblia and cryptosporidium have been found to be associated diarrhoea.

The commonest bacteria responsible for diarrhoea in children are EPEC, ETEC and Shigellae (Sanyal et al, 1977; Mahalanabis, 1975; Black et al, 1981). Vibrio cholerae becomes important in endemic areas.

Rotavirus is the most important cause of viral diarrhoea. It is responsible for upto 50% of acute diarrhoea in children in 6-24 months group visiting treatment facilities and 5-10% of all diarrhoeas in the community (WHO, 1980).

Amongst parasites E. histolytica and G. lamblia are dominant agents (Sanyal, 1977 and Mahalanabis, 1977).

Bacterial enteropathogens express a wide range of virulence factors or specific mechanism that enable
them to overcome host defence mechanism. They may produce diarrhoea by one or more of the following mechanisms.

1. Invasion of mucous with inflammation and ulceration.
2. Elaboration of cytotoxins that greatly alter the mucosal surface.
3. Elaboration of protein enterotoxins that greatly alter the intestinal salt and water balance without affecting mucosal morphological features.
4. Colonization and adherence to the surface.

**BACTERIAL PATHOGENS GROUPED BY PATHOGENIC MECHANISM**

**INVASIVE**
- Shigella
- *V. enterocolica*
- *V. parahaemolyticus*

**CYTOTOXIC**
- Shigella
- Enterohaemorrhagic E.Coli

**TOXIGENIC**
- E.T.E.C.
- *Vibrio cholerae* 01 and Non 01
- *K. pneumoniae*
- *Aeromonas hydrophila*
- *Plesiomona shigelloides*

**ADHERENT**
- E.P.E.C.
- Enterohaemorrhagic E.Coli

**VIRAL DIARRHOEA**

For many years viruses were suspected by paediatricians of causing a significant proportion of episodes
of childhood gastroenteritis which previously would have been undiagnosed. This suspicion seems to have been well founded, because over recent years, viral infections have become accepted as a major cause of diarrhoeal disease, particularly in children below 2 years of age (Cukor and Blacklow, 1984).

Rotavirus is best known of these viral agents, but there are many others including Norwalk agents adenoviruses, coronaviruses, calciviruses, small round viruses (SRV).

**ROTAVIRUS**

Rotavirus is probably the commonest virus which infects humans and is responsible for a great deal of vomiting and diarrhoeal illness in infants and young children. Rotavirus is the major cause of severe dehydrating diarrhoea in both developed and developing countries. The organism is responsible for 40-60% diarrhoea cases requiring hospitalization in developed countries and it accounts for 20-40% of severe diarrhoeas among children in developing world (WHO, 1989).

Human rotavirus was first visualized in 1973 in Australia in duodenal biopsy specimen of infants and young children suffering from non bacterial gastroenteritis (Bishop et al, 1973) by electron microscopic examination. Later they were easily recognised in stool specimen directly by E. M. (Flewett, 1973). In relatively short time thereafter laboratories all over the world reported the presence of rotavirus in the stool specimen from infants
and young children with acute diarrhoea.

Rotaviruses are members of the family Reoviridae, the prefix "rota" means wheel which the virus resembles morphologically. The virus has an average diameter of 70 nm with an inner core of RNA, surrounded by a double shield capsid. It contains a genome of 11 segments of double stranded RNA, which is capable of reassortments.

Rotavirus disease is predominantly a disease of under 2 years old with peak incidence about 7-12 month of age (Brandt et al, 1983; Rodreugz et al, 1977; WHO Sci. group, 1980). The average incubation period is about 1 to 3 days (Davidson et al, 1975). The onset of illness is characterized by severe watery diarrhoea vomiting and low grade fever. Vomiting is particularly common feature of rotavirus diarrhea in children as compared with occurrence of this symptom in gastroenteritis due to other causes (Rodriquez et al, 1977). The mean duration of rotaviral illness in 5 to 8 days. The concentration of rotavirus in the faeces reaches its maximum peak shortly after the onset of illness and diminishes gradually until 9 to 10 days.

The stool are usually liquid and without blood Faecal leucocytes are uncommon and mucous is some times seen (Rodriquez et al, 1977; Hei-her et al, 1978). Common clinical feature of rotaviral illness is isotonic dehydration, occurring in 40-83% of the cases. The level of dehydration is usually less than 5% but can be greater
in severe cases.

In temperate climate most episodes occur during winter season. In tropics rotavirus enteritis tends to occur throughout the year although seasonal variation have been reported.

In a usual case of rotavirus enteritis vomiting is a prominent early feature and in many cases precedes the onset of watery diarrhoea. Mucous is found in stools in upto 25% cases, blood is rare. Mild temperature elevation is present in 30-50% cases. Upper respiratory symptoms have been reported (WHO, 1980). Symptoms of upper respiratory tract infection have been reported to be associated with rotavirus diarrhoea (Rodriquez et al, 1977; Lewis et al, 1979). But rotavirus has never been demonstrated to infect respiratory tract (Lewis et al, 1979). The association may be coincidental.

The importance of rotavirus illness has been well documented in developed countries. In the developed countries rotavirus is responsible for about half of the hospitalized cases of acute diarrhoeal illness in this age group (Brandt et al, 1983; Kapikian et al, 1976 and Rodriquez et al, 1977).

In studies from Bangladesh by Black et al(1981) in moderately severe to severe gastroenteritis, rotavirus were found to be most important pathogen below 2 years of age and younger, 46% of such patients shed
agent. Bacterial agents were detected more frequently than rotavirus among children of 2 years of age and older.

The greater degree of dehydration was observed in a Bangladesh study, during rotavirus diarrhoea 44% of the children experienced dehydration and 30% visited the treatment centre. In contrast ETEC diarrhoea only 14% cases below 2 years of age had dehydration and 5% visited treatment centre both \( p < 0.001 \) (Black et al, 1981).

Although rotavirus infection has been widely accepted as a major cause of gastroenteritis in infants and young children. Asymptomatic excretion is not uncommon. Champasur et al (1984) found asymptomatic virus shedding in 71% neonates, 50% of 1 to 6 months old infants, and 26% of children aged 7 to 24 months in a prospective study of patients admitted in Paris.

Infection with rota virus induces seroconversion and elevation of antibody titre. The prevalence of rota virus antibody is high in newborns due to transfer of passive antibody from the mother then it diminishes in first 6 months of life and again high titre are present by 2 to 3 years of age and maintained throughout the life. In a study in Washington, rotavirus antibody was detected in over 90% of children by third year of age (WHO, 1980).

**STUDIES IN INDIA**

In India first study was conducted in Vellore by Holmes et al (1974) first of its kind from India.
detected rotavirus in 3 of the five children between 4-22 months age group.

In another study from Vellore Maiya et al (1977) reported 26% hospitalised diarrhoea cases to be rotavirus positive. This study also showed seasonal pattern of diarrhoea associated with rotavirus.

Paniker et al (1977) reported an epidemic diarrhoea in north Kerala caused by rotavirus. They demonstrated rotavirus particles by E.M. examination in all the 10 faecal samples of patients 7 months - 4½ years of age old. All of them were admitted with diarrhoea and vomiting.

In 1981 another epidemic of rotavirus diarrhoea was reported from Manipur by Sen Gupta et al (1981).

Yet another hospital based study from Calicut, by Panikar et al (1982) carried out over a period of 16 months showed high prevalence of rotavirus diarrhoea in infants and young children. In this study rotavirus was detected by electron microscopy in stool of 70.7% of the children. Prevalence of virus was high nearly 100% of cases examined during Nov., to January and Lowest in May. Prevalence of rotavirus was high (75.1%) in infants from 6-23 months of age.

Samantray et al (1982) studied the prevalence and seasonal occurrence of rotavirus diarrhoea among 212 preschool children with diarrhoea from a community and 99 cases from hospital in Delhi. The detection rate of
rotavirus was 21.2% in the community and 32.2% in hospital cases. There were no conspicuous peaks in the detection rates throughout the year, though a relatively lower peak was detected during July through September. The clinical features of rotavirus diarrhoeal disease did not show any significant difference.

Bhan et al (1987) in their study of etiology of acute diarrhoea in 204 children below 5 years of age detected rotavirus in 20.6% cases, from an outpatient dispensary.

Bhat et al (1985) studied the etiological role of rotaviruses in acute diarrheal illness in 0-5 years children admitted to a pediatric ward. Rota virus accounted for 16.3% of acute diarrhoea, peak detection rate was found in Jan. and Feb.

Mohandas et al (1987) detected rotavirus in 18% of children below 2 years who presented with acute diarrhoea in an outpatient clinic in Vellore. Syndrome of watery diarrhoea and vomiting was highly associated with rotavirus infection. Upper respiratory tract infection and fever was not significantly associated with rotaviral diarrhoea in this study.

An epidemiological study of rotavirus infection initiated by the National Institute of Virology (NIV) Pune in January, 1981. For the base line data, hospital records in a large Government teaching hospital in Pune, were screened retrospectively for years 1979-80. Stool
specimens from a representative sample of 213 hospitalized children with diarrhoea and from an equal number of non diarrhoeal controls were investigated, both by EM examination and ELISA for detection of viruses. Rotavirus were observed in 28.6% of diarrhoeal patients less than 12 years of age and only 1.4% of non/diarrhoeal controls. The prevalence of rotavirus was much higher 96.7% in children aged from 6-24 months. Seasonwise analysis showed significant number of children with rotavirus during colder months of the year (ICMR Bulletin, 1986).

There are 4 serotypes of rotaviruses designated 1 to 4. While they all cause disease, serotype-1 appears to be most common cause of epidemic rotavirus disease in countries with temperate climate. Information on distribution of rotavirus according to serotype in developing countries is limited (WHO, 1989).

It has been estimated that effective rotavirus vaccine could reduce all diarrhoeal deaths by 30% in the age group of 6-24 months and overt 500,000-1000,000 deaths in children annually (WHO, 1989).

E. coli

E. coli, the most familiar and numerous organism in the faecal flora of the humans and other animals, is a well known opportunistic pathogen when outside its normal etiological niche. Although E. coli has been suspected also for many years as a possible etiology of
diarrhoeal disease with its habitate, this association was not conclusively proved until mid 1940's when hospital nursery outbreaks of severe lethal diarrhoea occurred which were shown to be due to single serotype of E. coli (Bray, 1945; Taylor et al, 1949).

In the evaluation of these outbreaks, serotyping was shown to be an excellent epidemiological marker for recognition of bacterial virulence and these organisms were termed enteropathogenic E. coli (EPEC). Although the mechanisms whereby these organisms cause diarrhoea were not known. Enterotoxins were suspected as being virulence factor as early as 1956 by De et al and later by Taylor and Bettlemiem (1966) but their existence could not be conclusively demonstrated. In mid to late 1960's enterotoxin producing E. coli was first isolated from domestic young animals with severe diarrhoea. Shortly thereafter strains of ETEC were described in the etiology of severe cholera like illness in humans in Calcutta (Sack et al, 1971).

The understanding of pathogenesis of diarrhoea due to E. coli has undergone considerable change in past two decades. Today it has been accepted practice to identify and to distinguish the E. coli into 4 types
(1) Enterotoxigenic E. coli (2) Enteropathogenic E. coli
(3) Enteroinvasive E. coli (4) Enterohaemorrhagic E. coli.
ENTEROTOXIGENIC E. COLI

ETEC can produce one or both of the two recognised enterotoxins: a heat labile enterotoxin that is immunologically related to cholera toxin (LT) and a heat stable, low molecular weight, non antigenic enterotoxin (ST), thus there are LT strains, ST strains and LT/ST strains. The genetic material that controls the production of these enterotoxins is located on plasmids and thus relatively easily transferable to recipient strains (WHO Scientific group, 1980).

Like cholera toxin, LT induces a secretory diarrhoea through increased production of adenylase cyclase and with a subsequent increase in cyclic-AMP. In case of ST, it has been shown to cause secretory diarrhoea by stimulating guanylyl cyclase activity, leading to persistent increase in cyclic GMP.

We now know that these organisms are a major cause of diarrhoeal illness in children in developing part of world (WHO Scientific group, 1980). Studies carried out in developed countries notably in USA, Canada, Japan and England have shown that ETEC are an infrequent cause of diarrhoeal illness (Merson and Black, 1980).

During past decade enterotoxogenic E.coli has appeared as one of the most prevalent diarrhoeagenic agent in children in developing world. However, isolation rates of ETEC show a wide variance in different

This variation in different studies represent true geographical differences, the time of the years of
study and different assay employed for heat labile enterotoxin may influence incidence rates (Deb et al, 1983).

Paul et al (1980) reported ETEC in 8.67% of hospitalised children with diarrhoea, but in this study
difference in prevalence rates of enterotoxigenic E. coli in children with diarrhoea and controls was not significant statistically. This study was conducted over a limited period of time and over a small number of cases.

Panhotra et al (1980) conducted a year long study in Chandigarn and isolated ETEC in 13.8% children with diarrhoea. In this study a total of 99 strains of E.coli were isolated from 127 children with acute diarrhoea below 2 years of age. Only 13 of them were enterotoxigenic 5 strains showed production of LT/ST, 4 produced only ST and 4 only LT.

Black et al (1980) conducted a study at Matlab Hospital in Bangladesh. Over 6500 stool specimens were examined in 2 years period (They also examined ETEC in diarrhoea in other age groups). ETEC were found to be responsible for 26% of all diarrhoea cases seen at the hospital. The incidence was highest in age group below 2 years.
In a study in rural Bangladesh 197 diarrhoeal children age 2-60 months were studied for its aetiology. The ETEC were isolated most frequently (27%) followed by rotavirus and shigella. 85% of ETEC-ST were associated with the diarrhoea compared with only 62% of ETEC-LT of 70% ST/LT-ETEC were associated with diarrhoeal illness (Black et al, 1981).

Deb et al (1983) studied 201 preschool children suffering from acute diarrhoeal illness and investigated them to determine the prevalence and seasonal occurrence of ETEC diarrhoea in a periurban community near Delhi. 77 age matched children formed the control group. ETEC was isolated from faecal specimen of 22.9% patients and 7.9 in No control group (p < 0.01) Seasonal fluctuation was demonstrated.

Bhan et al (1987) conducted a study in slum community near Delhi. This included 204 children below 5 years of age and 98 controls. ETEC in this study was present in 23% children with acute diarrhoea. Peak incidence of ETEC was observed during second and third years of life (26.1% and 29.1% respectively).

Bhat et al (1985) reported 7.4% incidence of ETEC diarrhoea in a hospital based study from Bangalore in children under five years of age.

Jaysheela et al (1989) studied the characteristics of 75 E. coli isolates from cases of diarrhoea in infant and children from different parts of the country and
concluded that (i) ETEC is the most important cause of E. coli diarrhoea amongst infants and children in our country followed by EPEC and ETEC (ii) LT producers are more common in our country than LT/ST or ST strains.

**CLINICAL FEATURES**

The clinical illness caused by ETEC is largely the same whether the strains produce one or both of the enterotoxins, range from mild diarrhoea to severe cholera like disease. Both the enterotoxins produce a secretory diarrhoea in small intestine (WHO Scientific group, 1980).

Black et al (1981) in their study indicated that ETEC diarrhoea last considerably longer in infants than adults. In children below two years of age they observed along with watery diarrhoea in all 58 infants, 53 had vomiting and 30 had fever. The mean duration of diarrhoea was 39.5±3.8 hours before hospitalisation, 61.8±5.5 hours after hospitalisation and total duration was 101.4±6.7 hours.

Asymptomatic infections with ETEC have been well documented in many studies of non hospitalised children (Black and Merson, 1981).

**ENTEROPATHOGENIC E. COLI (EPEC)**

Diarrhoea associated with faecal E. coli has been recognised for almost a century but the presence of E. coli in normal stools made it hard to distinguish which type of E. coli can cause diarrhoea and which are normal commensals in gastrointestinal tract. A particular serological type
of *E. coli* was associated with most episode of summer diarrhoea in infants in Britain (Bray, 1945) and this was followed by introduction of serotyping to identify strains of *E. coli* in outbreaks of diarrhoea. Identification of *E. coli* by serotyping was used widely and by early 1960's there were 170 known serotypes of *E. coli* although only a dozen or so were found commonly. When enterotoxins became recognized it was found that most strains of EPEC were enterotoxigenic, since then setotyping became unpopular as a routine diagnostic procedure by late 1970's (Gracey, 1980). EPEC seems to have relatively unimportant as a cause of diarrhoea in infants and young children in developed countries. But EPEC continue to be important in developing countries.

Strains of EPEC which are non-invasive and which do not produce LT or ST, have been found, which are nevertheless able to cause diarrhoea (Annohymus, 1983). Other toxins might be involved in diarrhoea pathogenesis for example Vero toxin (VT) (Konowalchuk et al, 1977). Attachment of EPEC to intestinal mucosa is an essential virulence mechanism and this, itself may be involved in diarrhoea causation by production of faecal areas of mucosal damage to intestinal brush border at site where EPEC attach to the gut (Clausen and Christie, 1982).

The epidemiology of EPEC disease in developing countries is not so well defined. EPEC in these areas are more frequently isolated from diarrhoea cases in
second six months of life. Institutional outbreak have been less common and community outbreaks are more common (WHO, Scientific group, 1980).

Sanyal (1981) in his review of "epidemiological importance of diarrhoeal agents in India", stated that EPEC constitute most important etiologic agents of diarrhoea in infants and children in India. He observed that amongst commonest serotypes 026 is found in all three region of the country viz. north, south, and the east. The commonest serotypes in north zone 020, 026 and 086 from south zone 0.26 0.55 and 011 and from the east zone are 026, 0127 and 0128. The reported incidence of EPEC diarrhoea from India ranges between 5 to 18% (Sanyal, 1981).

Sarkar et al (1980) studied the role of enteropathogenic E. coli associated with diarrhoeal disease in children admitted in a hospital in Delhi. Out of a total 1326 patients, 223 strains of E. coli isolated in pure culture were serotyped. A total 58.8% strains could be serotyped. 018, 026, 020, 086 and 0126 were most prevalent serotype, in that order.

Agarwal et al (1981) studied bacterial aetiology of acute diarrhoea in infants and children below 2 years of age in an out patient clinic in Chandigarh. 127 children with acute diarrhoea were studied. In acute diarrhoeal group E. coli was isolated as predominant growth in 77 (56.66%) of cases, only 10% strains belonged to classical serotypes. Enteropathogenic serotypes of E. coli were recovered from 8% of control cases.
Gupta et al (1985) in a prospective epidemiological study of acute diarrhoea in children below 3 years of age in semiurban slum community observed that *E. Coli* contributed for 23.59% possible etiological agent. 1/4th of isolated strains were typable with 15 antisera used. *O:18* was the commonest serotype.

Sen et al (1985) in hospital based study in Calcutta, in children under five years, implicated EPEC as possible etiological agent in 17.2% cases of acute diarrhoea. EPEC was predominant agent isolated in infants below 6 months.

Bhat et al (1985) in hospital based study from Bangalore found EPEC as etiologic agent in 9.7% cases of acute diarrhoea in admitted patients below 5 years of age.

Bhan et al (1987) reported incidence of EPEC diarrhoea 7.8% of children with acute diarrhoea attending a dispensary.

**SHIGELLA**

Shigellosis is one of the common causes of diarrhoea or dysentry among young children (Agarwal et al, 1981). Shigellosis is some times known as bacillary dysentry. There are four recognized species of *Shigella* - *S. dysenteriae*, *S. flexneri*, *S. boydii* and *S. Sonnei*. These micro-organisms invade the large intestine, some times into the terminal ileum and cause intraepithelial proliferation and inflammation, penetration beyond lamina
propria is rare. Invasiveness can be demonstrated by
guinea pig kerato conjunctivitis model (The sereney test) or
in the cell culture. Some patients may have predominantly
watery diarrhoea, instead of more common typical dysen-
teric features. The watery diarrhoea is produced by
*shigella enterotoxin* (which has molecular weight 30,000)
and have cytotoxic property. The exact role of this toxin
is not known.

*Shigella*, one of the most important bacterial
agent of acute diarrhoea has been studied extensively.
The reported incidence of this organism in diarrhoea
ranges from 4-39 percent. *Shigella* has been found to be
present in endemic, epidemic and localised outbreaks of
acute diarrhoea. Analysis of species and serotype
distribution shows *S. flexnari* to be most prevalent
species in India (Sanyal, 1981).

Feldman et al (1970) reported the prevalence of
*Shigella* in 6.7% preschool children in a southern Indian
semiurban community. The incidence of infection below
6 months was low (1.3%). The commonest strain identified
was *S. flexnari* followed by *S. Sonnei*. The percentage
of isolation for any *Shigella* serotype was highest in
1-2 year age group.

Sanyal et al (1977) isolated *Shigella* in 6.3
percent children with acute diarrhoea. All the 4 strains
were prevalent in their study.
Agarwal et al (1981), in their study of bacterial etiology of acute diarrhoea in children below 2 year of age isolated 43.3% bacterial enteropathogen. *Shigella* constituted 14.9% of the isolated enteropathogen.

Stoll et al (1982) conducted a study at ICDDR Bangladesh in patients attending treatment centre over a period of one year. They isolated *Shigella* from 11.6% of 3350 patients studied. And it was second most common enteropathogen over the age of 2 years. The clinical manifestation found were :-

1. Watery diarrhoea occurring in young children and associated with shorter duration of illness and with more vomiting and dehydration.

2. Dysentry with stool blood and abdominal pain were the most useful sign and symptoms for diagnosis of shigellosis. Simple visual inspection of stool blood was correctly identified in 44% of all the cases infected by *shigella*.

Santhanakrishanan et al (1987) studied the clinical spectrum of disease in children under: 5 years of age. Among 250 stool samples, examined *Shigella* species were isolated from 22% cases. Fever (69.09% cases) Vomiting (71%), Tenesmus and rectal prolapse (50%) and dehydration were presenting features. Children under 2 years of age were predominant victims and 80% of cases identified were under two years of age. Measles and malnutrition played a greater role in predisposition to diarrhoea and dysentry.
Associated infections like pneumonia and septicemia are significant contributory factors for increased morbidity and mortality among children with shigellosis (Alam et al, 1984). Hemolytic uremic syndrome with acute renal failure has been an important complication of shigellosis reported from Sri Lanka (Lambadsuriya, 1986).

Mohandas et al (1987) in their etiological study of patient (≤3 years of age) attending an outpatients clinic in Vellore, identified shigella in 15% cases. Out of total 245 children studied 36 had Shigella infection. Mucous, blood in stool was present in 12, 8 had watery diarrhoea, half of the children had fever, 19 had abdominal cramps. The syndrome of classical dysentery was associated (p ≤0.001) with shigellosis. It was also observed that infants younger than 6 months, breast fed children were unlikely to have shigella infection. Fever and presence of mucous in stools was not significantly associated with shigella infection in this study.

Dutta et al (1989) studied the clinical and bacteriological profile in shigellosis in Calcutta before and after an epidemic (1984-1987) in children (below 5 years of age) hospitalized for shigellosis over a period of 4 years. During 1984 epidemic of shigellosis - it was isolated from 46.6% of dysentry patients and from 22.8% patients of watery diarrhoea. The predominant serotype observed was S. dysenteriae type I from dysentry(37.3%)
and watery diarrhoea patients (17.1%). During post epidemic period in 1985 and 87, 27.9% and 8.3% Shigella were isolated from dysentry and watery diarrhoea patients respectively. Then the isolation rate of Shigella flexnery increased

Shigella infected patients presented with both syndrome of dysentry and watery diarrhoea. Vomiting was more common with the watery diarrhoea while fever was seen in both patients with dysentry and watery diarrhoea.

**CAMPYLOBACTER JEJUNI**

*Campylobacter jejuni* (formerly referred to as a related vibrio) is a relatively recent addition to the growing list of agents causing infective diarrhoea. In several developed countries, the frequency of isolation of this organisms from patients of acute diarrhoea has transcended that of conventional enteropathogens like *shigella* and *Salmonella*. In recent years the significance of *C. jejuni* as an etiologic agent of human enteric disease has been established in developing countries. However, the detection of large number of inapparent infections particularly among infants and children in developing countries makes it difficult to assess the extent of the problem of campylobacteriosis.

The organism has been isolated from 4 to 15% of children with acute diarrhoea in both developed (Buczler et al, 1973 and Pai et al, 1979) and underdeveloped
(Stoll et al., 1982 and Blaser et al., 1980) countries. From developed countries the organism was rarely isolated from healthy individuals.

Nayyar et al (1983) studied the prevalence of *C. jejuni* diarrhoea among 155 children suffering from acute diarrhoeal illness. *C. jejuni* was isolated from 16(10.3%) of the patients and 2(4.7%) of the controls (p 70.05). The difference in excretion rate of *C. jejuni* from patients with diarrhoea and controls was insignificant in this study. The highest frequency of isolation was in 61-144 months age group. The organisms was not isolated from any child below 5 years of age. The clinical features consisted of fever (68.8%), abdominal pain (43.8%) blood with stools (43.8%), the usual duration of diarrhoea was more than 1 week.

Rajan et al (1982) reported 14.8% isolation of *C. jejuni* from healthy children in a random sample from southern India.

In another study from Calcutta (Nair et al, 1984), *C. jejuni* was isolated from 7.7% of 392 hospitalised cases with acute diarrhoea. The recovery rate from normal healthy individuals was 4.4%. The preschool children were most commonly affected. In this study the high incidence of mixed infection was observed with other known enteropathogens. Khatua et al (1984), in their study, isolated *C. jejuni* in 2% cases and none from asymptomatic controls.
The clinical features of patients with \textit{C. jejuni} appears to be quite different from that encountered in the developed world. The majority of the patients excreting \textit{C. jejuni} as the sole pathogen had watery diarrhoea (Similarly in Bangladesh, the complaints of all diarrhoeal patients versus those with \textit{C. jejuni} infection were identical with two exception: abdominal pain was less common among patients with \textit{C. jejuni} and watery diarrhoea was slightly more common.

\textbf{NON TYPHOID SALMONELLAES}

Salmonellae is well known organisms in causation of acute diarrhoea. It is commonest in children under age of 5 years and particularly in infants under 12 months of age. The disease can be spread through contaminated food (such as poultry) milk or water and perhaps requires a relatively large inoculum. A wide range of species can affect human, and all serotypes of \textit{salmonella} except \textit{S. typhi}, and \textit{S. paratyphi A}, can cause gastroenteritis in man and animals. The incidence of gastroenteritis caused by different serotype varies from time to time and place to place (WHO, 1980).

Diarrhoea initiated by \textit{Salmonella} may be produced by several mechanisms. Many patients present with non-specific watery diarrhoea, clinically identical to that caused by enterotoxigenic \textit{E. coli}, several toxins have been identified but whether they are responsible for excess
intestinal fluid production in human remains to be proved. *Salmonella* can also initiate diarrhoea by indirect stimulation of energy system within epithelial cells. *Salmonella* can penetrate superficial layer of mucosal lining without destroying epithelial cells and sometimes *Salmonella* infection can disseminated.

The incubation period of the salmonella diarrhoea is short, 8 to 48 hours. It is characterised by nausea, vomiting, abdominal pain, loose watery diarrhoea, which sometimes may contain mucous and blood. Vomiting is usually not severe fever $10^\circ \text{F}$ to $102^\circ \text{F}$ is seen in as many as 70% of patients. Septicemia to Salmonella is more common to first three months of life (Fiegin, 1987).

*Salmonella* is a causative agent of diarrhoea in India have remained relatively of less importance due to food habit even though strains are isolated in community based studies and also in outbreaks (Sanyal, 1981). The incidence of Salmonella in acute diarrhoea varies from 0.10% in different studies. (Sanyal et al (1977) failed to isolate Salmonella species in the study of 206 diarrhoeal children. Bhan et al (1987) isolated 2.5% *Salmonella* in their study. Similarly Sen et al (1985), Gupta et al (1985) have reported relatively lower incidence of *Salmonella* (0.9%, 1%) respectively). Bhat et al (1985) from Southern India have reported 10.8% prevalence rate of *Salmonella* in causation of acute diarrhoea. Fule and Kaundinya (1985) reported incidence of isolation to be
4.91% from a rural hospital of Maharashtra, in this study Salmonella typhymurium was the commonest strain (80%). Ram et al (1987) detected in Salmonella 10% (178 positive patients out of total 1980 patients) with diarrhea attending a hospital, S. typhimurium and S. senftenberg comprised the bulk of serotype isolated. The incidence of diarrhea due to Salmonella was maximum amongst the patient below one year of age and it decreased gradually with increase of the age.

Although Salmonella seems to constitute 2-5% cases of diarrhea, they have potentiality of causing severe, possibly lethal illness.

**ACUTE DIARRHOEA IN BREAST FED VS NONBREAST FED**

Breast milk provides not only nutrition for the growing infants but also active protection against the development of infections, particularly those of gastro-intestinal tract. Apart from being hygeinic, largely uncontaminated, breast milk is also endowed with many protective substances such as immunoglobulins, lymphocytes, macrophages, lysozymes and lacto-ferritin which may play an anti-infective role particularly in the gut (Goldman and Smith, 1973).

Educated and affluent section of the community living under conditions of good hygiene can bottle feed their babies safely (Clavano, 1982). Most mothers in
developing countries have neither the knowledge nor the money, time, sanitary conditions, nor the basic facilities to bottle feed their babies. For many of these mothers feeding bottle is indeed a baby killer (Muller, 1975). Lack of hygiene and education allows the feeding bottles to be heavily contaminated with bacteria and causing the baby to have frequent episodes of diarrhoea.

Studies from the developing countries have unequivocally shown the protective role of breast feeding in infectious disease (Mata et al, 1976 and Kumar et al, 1981). Mata et al (1976) in their prospective study found that adequate growth and survival were characteristics of exclusively breast fed infants in first months of the life. Despite high rate of infection, children exhibited considerable resistance to intestinal protozoa, enterobacteri-aace and enteric viruses. Resistance against colonic invaders is attributed to bifidus flora and that against agents acting in small bowel. In this study diarrhoeal disease was least during breast feeding period and increase with the weaning to reach maximum peaks at the time of weaning.

Kumar et al (1981) in their prospective study carried out from birth to one year of age on underprivileged rural Indian infants and privileged urban to study the effect of feeding pattern on morbidity and mortality. The lower mortality (p <= 0.01) and morbidity (p <= 0.01) were recorded in breast fed babies. Irrespective of place of
residence, socio-economic status and maternal education. Diarrhoea was less common ($p \leq 0.001$) among the breast fed infants. More so during the first four months of the life, in this study difference in morbidity becomes less marked during five to twelve months. As almost all of the breast fed babies were given some supplements and in this group maximum number of morbidity were noted. Incidence of diarrhoeal disease in mixed fed and bottle fed babies were significantly higher.

Saran et al (1979) from Varanasi found the higher prevalence of diarrhoeal illness in breast fed infants as compared to mixed fed infants and children. Bhatia et al (1980) also found that incidence of gastroenteritis is definitely lower in breast fed infants.

Many studies from more affluent countries in recent years have shown either a moderately decreased incidence in diarrhoeal disease and other infections or no significant difference.

Mittal et al (1983) in their hospital based study found that prevalence of breast fed infant among the non-diarrhoeal infants was significantly ($p \leq 0.01$) higher than in diarrhoeal infants. In the same study microbial flora of the gut was studied in relation to feeding pattern. No differences were observed in frequency of various organisms isolated from rectal swab of breast and bottle fed infants with or without diarrhoea. Highly pathogenic organisms EPEC, ETEC, Shigella and Salmonella were
frequently cultured from exclusively breast fed infants with diarrhoea. This study suggested that the breast feeding in the environmental conditions prevailing in communities is rather inadequate to protect against the development of diarrhoeal disease with highly pathogenic organisms.

Fallot et al (1980) however, failed to find any bacterial pathogen among hospitalised diarrhoeal infants who had been largely breast fed. Cushing and Anderson (1982) failed to find any protection against toxigenic E. Coli amongst breast fed infants. Weinberg et al (1984) observed that the incidence of Rotavirus infection, its average age of occurrence and severity among differently fed infants were largely comparable. The protection against rotavirus infection is only marginal in breast fed.

It is noteworthy that the diarrhoea morbidity and mortality continues to be significantly prevalent in areas of the world where the breast feeding is the dominant mode of feeding. Protective effects of breast feeding are more obvious in poor socio-economic areas with heavy environmental contamination. The protective effects observed even in these areas are also not absolute even among purely breast fed infants. The breast feeding can provide a significant but not absolute protection against diarrhoeal disease (Mittal, 1986).
ACUTE DIARRHOEA AND MALNUTRITION

Acute diarrhoea and malnutrition are commonly associated in many of the developing countries. Diarrhoea may affect nutritional status in several ways.

1. The intake of food due to anorexia is decreased.
2. Loss of macronutrients and micronutrients in the faeces (Einstein et al., 1972).
3. Decreased diarrhoeal gut enzyme activity.
5. Withholding the food as a measure to control diarrhoea.

Diarrhoeal disease is so devastating to infants (Synder and Merson, 1982) in regions of world where malnutrition is prevalent. It is suspected that somehow undernourished child may be particularly vulnerable to infectious diarrhoea. There are some clinical observations to suggest that acute diarrhoeal disease is more frequent and more serious among the malnourished subjects than among those of normal nutritional status (Hansen et al., 1962; Robertson et al., 1960 and Ghai and Jaishwal, 1970).

Based on a two year longitudinal study of diarrhoea in infancy and early childhood Ghai and Jaiswal (1970) reported spell frequency of diarrhoeal disease during the phase of undernutrition. In this study 60% undernourished children suffered from diarrhoea disease as compared to 20% of those with normal nutritional status. When children with diarrhoeal disease in preceding period of three months or more deteriorated nutritionally due to
dietary factors, the spell frequency of diarrhoea was 8.2 per 100 child weeks, during succeeding period of observations as compared to frequency of 3 episodes per 100 child weeks in children maintaining the normal nutritional status. Improvement in nutritional status likewise reduced the spell frequency.

Recent studies from NIN Hyderabad and Bangladesh have failed to show any increase in the attack rate of diarrhoeal illness. Chen et al (1981) on the basis of a prospective field study in Bangladesh reported that child nutrition appears to exert little effect on subsequent diarrhoeal incidence. This study suggested that impact of diarrhoea in predisposing and exacerbating malnutrition may be the most important of the bidirectional interaction. The predominant effect of nutrition on diarrhoea may be through disease incidence. Palmer et al (1976) demonstrated that duration of cholera purging among malnourished children was greater than among well nourished children, presumably because turnover and replacement of diseased gut epithelial cells were decreased due to malnutrition.

Mittal et al (1980) studied the clinical, biochemical and bacteriological profile of acute diarrhoea in malnourished children. In their study severe dehydration was more often seen in grade III malnutrition children. Serum sodium levels were significantly lower in malnourished children but it had no effect on outcome. On the other hand hypokalemia in malnourished children was more often fatal.
Bacteriological flora was significantly different in these two groups. Pathogens like *Salmonella*, *Shigella* and *Klebsiella* were more often grown in malnourished group as compared to well nourished group.

Malnourished children with already compromised nutritional status could be expected to tolerate diarrhoea poorly. Chen et al (1980) have shown as increase of 3 to 4 times in diarrhoeal mortality among malnourished children compared to that in normal nourished children. Mittal et al (1980) observed a mortality rate of 10.5% among malnourished children as compared to 2.6% in normal nourished children. In their study fluid loss and electrolyte imbalance was the major cause of the morbidity and mortality in these cases.

Ray et al (1986) studied the specific enteropathogens in relation to severe malnutrition in children with acute gastroenteritis. Enteropathogenic profile was studied in 65 malnourished children and 50 well nourished children with acute diarrhoea. Pathogenic organisms like *Salmonella* and *Shigella* were isolated in significantly higher number in malnourished children with diarrhoea as compared to well nourished children (p \( \leq 0.001 \)) while rotavirus detection was greater in well nourished children.

The relationship between malnutrition and infection are synergistic and each factor adversely
affects the other. Protein energy malnutrition has been identified as most frequent cause of acquired immuno-deficiency in man (Seth, 1985). There may be general increased susceptibility to conventional entropathogens and associated malnutrition may adversely affect mucosal and enzymatic functions.