# “CLINICAL PROFILE OF ACUTE VIRAL GASTROENTERITIS IN ADULTS – A ONE YEAR CROSS-SECTIONAL STUDY”

REG NO. BG0110004

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

**DEPARTMENT OF MEDICINE,**
**JAWAHARLAL NEHRU MEDICAL COLLEGE,**
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# ENDORSEMENT

This is to certify that the dissertation entitled **"CLINICAL PROFILE OF ACUTE VIRAL GASTROENTERITIS IN ADULTS – A ONE YEAR CROSS-SECTIONAL STUDY"** is a bonafide research work done by **THE CANDIDATE REG NO. BG0110004**.


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# LIST OF ABBREVIATIONS USED

| | |
|---|---|
| µg | - Micro gram |
| $^0$C | - Degree Celsius |
| Ad | - Adenovirus |
| AIDS | - Acquired immunodeficiency syndrome |
| ARD | - Acute respiratory disease |
| CD | - Cluster of differentiation |
| CDC | - Centre for Disease Control |
| d | - Day |
| DNA | - Deoxyribo nucleic acid |
| EIA | - Enzyme immuno assays |
| ELISA | - Enzyme Linked Immuno Sorbent Assay |
| HIV | - Human immunodeficiency virus |
| HS | - Highly Significant |
| IgA | - Immunoglobulin A |
| IgM | - Immunoglobulin M |
| IU/L | - International units/Litre |
| K+ | - Potassium |
| Kg | - Kilogram |
| meq/L | - Milli equivalent/Liter |
| mg | - Milligram |
| mg/dL | - Milligram/deciliter |
| mL | - Milli Liter |

| | |
|---|---|
| mOsm | - Milli osmole |
| n | - Number |
| Na+ | - Sodium |
| NS | - Not significant |
| NSP | - Non structural protein |
| p value | - Probability value |
| PCR | - Polymerase Chain Reaction |
| RNA | - Ribo Nucleic Acid |
| RRV-TV | - Reassortant Rotavirus vaccine |
| S | - Significant |
| SD | - Standard deviation |
| SGOT | - Serum glutamic oxaloacetic transaminase |
| SGPT | - Serum glutamic pyruvic transaminase |
| spp | - Species |
| SV40 | - Simian virus serotype 40 |
| U.K. | - United Kingdom |
| USA | - United States of America |
| VP | - Viral protein |
| WHO | - World Health Organization |

# ABSTRACT

## Background and objectives

It is now appreciated that viruses are the most common cause of diarrhoeal illness worldwide. Viruses like rotavirus and adenovirus are the most common causative agents of acute viral gastroenteritis. The present study was aimed to investigate the etiology and clinical profile among adult patients with acute viral gastroenteritis.

## Methodology

This one year hospital based cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 100 patients presenting with passage of more than three stools per day with decrease in stool consistency, increase in stool urgency and/or vomiting and/or abdominal discomfort from January 2011 to December 2011 were studied. The diagnosis of viral etiology (Rota virus, Adeno virus and co-infection) was determined by Rapid kit test.

## Results

In this study most of the patients (41%) had age less than 30 years followed by 30 to 45 years (33%). Acute gastroenteritis was present in 51% and 49% males. The most common symptoms were diarrhea (100%) followed by vomiting (51%). Based on skin elasticity, tongue appearance and patient appearance 37% of patient had signs of dehydration. Abnormal blood urea and serum creatinine levels were observed in 66% and 50% of patients. Abnormal

liver functions were reported in 89%, abnormal renal function in 73% and electrolyte imbalance was noted in 12%.

**Conclusion and interpretation**

The overall prevalence of viral gastroenteritis was 26%. Viral gastroenteritis was significantly associated with symptoms of vomiting, fever, reduced urine output, signs of dehydration, abnormal liver and renal function tests ($p<0.050$).

**Keywords**

Adenovirus; Diarrhoea; Rotavirus; Viral gastroenteritis;

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Chapter 1

# Introduction

# INTRODUCTION

Gastroenteritis is the term used to describe a condition in which there is a combination of nausea, vomiting, diarrhoea and abdominal pain. This term is usually taken to mean those of infectious origin.[1]

Gastroenteritis is caused by a variety of viral, bacterial and parasitic pathogens. Worldwide there are more than one billion cases and at least four million deaths per year attributed to diarrhoea.[1]

Infectious diarrhoea is the most common cause of diarrhoea worldwide and is responsible for more deaths than gastrointestinal cancers, peptic ulcer, or inflammatory bowel disease.[2]

All of the bacteria, parasites, and viral pathogens are considered among the causes of infectious gastroenteritis. The wide diversity of bacterial and viral infections that may cause diarrhea complicates accurate surveillance and diagnosis, especially in developing countries. Gastroenteritis caused by viral agents are gradually increasing particularly in the developed countries. Although the improvements in sanitation have significantly decreased the gastroenteritis cases caused by bacteria and parasites, it has little effect on viral gastroenteritis.[3]

Since Kapakian first identified a virus in the stool of a patient with diarrhoea in 1972, many viruses have been described that cause diarrhoea directly or indirectly. It is now appreciated that viruses are the most common cause of diarrhoeal illness worldwide.[4]

Viruses like rotavirus, astrovirus and adenovirus are the most common causative agents of acute viral gastroenteritis. Rotavirus remains the leading cause of diarrhoeal disease overall, with the newly designated calicivirus family causing the most outbreaks in the industrialized nations. As diagnostic techniques improve, however, the importance of virus and other previously under-reported pathogens is becoming more apparent and the number of viruses associated with gastroenteritis continues to increase.[4]

In 1997 and 1998, group B rotaviruses were identified as the cause of sporadic cases of diarrheal disease in adults in Kolkata, India, representing the first description of cases of human group B rotavirus disease outside China.[5]

The seasonal variation of rotavirus diarrhoea in India varies in different geographical regions with high incidence in winter months at low relative humidity in north India.[6]

Peak incidences of infectious gastroenteritis are found in younger age groups (less than five years) while, severe disease leading to hospitalization and resulting in death is most frequently observed in elderly patients (more than 60 years).[7]

The clinician encounters acute viral gastroenteritis in three settings. The first is sporadic gastroenteritis in infants, which most frequently is caused by rotavirus.[8] The second is epidemic gastroenteritis, which occurs either in semiclosed communities (families, institutions, ships, vacation spots) or as a result of classic food-borne or water-borne pathogens.[9] Most of these infections are caused by caliciviruses. The third is sporadic acute gastroenteritis of adults,

which most likely is caused by caliciviruses, rotaviruses, astroviruses, or adenoviruses.

The clinical spectrum of rotavirus disease varies from asymptomatic infection to acute, severe, dehydrating diarrhea with vomiting that can be fatal. Initially, rotavirus replication was thought to be limited to the gastrointestinal tract in patients with gastroenteritis. This idea has prevailed despite repeated associations of rotavirus infection with systemic symptoms and non-gastroenteric clinical diseases, including respiratory illness and neurological syndromes. Rotavirus ribo nucleic acid (RNA) and proteins have been detected in the blood of infected children as well as in non-intestinal tissues such as the liver, heart, lung, and central nervous system. The role of this antigenemia and viremia in rotavirus disease is puzzling since rotavirus infections have not traditionally been linked to illness outside the gut.[10]

Rapid antigen testing of the stool, either by EIA or latex agglutination tests, is used to aid in the diagnosis of rotavirus infection. The rapid antigen detection tests have ensured rapid diagnosis with high sensitivity and specificity (>98% sensitivity and specificity) in several infectious diseases.[11] The antirotavirus antibodies (IgM, IgA) excreted in the stool after the first day of illness and antibody tests can remain positive for 10 days after primary infection and longer after reinfection; therefore, they can be used to confirm the diagnosis.

The rapid antigen detection tests for rotavirus and adenovirus have begun to be used widely in clinical setting and their use for the other viruses is also becoming widespread.[3]

Several studies have focused on the etiology of infectious diarrhea in hospitalized children.[12] However, the epidemiology of hospitalizations associated with gastroenteritis in adults remains least explored and not well investigated so far even though; it imposes a major burden on the patient and health care system.[13] Though, viral gastrointestinal infections remain a significant cause of morbidity and mortality worldwide, effective pharmaceutical treatments are lacking and guidelines from the 1980s remain the basis for our current management. No effective treatments have been developed for viral gastroenteritis. Current efforts are targeted at the development of suitable vaccines and the implementation of infection control measures.[4]

Considering the above facts, the present study was undertaken to investigate the etiology and clinical profile among adults patients with acute viral gastroenteritis and to provide data for recommendations concerning routine testing panel to guide clinicians in the rationale use of diagnostic methods by assessing the systemic manifestations including biochemical parameters.

Chapter 2

# Objectives

# OBJECTIVES

The objectives of the present study were;

1. To study clinical profile among adults patients with acute viral gastroenteritis.

2. To assess the systemic manifestations including biochemical parameters in adults patients with acute viral gastroenteritis.

Chapter 3

# Review of Literature

# REVIEW OF LITERATURE

Gastroenteritis is a term used for various pathological states of the gastrointestinal tract. The primary manifestation is diarrhea, but it may be accompanied by nausea, vomiting, and abdominal pain.[14]

Diarrhea (or diarrhoea) (from the Greek *dia* meaning "through" + *rheo* "flow" meaning "flowing through") is the condition of having three or more loose or liquid bowel movements per day.[15]

Acute diarrhea is defined as the abrupt onset of three or more loose stools per day. The augmented water content in the stools (above the normal value of approximately 10 mL/kg/d in the infant and young child, or 200 g/d in the teenager and adult) is due to an imbalance in the physiology of the small and large intestinal processes involved in the absorption of ions, organic substrates, and water. A common disorder in its acute form, diarrhea has many causes and may be mild to severe.[15]

Diarrheal episodes are classically distinguished into acute and chronic (or persistent) based on their duration. Acute diarrhea is thus defined as an episode that has an acute onset and lasts no longer than 14 days; chronic or persistent diarrhea is defined as an episode that lasts longer than 14 days. The distinction, supported by the World Health Organization (WHO), has implications not only for classification and epidemiological studies but also from a practical standpoint because protracted diarrhea often has a different set of causes, poses different problems of management, and has a different prognosis.[15]

**Epidemiology**

Frequency is difficult to determine because of underreporting, especially of mild illness, resulting in wide variations of estimated numbers of cases, hospitalizations, and deaths. As many as 100 million cases occur per year with several million healthcare visits and thousands of hospitalizations.

Diarrhea is the third leading cause of death related to infectious diseases all over the world; the rate of death due to diarrheal diseases is estimated as two millions a year (1.7 - 2.5 millions).[3]

Diarrhea is a leading cause of morbidity and mortality across all age groups and regions of the world. Among children 0-59 months of age, diarrhea is responsible for 1.236 million deaths annually and is the second leading cause of death in this age group.[16] Though mortality rates among older children, adolescents, and adults are lower than those observed in children under five, diarrhea still poses a substantial burden accounting for approximately 2.8 billion diarrhea episodes among older children, adolescents, and adults.[17]

A recent review reported that, total envelope of diarrhea cases among individuals ≥ 16 years of age is comprised of approximately 430 million annual episodes of diarrhea.[17] Study estimated that approximately 408.5 million episodes are mild (95%); 21.3 million are moderate (4.95%); and 0.2 million are severe (0.05%). Another study reported that, diarrhea affects almost every adult in the United Kingdom every year,[18] though most people do not consult a doctor about it.[19,20] The significantly higher mortality is observed among non-Hispanic whites.[21] Significantly higher mortality is observed among women.[21]

Gastroenteritis may occur at any age. Morbidity and mortality are much higher in the very young and the very old. It is a major cause of mortality among children younger than five years in developing countries, and persons aged 65 years or older account for the majority of hospitalizations and deaths in the United States.[21]

However, in Indian context studies on the prevalence of diarrhoea among adults are lacking. Few studies have reported the prevalence so far which are decade old. The incidence of diarrhea was assessed in a survey conducted among 6285 persons living in 1090 households in three Jhuggi clusters in Delhi, India. The survey revealed an overall incidence of diarrhea in the two weeks preceding the interview of 29.1/1000. This rate was higher among children under five years of age (60.2/1000) than among adults (13.8/1000). Dysentery was present in 13.1% of cases.[22]

Surveys in the United States suggest nearly every American will have one or more episodes of viral gastroenteritis per year. Of these cases, approximately 450000 adults and 160000 children will be hospitalized, and more than 4000 deaths will occur.[23]

The Centre for Disease Control (CDC) reported enteritis deaths more than doubled in the United States, an increase to 17,000 in 2007 from about 7,000 in 1999. Adults older than 65 years accounted for 83% of deaths and the majority of hospitalizations. Norovirus was associated with an estimated 797 deaths annually, causing the majority of gastroenteritis outbreaks, although 50% more deaths occurred in years when epidemics were caused by new strains of the virus.[24]

Viral infections cause 30-40% of gastroenteritis cases in industrialized countries. About 20% of the UK population develop infectious intestinal disease each year.[1]

A study[25] reported human viral gastroenteritis is of global significance since thousands of outbreaks have been reported in North America, South America, Europe, Africa, Asia and Australia. It is estimated that 1.4 billion non-fatal episodes occur on an annual basis.[26]

In 1997 and 1998, group B rotaviruses were identified as the cause of sporadic cases of diarrheal disease in adults in Kolkata, India, representing the first description of cases of human group B rotavirus disease outside China.[5] The seasonal variation of rotavirus diarrhoea in India varies in different geographical regions with high incidence in winter months at low relative humidity in north India.[6]

**Pathophysiology**

Diarrhea is the reversal of the normal net absorptive status of water and electrolyte absorption to secretion. Such a derangement can be the result of either an osmotic force that acts in the lumen to drive water into the gut or the result of an active secretory state induced in the enterocytes. In the former case, diarrhea is osmolar in nature, as is observed after the ingestion of nonabsorbable sugars such as lactulose or lactose in lactose malabsorbers. Instead, in the typical active secretory state, enhanced anion secretion (mostly by the crypt cell compartment) is best exemplified by enterotoxin-induced diarrhea.[27]

In osmotic diarrhea, stool output is proportional to the intake of the unabsorbable substrate and is usually not massive; diarrheal stools promptly regress with discontinuation of the offending nutrient, and the stool ion gap is high, exceeding 100 mOsm/kg. In fact, the fecal osmolality in this circumstance is accounted for not only by the electrolytes but also by the unabsorbed nutrient(s) and their degradation products. The ion gap is obtained by subtracting the concentration of the electrolytes from total osmolality (assumed to be 290 mOsm/kg), according to the formula: ion gap = 290 – [(Na + K) × 2].[27]

In secretory diarrhea, the epithelial cells' ion transport processes are turned into a state of active secretion. The most common cause of acute-onset secretory diarrhea is a bacterial infection of the gut. Several mechanisms may be at work. After colonization, enteric pathogens may adhere to or invade the epithelium; they may produce enterotoxins (exotoxins that elicit secretion by increasing an intracellular second messenger) or cytotoxins. They may also trigger release of cytokines attracting inflammatory cells, which, in turn, contribute to the activated secretion by inducing the release of agents such as prostaglandins or platelet-activating factor. Features of secretory diarrhea include a high purging rate, a lack of response to fasting, and a normal stool ion gap (ie, 100 mOsm/kg or less), indicating that nutrient absorption is intact.[27]


**Figure 1. Evaluation of the acute diarrhoea patient**[28]


**Figure 2. Classification of episodes of diarrhoea**[28]

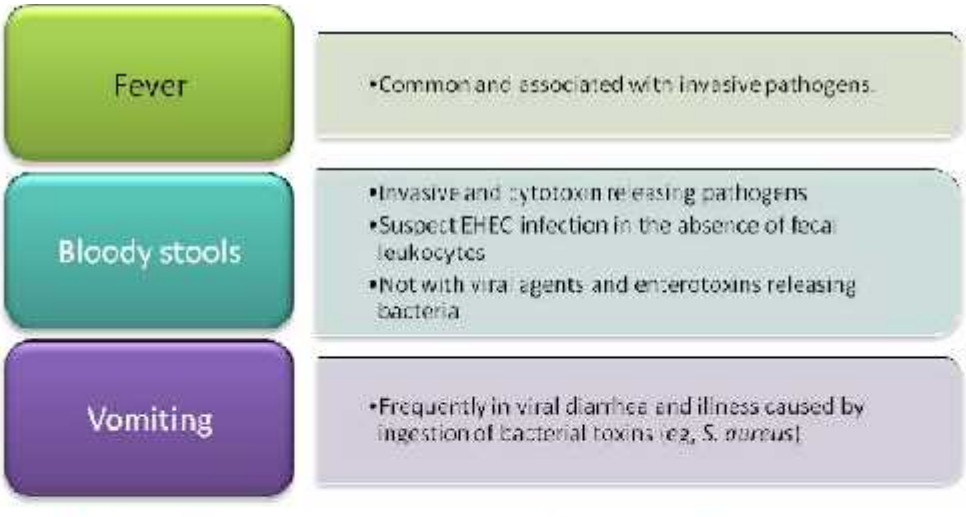


**Figure 3. Main symptoms to the causes of acute diarrhoea – EHEC, enterohemorrhagic, Escherichia coli.**[28]

**Clinical features**

A well-taken history, considering important epidemiologic factors, can help to identify not only the cause of diarrhea but also the patient at risk for complications. History in infectious and food poisoning cases varies depending on the agent, with variation in the onset; the frequency and consistency of the stools; the presence or absence of blood and mucus, and associated vomiting, cramps, or fever. The history should also identify risk factors for unusual causes of acute gastroenteritis and possible reasons to suspect noninfectious etiologies. Indications of dehydration or sepsis should also be sought.[27]

Duration of illness

- Duration and rapidity of symptom onset are important in determining the incubation period and possible infecting organism and in directing further care.

- Diarrhea that lasts longer than a month requires consideration of a different spectrum of etiologic factors than diarrhea that lasts less than 1-2 weeks.[27]

Fever

The presence of high fever (with or without chills) generally suggests that an invasive organism is the cause of diarrhea, although many extraintestinal illnesses can present with both fever and diarrhea, especially in children.[27]

Vomiting

- Vomiting, a symptom common to a host of illnesses, implies proximal bowel involvement.

- Vomiting is a leading symptom of intestinal obstruction, usually coupled with distention or if the patient has had gastric bypass surgery; however, distention may not be significant if the obstructing lesion is very proximal. Vomiting without diarrhea must always prompt a search for noninfectious causes and cannot be referred to as gastroenteritis.[27]

Pain

- The location and character of pain may be indicative of the area of infection because colonic involvement is usually associated with tenesmus and pain in either of the lower quadrants or the lower back, whereas jejunoileal infection may result in periumbilical pain.

- Cramps may be caused by an electrolyte imbalance.

- Pain, especially in patients older than 50 years, should raise the suspicion of an ischemic process.[27]

Stools

- Ask about frequency, amount, color, consistency (ie, watery, semisolid, odor), and presence of blood and/or mucus.

- Large volumes of stool are usually associated with enteric infection, whereas colonic infection results in many small stools.

- The presence of blood may indicate colonic ulceration (bacterial infection, inflammatory disease, ischemia).

- White bulky feces that float (high fat content) are due to a small bowel pathology that leads to malabsorption.[27]

Extraintestinal causes

- A history of any nonintestinal illnesses that can lead to diarrhea should be obtained. Vomiting and/or diarrhea may be a manifestation of that illness or a result of its treatment. Obtaining a history of recent surgery or radiation, food or drug allergies, and endocrine or gastrointestinal disorders is extremely important. The patient should always be questioned regarding prior episodes.

- Malaria, Whipple disease, irritable bowel, incomplete bowel obstruction, inflammatory bowel disease, nutritional disease, and carcinoid and malabsorption syndromes can all result in diarrhea and are examples of the numerous possible noninfectious cases.

- Drugs such as colchicine, quinidine, antimicrobials, cancer chemotherapeutic agents, and magnesium-containing antacids frequently cause diarrhea.[27]

Dehydration

- Orthostasis, lightheadedness, diminished urine formation, and a change in mentation are symptoms of marked dehydration, requiring aggressive treatment.

- These symptoms are particularly important in elderly patients, a group that is most at risk from diarrhea.

- Severe dehydration may also be associated with significant electrolyte imbalances.[27]

Epidemiologic factors

- A number of historical questions may provide clues to the etiology of the illness, including foreign travel, recent camping, recent antibiotic use, daycare attendance, and/or ingestion of raw, possibly spoiled, or new marine products, as well as similar illnesses in family, friends, or close contacts.

- An epidemiologic factor may be travel to developing countries where bacterial or parasitic agents are endemic and can cause infection or to campgrounds in developed regions.

- As many as 12% of diarrheal illness cases may be caused by rotavirus in travelers to Asia, Africa, and South America.

- Infections via the fecal-oral route are prevalent in children who attend daycare centers. Rotavirus has an infection rate of nearly 100% in

exposed children younger than 2 years. Other family members are also at risk for infection.

- Exposure to a public vomiting episode in a public location such as cruise ship or casino can lead to exposure to aerosolized norovirus infection.[27]

Though most diarrhea episodes are self limiting and dehydration can usually be controlled with oral rehydration therapy, it would be ideal to be able to prevent diarrhea, especially the more severe episodes which have a higher likelihood of progressing to complications or death. Some prevention strategies such as improved water and sanitation and basic hygiene practices are generalizable and thus do not require knowledge of diarrhea etiology, but others such as vaccines would benefit greatly from a comprehensive understanding of the overall burden of pathogen specific diarrheal disease.[28]

**Causative agents and pathogenic mechanisms**

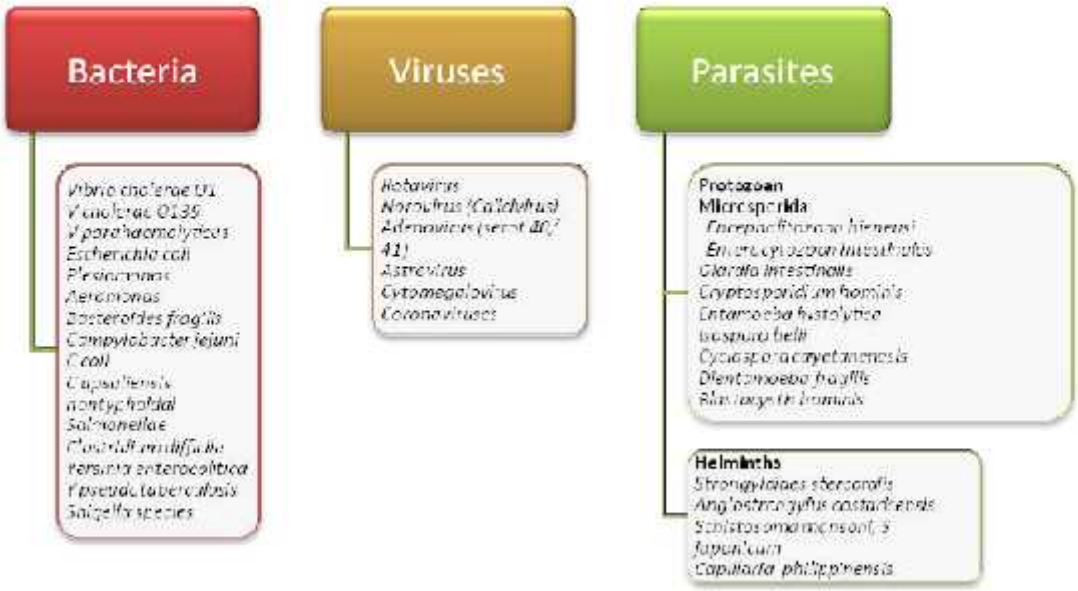


**Figure 4. Causative agents and pathogenic mechanisms**[28]

**Clinical features of infection with selected diarrhoeal pathogens**[28]

| | Pathogens | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clinical features | *Shigella* | *Salmonella* | *Campylobacter* | *Yersinia* | *Norovirus* | *Vibrio* | *Cyclospora* | *Cryptosporidium* | *Giardia* | *Entamoeba histolytica* | *Clostridium difficile* | Shiga toxin–producing *E. coli* (including O157:H7) |
| Abdominal pain | | | | | | V | V | V | | O | O | |
| Fever | | | | | V | V | V | V | | O | O | A |
| Fecal evidence of inflammation | | | | O | | V | | O | | V | | N |
| Vomiting and/or nausea | | O | O | O | | V | O | O | O | V | | O |
| Heme-positive stool | V | V | V | O | | V | | | | | O | |
| Bloody stool | O | O | O | O | | V | | | | V | O | |

*O=Occurs; V=Variable, not common; A=Atypical; N=Often not*

Viral agents

In industrialized countries, viruses are the predominant cause of acute diarrhea and show distinct winter seasonality.[28]

*Rotavirus*

- Leading cause of severe, dehydrating gastroenteritis among children.
- One-third of diarrhea hospitalizations and 500 000 deaths worldwide each year.
- Nearly all children in both industrialized and developing countries have been infected with rotavirus by the time they are three to five years of age. Neonatal infections are a common occurrence, but are often asymptomatic.
- The incidence of clinical illness peaks in children between four and twenty three months of age.
- Rotavirus is associated with gastroenteritis of above-average severity.[28]

*Human caliciviruses (HuCVs)*

- Belong to the family *Caliciviridae*, the noroviruses and sapoviruses.
- Previously called “Norwalk-like viruses” and “Sapporo-like viruses.”
- Noroviruses are the most common cause of outbreaks of gastroenteritis, affecting all age groups.
- Sapoviruses primarily affect children.
- May be the second most common viral agent after rotavirus, accounting for 4–19% of episodes of severe gastroenteritis in young children.

*Adenovirus*

- Adenovirus infections most commonly cause illness of the respiratory system. However, depending on the infecting serotype and especially in children, they may also cause gastroenteritis.

**Rotavirus**

Infective gastroenteritis causes substantial morbidity and mortality worldwide. Although various bacterial species have long been associated with gastrointestinal disease, specific viral causes of these infections were not delineated until the early 1970s. However, with the discovery of Norwalk virus in 1972 and rotavirus in 1973, the causative agents for most non bacterial gastroenteritis infections were identified. Almost immediately, the spectrum of viruses causing gastrointestinal infection in adults was recognised as differing from that in children. Among children younger than two years, nearly half of all cases of diarrhoea requiring admission to hospital can be attributed to rotavirus infection. By contrast, among adults most non-bacterial outbreaks of gastroenteritis can be linked to the Norwalk-like viruses. The important part played by viral pathogens besides the Norwalk-like viruses in adults with gastroenteritis is not yet fully appreciated. Specifically, the contribution of pathogens that typically affect children is not recognised by most clinicians who take care of adults. Such is the case for adult infections caused by the common paediatric pathogen rotavirus.[29]

Structure

In 1973, Bishop and colleagues described unique viral particles obtained from the duodenal mucosa of children with gastroenteritis.[30]

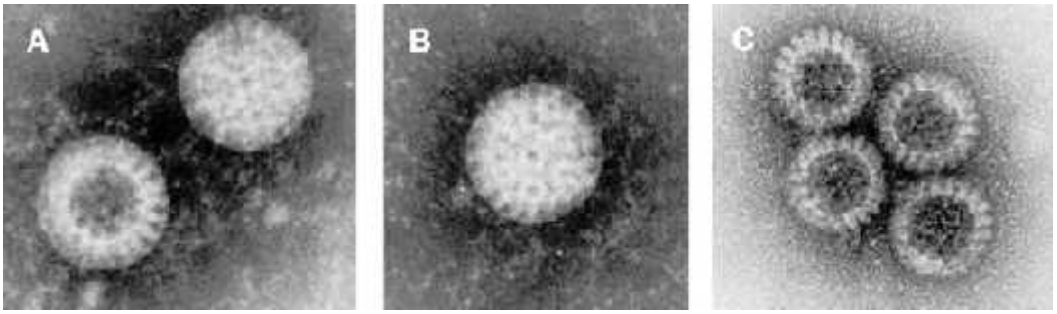


**Figure 5. Electron micrographs of a human strain of rotavirus B. (A,B) Completevirus; (A,C) stages in the breakdown of virus particles as seen inpreparations of stool samples (courtesy of Cornelia Büchen-Osmond, ICTVdB, the universal virus database of the International Committee onTaxonomy of Viruses)**[29]

Viruses with similar morphological appearance had been seen in 1963 in the intestinal tissue of mice with diarrhoea. Under the electron microscope, the 70 nm diameter viral particles first described in these reports had a wheel like appearance, prompting the name rotavirus, from the Latin rota. Rotavirus is a non-enveloped virus now classified within the Reoviridae family. 11 segments of double stranded RNA reside within the core. The RNA encodes six viral proteins (VP) that make up the viral capsid, and six non-structural proteins (NSP). The core is surrounded by an inner capsid, composed mostly of VP6, the primary group antigen and includes the epitope detected by most common diagnostic assays. Other structural proteins also seem to confer some degree of group specificity. The outercapsid is primarily composed of VP4 and VP7. VP4

contributes the spoke-like projections to the wheel-shaped appearance of rotavirus. This VP is cleaved by trypsin in vitro to yield VP5* and VP8*, which appear to play an important part in cellular attachment. The inner and outer capsids give the viral particle the double-layered icosahedral structure visualised on negative-stain electron microscopy.[29]

Seven distinct groups of rotavirus (named A to G) have been shown to infect various animal species. Of these, only groups A, B, and C have been reported as human pathogens.[31]

Group A is the primary pathogen worldwide and is the group detected by commercially available assays. Additional subgroups and serotypes can be identified by further characterization of VP4, VP6, and VP7 antigens. Group B seems to be limited to causing epidemic infection in Asia and the Indian subcontinent, whereas group C rotavirus causes endemic infections that frequently go unrecognised.[29]

Pathogenesis

Rotavirus spreads from person to person, mainly by faecaloral transmission. Although rotavirus has been detected in urine and upper-respiratory samples, these body fluids are not believed to be commonly associated with transmission. After ingestion, rotavirus particles are carried to the small intestine where they enter mature enterocytes through either direct entry or calcium dependent endocytosis. After cytolytic replication in the mature enterocytes of the small intestine, new rotavirus particles can infect distal portions of the small intestine or be excreted in the faeces. The amount of rotavirus excreted by adults

might be more variable. In at least one study shedding was 10–100-fold lower in travellers' diarrhoea. Symptom-free adults can shed rotavirus in quantities so low as to be undetectable by most routine assays.[29]

The mechanism by which rotavirus induces diarrhoea is poorly understood. Few investigations have incorporated the study of human mucosal samples. The reports that are available describe various findings: villous shortening, flattening, and atrophy, denudation of microvilli, mitochondrial swelling, distension of the endoplasmic reticulum, depressed disaccharidase concentrations, and infiltration of mononuclear cells.[32,33,34]

**Immunity to rotavirus**

Resolution of rotavirus gastroenteritis depends greatly on the immunological response of the host. In a normal host, rotaviral antigens are transported to Peyer's patches, undergo processing by B cells, macrophages, or dendritic cells and are presented to helper T cells. This cascade culminates in stimulation of rotavirus-specific B cell and cytotoxic T-lymphocyte-precursor expansion.[35]

Bernstein and colleagues[36] noted that stool rotavirus IgA concentrations peaked 14–17 days after infection and persisted for longer than 1 year, but at declining concentrations. The researchers[36] suggested that serum rotavirus IgA is a more consistent marker of rotavirus immunity than other antibody measurements.

However, rotavirus-specific IgA is frequently undetectable in duodenal fluid or faeces in the first week of infection, although symptoms might resolve within that time. This pattern suggests a mechanism independent of humoral immunity.

Offit[35] notes that infected mature villous epithelial cells are steadily replaced by less-mature enterocytes, which may be less susceptible to rotavirus invasion. Increased peristalsis improves clearance of viral particles and the non-specific activity of interferons can prevent VP translation.[35]

De Bouissieu[37] has reported that interferon concentrations correlate with a trend towards shorter duration of diarrhoea among patients who have rotavirus infection. Although many physicians presume that rotavirus infection will confer lifelong immunity, multiple investigations show that re infection can occur.

Bishop and colleagues[38] noted that infection with rotavirus during the neonatal period did not protect against developing rotavirus infection during the first three years of life but did lessen the severity of such infections. Rotavirus can elude host defences and induce repeat infection through several mechanisms. There are multiple groups, subgroups, and serotypes of rotavirus. Initial antibody response to infection is serotype specific, with limited production of cross-reactive antibodies. Subsequent rotavirus infections increase antibodies that cross-react with multiple serotypes.[39]

Additionally, certain elements of the rotavirus-specific immune response are short-lived. Rotavirus-specific secretory IgA is sometimes not detectable in faeces as early as one year after infection.[40]

**Clinical presentation**

An appreciation of the typical presentation of rotavirus infection in children is critical to understanding the spectrum of disease among adults. Primary infection with rotavirus typically occurs in infants between ages 6 months andtwo years, although infection in neonatal intensive-care units and severe infection in infants younger than six months are well documented.[41,42]

In all age-groups, the classic presentation of rotaviral infection is fever and vomiting for two to three days, followed by non-bloody diarrhoea.[43]

The diarrhoea may be profuse, and 10–20 bowel movements per day are common. When examined, the stool from affected patients is generally devoid of faecal leucocytes. Especially when associated with vomiting, the diarrhoea of rotavirus infection can precipitate severe and even life-threatening dehydration. Infants with repeat rotavirus infections are generally less-severely affected than those with primary disease.[44]

Among adults, rotavirus infection has been associated with a wide spectrum of disease severity and manifestations. As such, it is difficult to provide a concise description of a typical clinical presentation. Nevertheless, prospective studies of voluntary rotavirus ingestion have provided some insight, although the participants in these studies were primarily young healthy adults.

Data from several such trials[45-49] indicates that, volunteers illness most frequently began two to six days after ingestion and continued for one to four days. About two-thirds of study participants had an antibody response, with more

than half of all participants eventually shedding rotavirus. Symptoms were less common than evidence of infection, but most frequently included diarrhoea, fever, headache, malaise, nausea, or cramping. One participant passed 11 stools in one day.[45]

Among the volunteers, rotavirus particles were detectable in the stool from the start of symptom onset and persisted for more than 10 days in some. Three studies document rotavirus readministration to volunteers, noting that symptoms and antibody response were much less common.[45,47,49]

In several reports of rotavirus outbreaks among adults similar symptoms have been described.

In a prospective study[50] of 98 families with neonates followed up from shortly after birth, only 17 of 43 adults who had serological evidence of rotavirus infection were symptomless. 14 had diarrhoea and 11 had abdominal cramping. None had symptoms that necessitated medical care or absence from work.

In a separate study,[51] 14 parents of children with rotavirus gastroenteritis developed serological evidence of infection, but only three had diarrhoea.

Grimwood and colleagues[52] found, in a study of children with rotavirus in 28 families, that 18 of 54 adult family members exposed to rotavirus developed evidence of infection, and all but four were symptomatic.

In a study[53] of college students during a rotavirus outbreak, of the 83 individuals who met the criteria for rotavirus infection, 93% had diarrhoea, 90% abdominal pain or discomfort, 83% loss of appetite, 81% nausea, and more than

50% had fatigue, vomiting, headache, chills, subjective or low-grade fever, or myalgia.

Patients with underlying immunodeficiency are at risk of sustained symptoms and rotavirus dissemination, a phenomenon already recognised among children. This pattern was first described in 1980 when two of four children with underlying primary immunodeficiency who had rotavirus infection developed chronic diarrhoea that at least temporarily responded to administration of human milk containing a high titre of rotavirus antibodies.[54]

A geriatric patient with impaired natural killer-cell activity and impaired cellular and humoral immunity had rotavirus shedding for at least 35 days.[55]

Gilger and colleagues[56] noted that in four children who had various immune deficits and chronic diarrhoea from rotavirus, rotavirus was identified in the liver and kidney. Whether the involvement of liver or kidney was important is unclear.

Other investigators have assessed the course of rotavirus infection in patients with malignant disease. A wide spectrum of clinical manifestations and severity of illness have been reported.

Bolivar[57] screened 90 adults who had various solid tumours and leukaemia, with and without diarrhoea. He noted that two patients had rotavirus infection, both of whom had undergone bone-marrow transplantation and had developed graft-versus-host disease.

Troussard and colleagues[58] also prospectively assessed patients undergoing bone-marrow transplantation and noted rotavirus infection in eight of 94 patients. Adenovirus occurred concomitantly in two patients. Seven of the patients had isolates positive for rotavirus in the winter months, with acute onset, vomiting, and diarrhoea.

Rotavirus infections in adult patients infected with HIV-1 frequently present as a chronic diarrhoea with sustained viral shedding in stools. Albrecht and colleagues,[59] between 1987 and 1991, detailed a retrospective assessment of 106 samples from 66 patients infected with HIV-1 who had otherwise unexplained diarrhoea. 35 samples from patients without diarrhoea served as controls. 13 samples from nine case patients were positive for rotavirus; two of these samples were rotavirus recurrences 6 months after the initial episode. No symptom-free patients had rotavirus infection. Rotavirus was associated with diarrhoea of 2–8 weeks' duration in all patients and with abdominal cramping in eight patients.

Thomas and colleagues[60] looked prospectively at 862 samples from 377 UK HIV-1-positive patients with diarrhoea. Rotavirus was third in frequency to adenovirus and coronavirus, occurring in 11 (2·4%) samples. The median CD4 count of patients with rotavirus infection was nine.

Epidemiology

Five typical settings for rotavirus infections in adults are described however few modifications are proposed of these classifications to the following: endemic disease, epidemic outbreaks, travel related gastroenteritis, and infections

transmitted from children to adults. Although substantial overlap exists between the groups, our classifications clarify separate risk factors and clinical features.[29]

*Endemic disease*

Rotavirus infection in children is seasonal, with peak incidence in winter months in temperate climates.

Iturriza- Gomara and colleagues[61] noted that, in the UK between 1995 and 1998, notable numbers of infections began in December or January, peaking in March or April an falling to almost zero by July.

In the USA, Kapikian and colleagues[51] found that rotavirus cause 59% of diarrhoea cases necessitating admission to hospital in children between November and April, but could not be linked to cases from May to October.

In several studies findings suggest that adult disease is not as season-specific as childhood disease.

Cox and Medley[62] noted that IgM antibodies to group A rotavirus in adult serum in routine hospital samples are present throughout the year. IgM concentrations increased with older age, and antibodies reached 20% in March and fell to 10–11% during the summer months.

Cox and Medley[63] attributed the high rates to IgM persistence, IgM crossreactivity, or possibly to non seasonal high infection rates in adults. Other researchers have also found that rates of adult disease do not mirror the winter seasonality of infection in paediatric patients. These studies suggest that endemic

disease in adults may not arise solely from unrecognized transmission of rotavirus from children to adults.

The contribution of rotavirus as a cause of endemic gastrointestinal disease varies according to geographic distribution and characteristics of patients. In a small prospective study[58] in the UK, rotavirus caused 4.1% of acute diarrhoea in adults admitted to hospital.

Similarly, 3% of acute diarrhoea in Switzerland,[65] 3% of infectious diarrhoea pathogens in a Swedish clinic for infectious diseases,[66] 5% of adults with gastroenteritis requiring admission in Thailand,[67] 2–4% of adults older than 15 years with gastroenteritis presenting to their family physician in the Netherlands,[68] and nearly 4% of individuals older than 45 years in Michigan[69] were due to rotavirus.

In studies in other geographic areas even higher rates of infection have been seen.

In Japan, Nakajima and colleagues[63] reported that group A rotavirus had a role in 14% of patients with diarrhoea.

Pryor and colleagues[64] noted that rotavirus was second only to *Campylobacter* spp as a cause of diarrhoea among Australian adults, accounting for 17% of all cases.

In Indonesia,[65] 42% of patients presenting with diarrhoea had rotavirus-positive stools compared with 11% of control samples.

In a study of Mexican adults,[66] 63% of patients presenting with acute gastroenteritis during winter months were positive for rotavirus.

Even these results might underestimate the true prevalence of endemic rotavirus infection. Group C rotavirus is not routinely detected by commercial assays but it does contribute to endemic rotavirus infection worldwide. In a study[67] in the UK, 43% of patients were seropositive for group C rotavirus.

*Epidemic outbreaks*

Among adults, clusters of rotavirus infections most frequently occur in communities that are otherwise sheltered from more routine exposure to rotavirus-infected children.[68]

One of the largest outbreaks involved nearly 3500 people in 1964, in an isolated area of Micronesia.[69] Since then, other outbreaks have occurred among closed communities, including a Finnish military base,[70] an Israeli kibbutz,[71] and an isolated South American Indian community.

Outbreaks of rotavirus infection have also occurred in long-term health-care facilities, particularly those with close living quarters; compromised host immunity and multiple comorbid disorders might help facilitate the spread of infection.[72–76]

Cubitt and colleagues[73] described an epidemic of rotavirus among staff and patients in an extended-stay geriatric hospital, in which 15 of 39 residents developed symptoms and seven had confirmed rotavirus infection.

Halvorsrud and Orstavik[77] described an outbreak of 92 cases of acute gastroenteritis among nursing-home patients with identification of rotavirus by comparing acute and convalescent antibody titres. Rotavirus has been suggested as the causal pathogen in 5% of diarrhoea outbreaks in a study of institutions caring for elderly residents.[78]

Among adults, rotavirus outbreaks are not confined to geriatric populations. Group A rotavirus was associated with an outbreak of gastroenteritis among college students in the District of Colombia.[53]

Rotavirus also caused a waterborne outbreak of gastroenteritis in 1981 in Eagle-Vail and Avon, CO, USA in which severity of symptoms correlated with the amount of tap water consumed.[79]

Finally, Griffin and colleagues[80] screened 263 outbreaks of gastroenteritis in the USA between 1998 and 2000 and found that rotavirus was implicated in three outbreaks. Uniquely affecting Asia, group B rotavirus has been associated with outbreaks affecting large numbers of adults in broad geographic distributions of China and India.[5,81]

Diagnosis

Electron microscopy, which permits visualisation of the pathognomonic wheel-like appearance, was initially used for diagnostic purposes, but ELISA or EIA have become more commonly used. Commercial assays are reliable, convenient, and inexpensive, but require at least $10^4$–$10^7$ virions to generate a positive result.[82-84] The false-positive rate of commercial assays is 3–5%.[61] One

of the biggest limitations of most commercial assays is that they do not detect non-group-A rotavirus.[85,86]

Other more sensitive and newer methods are being used in research. One such method is PCR, which is up to 1000 times more sensitive than immunoassays.[84,87]

In one study[88] using PCR, 30% of otherwise healthy children shed virus for 25–57 days after symptoms developed. Although stool cultures are routinely tested for bacterial pathogens, the low frequency of detecting a positive result calls the usefulness of this practice into question.

Rotavirus infection can occur in a similar number of patients to some bacterial pathogens. Sending a sample of rotavirus antigen for testing by ELISA or EIA could potentially cut costs if by doing so either hospital stay or procedures could be avoided. Such a cost-benefit analysis in adult patients has not been published. One limitation is that adults might shed less rotavirus in faeces than do children, further hampering diagnosis.[89]

We suggest that obtaining rotavirus antigen testing for patients admitted to hospital with risk factors for rotavirus infection will be cost effective if additional inpatient studies can be avoided.[29]

Determination of rotavirus infection may also be beneficial if infectious patients can be isolated to prevent nosocomial spread. A positive rotavirus antigen test might also allow physicians to avoid prescribing antibiotics for travel-related rotavirus infection.[29]

*Travel-related gastroenteritis*

Rotavirus has been implicated as an important contributor to travellers' diarrhoea among adults, especially among those visiting Central America and the Caribbean. In a study of travellers returning from Jamaica, rotavirus was identified in 9% of individuals with diarrhoea, making the virus second only to enterotoxigenic *Escherichia coli* as a cause.[90]

In two studies of US students travelling in Mexico, electron microscopy identified rotavirus in about 25% of patients who had diarrhoea, compared with 3% and 15%, respectively, of symptom-free patients.[89,91]

In a third study,[92] a substantial rise of antibodies to rotavirus was seen in 17% of two student groups travelling to Mexico. By contrast, only 5–6% sero converted to Norwalk virus.

Ryder and colleagues[93] found rotavirus in 26% of Panamanian travellers to Mexico who had diarrhoea.

Sheridan and colleagues[94] similarly found that 36% of US Peace Corps volunteers and 30% of Panamanian travellers visiting Mexico had at least a four-fold increase in rotavirus antibody titres.

Adult travellers with rotavirus shed 10–100 times less rotavirus than do paediatric patients.[89,91]

*Infection transmitted from children to adults*

Although rotavirus can be linked to adult gastroenteritis in each of the other settings, adults who are in contact with children are at particularly high risk of infection. Transmission of rotavirus within families from children to parents seems to be a common event.[29]

Wenman and colleagues[50] showed prospectively that rotavirus infection occurred in 36 of 102 adults caring for children with rotavirus infection. By contrast, only four of 86 adults whose children had no documented rotavirus infection became infected.

Grimwood and colleagues[52] confirmed this finding in a report that a third of adult family members in New Zealand developed evidence of rotavirus infection. The same phenomenon has been seen among parents of more severely ill children.

Kim and colleagues[95] found evidence of rotavirus infection in 55% of adult contacts of children who were admitted to hospital with rotavirus, compared with 17% of adult contacts whose children were not infected. More casual contact might also be sufficient to facilitate rotavirus transmission from children to adults.

Rodriguez and colleagues[96] reported that nine of 12 adults experienced illness after exposure to children infected with rotavirus in a playgroup. Although substantial evidence is lacking, child-to-adult transmission of rotavirus is accepted to occur with some frequency on paediatric wards. Many paediatric

nurses, medical students, and house officers experience symptoms of gastroenteritis during the winter months when most paediatric rotavirus infections are encountered.

Von Bonsdorff and colleagues[97] described paediatric nurses at several different locations with acute gastroenteritis caused by rotavirus. Among seven hospital staff that developed diarrhoea after direct contact with children with diarrhoea staying in hospital, a rise in antibody titres was detected in three.104 Interestingly, in the same study, six of 45 medical students reported gastroenteritis. Three of the students had rotavirus particles present on electron microscopy and were noted to be more ill than the parents of the children who were infected. All had diarrhoea for 3–6 days and two of the three had low-grade fever and vomiting.

Another case report[98] supports transmission of rotavirus from children to hospital caretakers.

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Treatment

Treatment of rotavirus infections is primarily directed at symptom relief and restoration of normal physiological function. Oral rehydration should be attempted initially. In most developing countries, oral rehydration salt solutions are used extensively in children. Most adults can be managed by encouraging them to drink fluids. An additional intervention that has been used is administration of *Lactobacillus* spp bacteria to shorten the duration of diarrhoea.[99]

Although seldom used in children, codeine, loperamide, and diphenoxylate can help with symptom relief and control of the volume of diarrhoea. Bismuth salicylate, in a placebo-controlled double-blinded trial, was efficacious in treating the symptoms of rotavirus diarrhoea.[29]

Trial use of bismuth salicylate can be considered in adults when other coexistent infectious causes have been ruled out. If symptoms cannot be controlled and the patient becomes dehydrated, administration of intravenous fluids and hospital admission might be necessary. Rarely, extraordinary measures have been attempted to help resolve rotavirus infections. For example, human breastmilk has been provided to immunodeficient infected children to help resolve chronic diarrhoea.[54]

This option, however, is not practical in adults. Several groups report oral administration of human serum immunoglobulins possessing antirotavirus activity to bind free rotavirus antigen. Among adults, oral immunoglobulin

administration of 5–6 g daily for five days to bone-marrow-transplant recipients has been successful.[29]

Prevention

Prevention of rotavirus infection can be facilitated by avoiding exposures and faecal-oral spread. Contact with sick children and potentially contaminated food and water should be avoided. Since 43% of rotavirus virions placed on human fingers survive for 60 min, thorough hand washing is critical in prevention. Contact isolation for patients diagnosed with rotavirus infection is necessary, generally for the duration of hospital stay, because of sustained faecal shedding of low concentrations of virus. Gloves, gowns, isolation, and rigorous hand washing should be used in the care of individuals infected with rotavirus.[29]

Sattar and colleagues[100] reported that rotavirus survives best in low humidity on non-porous surfaces at room temperature or cooler. Phenolic disinfectants do not inactivate rotavirus; instead hypochlorite or sodium dichloroisocyanurate tablets with a free chlorine concentration of at least 20000 parts per million are recommended.[29]

A 70% ethanol solution is also effective in inactivation of rotavirus and can help to prevent environmental spread. Rotavirus infection in adults has been successfully prevented by use of a commercially available disinfectant spray on rotavirus contaminated fomites under experimental conditions.[29]

Given the substantial disease-related morbidity and mortality associated with rotavirus, the development of an effective vaccine is a priority. Although

multiple vaccines were under development, the tetravalent rhesus-human reassortant rotavirus vaccine (RRV-TV) seemed to produce the best results. The RRV-TV vaccine prevented about half of rotavirus infections, but was much more effective in preventing severe disease.[29]

Shortly after the vaccine was approved, the vaccine adverse-event monitoring system noted by mid-1999 an excess of cases of intussusception among recently vaccinated infants, eventually prompting the vaccine to be withdrawn. Two sharply differing perspectives on the risk and benefits of the RRV-TV vaccine and the Advisory Committee on Immunization Practices confirmation of its decision to withdraw its recommendation for the vaccine have been put forward.[101,102]

Other vaccines are under development. Vaccines have been primarily developed to attempt to decrease the severity of rotavirus infections in children. Although vaccines seem to be fairly safe in adults from the vaccine trials, we are unaware of any plan to consider vaccination in adult patients. Vaccination could theoretically be used in adult patients considering travel to Central America or the Caribbean or among immunocompromised patients to prevent or lessen the severity of rotavirus diarrhoea.[29]

**Adenovirus**

Adenovirus, a DNA virus, was first isolated in the 1950s in adenoid tissue–derived cell cultures, hence the name. These primary cell cultures were often noted to spontaneously degenerate over time, and adenoviruses are now

known to be a common cause of asymptomatic respiratory tract infection that produces in vitro cytolysis in these tissues.[103]

An extremely hardy virus, adenovirus is ubiquitous in human and animal populations, survives long periods outside a host, and is endemic throughout the year. Possessing 52 serotypes, adenovirus is recognized as the etiologic agent of various diverse syndromes. It is transmitted via direct inoculation to the conjunctiva, a fecal-oral route, aerosolized droplets, or exposure to infected tissue or blood. [103]

The virus is capable of infecting multiple organ systems; however, most infections are asymptomatic. Adenovirus is often cultured from the pharynx and stool of asymptomatic children, and most adults have measurable titers of anti-adenovirus antibodies, implying prior infection. Adenovirus is known to be oncogenic in rodents but not in humans.[103]

Adenovirus has been associated with both sporadic and epidemic disease and, with regard to infections among military recruits, is a significant cause of economic cost and morbidity because of the cessation of vaccine production in 1996.[103]

Of most recent interest is the role of adenoviruses as vectors in vaccination and in gene therapy. Adenoviruses can infect various cells, both proliferating and quiescent, and thus hold the promise of targeting many different tissues and diseased cell lines.[104-106]

The genome of adenovirus is well known and can be modified with relative ease to induce lysis or cytotoxicity of a specified cell line without affecting others.[103]

The virus itself can be engineered to remove its replicative capacity by removing essential genes. Additionally, specific genes can be inserted into the virus that then can repair defective metabolic, enzymatic, or synthetic pathways in the host. Suicide gene systems that convert nontoxic systemically delivered prodrugs to active chemotherapeutic agents have been delivered via adenoviral vectors directly into cancer cells. However, the greatest challenge in viral gene therapy, as might be expected, is the immune response to the viral vector itself.[103]

The complex mechanisms by which viral vectors may be incorporated into gene therapy and the rapid growth in this field put further discussion beyond the scope of this text.[103]

Pathophysiology

Adenovirus is a double-stranded DNA virus that measures 70-90 nm and that has an icosahedral capsid. The site of entry generally determines the site of infection; respiratory tract infection infections result from droplet inhalation, while gastrointestinal tract involvement results from fecal-oral transmission. Upon infection with adenovirus, one of three different interactions with the cells may occur.[103]

The first is lytic infection, which occurs when an adenovirus enters human epithelial cells and continues through an entire replication cycle, which

results in cytolysis, cytokine production, and induction of host inflammatory response.[103]

The second is chronic or latent infection, the exact mechanism of which is unknown, which frequently involves asymptomatic infection of lymphoid tissue. Lastly, oncogenic transformation has been observed in rats. During oncogenesis, the replication cycle is truncated, and adenoviral DNA is then integrated into the host cell's DNA. Thereafter, adenovirus produces potent E1A proteins that immortalize primary rodent cells by altering cellular transcription, ultimately leading to deregulation of apoptosis and malignant transformation. A clear role for adenovirus in human oncogenesis has not been established.[103]

Epidemiology

*Prevalence*

Adenovirus is isolated most commonly in infants and children. An increased incidence of infection was found in military recruits until the introduction of an effective vaccine against serotype 4 (Ad4) and serotype 7 (Ad7) in 1971. The economy-driven cessation of vaccine production by its sole producer in 1996 resulted in re-emergence of outbreaks, with Ad4 predominating in 98% of cases. The reservoirs exist within the training environment itself, and Ad4 has been detected on lockers, rifles, and bedding. Ad4 seropositivity of new recruits has been demonstrated to rise from 30% to almost 100%. Prolonged pharyngeal shedding and communal quarters contribute to outbreaks, with illness most commonly arising in weeks 3 to 5.[103]

Lost productivity and interrupted military training have prompted reinvestigation of vaccine production. Notably, co-infection with non-vaccine strains (B1 and E) have developed following vaccination,[107] and surveillance for emerging non-vaccine strains is still needed.

*Mortality/Morbidity*

- Severe morbidity and mortality associated with adenovirus infections are rare in immunocompetent hosts. Uncommon complications that increase the risk of mortality include meningoencephalitis and pneumonitis.

- Severe adenovirus infections have been reported in immunocompromised patients, such as transplant patients and those with inherited and acquired immunodeficiency states. Mortality rates associated with adenovirus infections among pediatric and adult transplant recipients have varied from 6%-70%.[108]

- Morbidity and deaths due to pronounced host inflammatory responses have occurred in past gene vector trials.

- As with polio vaccines, live adenovirus vaccines in the 1950s became contaminated with simian virus 40 (SV40), with resulting concern that this virus caused various cancers. After subsequent long-term follow-up, some studies have found a moderate association between SV40 and human cancers as a transforming virus, while some other studies have reported no such findings.[109,110]

*Race*

No racial predilection has been described.[103]

*Sex*

Adenovirus urinary tract infections are more common in males. The prevalence of other syndromes does not appear to be affected by the sex of the individual.[103]

*Age*

Adenovirus infection typically affects children from infancy to school age, but children of any age may be affected, including neonates. Young adults in any setting of close quarters and stress may be affected, as with military trainees.[103]

History

Because the manifestations of adenovirus infections are protean, the major syndromes are discussed separately. The major syndromes covered in this article include (1) acute respiratory disease (ARD), (2) pharyngoconjunctival fever, (3) epidemic keratoconjunctivitis, (4) acute hemorrhagic cystitis, (5) gastroenteritis, and (5) adenoviral infections in immunocompromised hosts.[103]

Given the range of manifestations, the varying levels and effects of immunosuppressive therapies, and rapid advances in molecular methods of detection, a comprehensive review of adenovirus infection in the immunosuppressed host is beyond the scope of this article; however, the author

plans to report the most salient features and general updates here. The reader is encouraged to review the literature for more detail regarding infection in specific settings.[103]

Acute respiratory disease (predominantly adenovirus types 1, 2, 5, and 6; occasionally, 3 and 7). As with many other viral syndromes, ARD is more common in spring and winter months. Approximately half of adenovirus respiratory infections do not cause symptoms. Adenoviruses account for 10% of all childhood lower respiratory tract infections. The contagiousness of adenovirus is facilitated by very high levels of viral particles (100,000-1,000,000/mL) in the sputum or oral secretions of infected adults. Additionally, adults who lack antibody may be infected by the inhalation of as few as 5 virions in droplet nuclei.[103]

Fever, rhinorrhea, cough, and sore throat, usually lasting 3-5 days, are typical symptoms of adenoviral ARD. Causes of sore throat may include pharyngitis, adenoiditis, or tonsillitis. Tonsillitis and otitis media were reported in up to 60% and 30%, respectively in a series of young children with serotype 4 predominance. Prolonged fevers, leukocytosis, and elevations in C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were also noted in over half of cases, suggesting potential for confusion of this viral syndrome with bacterial infections.[111]

Lower respiratory tract infections, including tracheobronchitis, bronchiolitis, and pneumonia, may mimic respiratory syncytial virus infection or

influenza. Notably, conjunctivitis in the presence of bronchitis suggests adenoviral infection.[103]

Fatal pneumonia is uncommon but is more likely in neonates and has been associated with serotypes 3, 7, 14, 21, and 30.[112]

Encephalitis, hepatitis, and myocarditis are uncommon.

From the 1950s to 1971 (prevaccine era), adenoviruses accounted for significant acute disease in 70% of military recruits. Adenovirus serotypes 4 and 7 were primarily involved. A live enteric-coated oral vaccine against these serotypes was introduced in 1971 and reduced adenovirus-related respiratory illness by more than 95% in recruits and thus attenuated outbreaks. Vaccine production ceased in 1996 for economic reasons, and vaccination administration was limited to high-risk periods until supplies ran out in 1999. In 1997, a large epidemic of more than 500 cases associated with serotypes 3 and 7 occurred in US Navy recruits. Most recent analyses suggest that serotype 4 has caused most military outbreaks since 1999, with the exception of Ad14.[113,114]

Adenovirus serotype 14

Ad14, referred to as the "super cold" in the media, has caused rare outbreaks of ARD since 1955.

Between May 2006 and June 2007, 141 cases of Ad14 infection were reported in clusters in New York, Oregon, Texas, and Washington. Almost 40% of affected persons were hospitalized, almost half in intensive care, with a 5% overall mortality rate. The cases in Texas involved military trainees at Lackland

Air Force Base, and subsequent cases were reported at Lackland, three other Texas military bases, and one eye culture in a civilian unassociated with the military. Adenovirus may be isolated from children with whooping cough syndrome in the presence or absence of Bordetella pertussis infection; however, whether adenovirus is an etiologic cause of the syndrome remains unclear.[115,116]

Pharyngoconjunctival fever (predominantly serotypes 3, 4, and 7)

This syndrome most often affects school-aged children. Contagious in nature, sporadic outbreaks of adenovirus infection occur in small groups, especially summer camps in the setting of an inadequately chlorinated water source such as a pool or lake. Interestingly, water sample cultures are often not confirmatory. Spread occurs via the respiratory route and contact with ocular secretions during the acute illness. The classic presentation is characterized by fever, sore throat, coryza, and red eyes. Upper respiratory tract symptoms may precede ocular findings or may be absent.[103]

Acute conjunctivitis may occur with or without pharyngitis or a respiratory syndrome. Encephalitis may occur but is rare. Conjunctivitis usually begins in one eye and then spreads to the other, although both eyes may be affected simultaneously. Severe pain is atypical, but mild pain or discomfort, tearing, pruritus, and morning crusting are common. It usually is self-limited to 5 days (incubation period is 5 d). Uncommonly, an exanthem or diarrhea may occur. Epidemic keratoconjunctivitis (predominantly serotypes 8, 19, and 37).[103]

This is highly contagious, with approximately 10% transmission in household contacts via hands and fomites. Transmission has also been associated

with instrumentation, industrial trauma (shipyard workers [ie, shipyard eye], welders, airborne particles), contaminated ophthalmic solutions, and the hands of health care workers.[117] Corneal trauma facilitates infection.

After an eight day incubation period, an insidious onset of unilateral red eye occurs, spreading to involve both eyes. Patients have photophobia, tearing, and pain (indicating corneal involvement). Children may have fever and lymphadenopathy. Malaise and headache are reported, inflammation may persist for weeks, and residual scarring and visual impairment may occur. Acute hemorrhagic cystitis (serotypes 11 and 21)/nephritis. Acute hemorrhagic cystitis usually affects children aged 5-15 years but may also affect immunosuppressed adults (from kidney or bone marrow transplantation, AIDS). Boys are affected more often than girls.

Dysuria, frequency, and grossly bloody urine are reported. Hematuria is self-limited to three days, and other symptoms resolve later. Symptoms may be more prolonged in hematopoietic stem cell recipients. Nephritis has occurred in recipients of hematopoietic stem cell transplants and is associated with fever, hematuria, and flank pain.[118-119]

Gastroenteritis (most commonly associated with serotypes 40 and 41, but others may be involved). Enteric adenovirus infection is a common cause of infantile diarrhea in the daycare setting, but less common than rotavirus infection and, in some settings, less common than infection with astroviruses. It can also affect adults; in addition, a nosocomial outbreak in a hematology unit has been reported.[120]

Adenoviruses replicate readily in the human intestine and may be cultured from asymptomatic individuals; thus, their presence in the setting of a diarrheal syndrome may be incidental.[103]

Many serotypes are fastidious in culture. Serotypes 40 and 41 had been termed "noncultivatable." However, they have been cultured in the setting of diarrheal syndromes using newer cell lines. Monoclonal antibody assays, enzyme-linked immunosorbent assay, and electron microscopy support the association of these strains with enteric disease. However, one cannot assume that enteric disease is limited to these strains. In fact, various serotypes of adenovirus have been associated with infectious diarrheal syndromes in recipients of hematopoietic stem cell transplants. Fever and watery diarrhea are usually limited to one to two weeks.[103]

Mesenteric adenitis and intussusception have been associated with nonenteric adenovirus serotypes (types 1, 2, 3, 5, 6). Approximately 40% of infants with intussusception have positive findings from cultures of stool or mesenteric lymph nodes for nonenteric serotypes, and most have no evidence of infection with enteric strains (40, 41). The role of adenovirus in this setting is unclear. Mesenteric lymphadenitis or hyperirritable small bowel associated with nonenteric adenoviral infection has been postulated to lead to intussusception. However, most patients with intussusception have no evidence of adenoviral infection (based on culture, serology, or histopathologic viral inclusion findings); thus, intussusception may be related to multiple etiologies. Adenoviral infections in immunocompromised hosts (multiple serotypes).[103]

Adenovirus is increasingly known to cause disease during the posttransplantation period in patients who have received hematopoietic stem cell transplants. Risk factors for adenovirus disease include allogeneic stem cell transplantation, T-cell depletion and nonmyeloablative conditioning regimens such as high-dose alemtuzumab (Campath) antibody therapy, lymphopenia, young age, and graft versus host disease. Prolonged neutropenia or immunosuppression also enhances the risk of adenoviral infections. Manifestations may vary but include hemorrhagic cystitis/nephritis, pneumonitis, hepatitis/liver failure, and gastroenteritis, particularly during the acute posttransplantation period prior to engraftment. In one series, nephritis was associated with acute renal failure in more than 90% of patients. Adenovirus should be considered in patients with a fever, hematuria, flank pain, and worsening renal function.[108,121]

Uncommonly, T-cell immunodeficiency related to HIV infection has been associated with adenoviral infections, particularly in infants and children infected with HIV. Pneumonitis and hemorrhagic cystitis are cited most often. Cholecystitis, severe hepatitis, and liver failure have been reported.[122]

Immunosuppression in recipients of solid organ transplants has also been associated with the above syndromes, as has diffuse adenoviral infection of the allograft itself. Both allograft loss and recovery have been reported.[121] Adenoviral infection following pediatric lung transplantation has been reported.[123]

Importantly, note that a prior history of adenoviral infection in a patient with recovered immunocompetence may herald recurrence when the patient again becomes immunosuppressed. A high level of suspicion for adenovirus is warranted in these cases.[103]

Diagnosis

Pulmonary infiltrates are often diffuse and reticulonodular, but they may be lobar. Hematuria may occur in the setting of nephritis or hemorrhagic cystitis. Abnormal transaminase levels, which may be dramatic, may indicate adenoviral hepatitis. Diarrhea may indicate adenoviral gastroenteritis.[103]

*Laboratory Studies*

Culture: Adenovirus is stable in routine viral transport medium, including specimens of nasopharyngeal, rectal, and corneal secretions; urine; and unfixed biopsy tissue. Detection is enhanced if specimens are collected early in the clinical course and promptly shipped cold or frozen to the appropriate laboratory. Many adenovirus serotypes can be isolated in cell culture lines commonly used in diagnostic virology laboratories; a few, such as types 40 and 41, fail to grow. Primary human embryonic kidney cells support growth of many fastidious adenovirus serotypes, but their additional cost may be prohibitive in some settings. Other cell lines may not support the growth of ocular strains well, may be less sensitive, or may not be maintainable to support slower-growing strains.[103]

Serology: Seroreactivity to adenovirus is common. By age 4 years, approximately half of all children have positive adenovirus titers. As a result, serology is less useful in the acute clinical setting. If a serologic diagnosis is pursued, serum should be obtained as early as possible in the clinical course, followed by a second titer 2-4 weeks later. A 4-fold rise in acute titers to convalescent titers is diagnostic.[103]

Antigen tests: Indirect immunofluorescence assays may be used for direct examination of tissue specimens.[103]

Polymerase chain reaction (PCR): PCR is being used with high specificity on various specimens (eg, respiratory, tissue, urine, blood) to identify adenovirus.[108,124]

Serotyping is generally in the domain of epidemiology and research and is not typically used in clinical practice. However, as specific syndromes are associated with specific serotypes, tests can be performed in a reference laboratory.

Certain serotypes of enteric adenovirus have been seen in stool specimens using electron microscopy, but they have been difficult to isolate in routine tissue culture. These types have been referred to as noncultivatable enteric adenoviruses. Adenovirus has been identified using electron microscopy and immunohistochemistry techniques. The isolation of enteric adenovirus infection in recipients of small bowel transplants in whom allograft damage is a risk may warrant stool cultures or biopsy.[103]

Chapter 4

# Methodology

# METHODOLOGY

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

**Study design**

The study design was a one year hospital based cross sectional study.

**Study period and duration**

This study was conducted from January 2011 to December 2011.

**Place**

This study was conducted at Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum a teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum.

**Source of Data**

Patients presenting with history of passing more than three stools per day with decrease in stool consistency, increase in stool urgency and/or vomiting and/or abdominal discomfort at Department of General Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were studied.

**Sample size**

A total of 100 patients were selected for the study.

**Sampling procedure**

The sample size was calculated based on the formula as mentioned below.

$n = 4 X p X q / d^2$

Where p = Prevalence.

q = 100 – p

d = Absolute error 10

n = 100

Based on the above formula sample size was calculated as a total of 100 patients.

**Sampling method**

Simple random sampling was employed where every third patient who fulfilled the selection criteria was included in the study.

**Selection criteria**

***Inclusion Criteria***

- Age more than 18 years.
- Patients with passage of more than three stools per day with decrease in stool consistency, increase in stool urgency and/or abdominal discomfort.
- Diarrhoea less than two weeks duration.

***Exclusion Criteria***

- Non infectious causes of acute diarrhoea.

- Patients presenting with dysentery.
- Patients proven positive for bacterial and parasitic infection by stool routine and microscopy, stool hanging drop test and stool culture and sensitivity.

**Ethical clearance**

Before the commencement of the study, the ethical clearance was obtained from the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belgaum.

**Informed Consent**

All the patients fulfilling selection criteria were explained about the nature of the study and a written informed consent was obtained before enrollment (Annexure I).

**Method of collection of data**

Demographic data such as age and sex, were recorded. Patients were interviewed for the history such as vomiting, diarrhoea, abdominal pain and reduced urine output. Thorough physical and clinical examination was conducted to assess signs of dehydration such as skin elasticity, tongue appearance and patients appearance. These findings were recorded on a predesigned and pretested proforma (Annexure II).

**Investigations**

Further, these patients were subjected to routine investigations such as haemoglobin, chest X-ray and urine routine, serum creatinine, fasting blood sugar and complete biochemical profile which included liver function tests (serum bilirubin total and direct, SGOT, SGPT), renal function test (blood urea, serum creatinine) and serum electrolytes (serum sodium and potassium). The diagnosis of viral etiology (Rota virus and Adeno virus) was determined by Rapid kit test.

Rapid kit test for Rota virus and Adeno virus[125-127]

*Materials provided / Active ingredients of main components*

- BIOLINE Rota/Adeno Rapid test device.
- Sample collection tube.
- Assay diluent.
- Sample collection swab.
- Disposable dropper.
- Instructions for use.

*Active ingredients of main components*

- 1 test strip includes;
    - Gold Conjugates (as main component): Mouse monoclonal anti-rotavirus – gold colloid (0.18±0.036 µg), Mouse monoclonal anti-Adenovirus – gold colloid (0.06±0.012 µg)
    - Test Line 1(as main component) : Mouse monoclonal anti-adenovirus (0.32±0.064 µg)

- Test Line 2 (as main component) : Rabbit polyclonal antirotavirus (0.96±0.192 µg)
- Control Line (as main component) : Goat anti- mouse IgG (0.64±0.128 µg)

- Assay diluent includes; 20 mM Phosphate buffer (q.s), Sodium azide (0.01%)

*Kit Storage and Stability*

- The SD BIOLINE Rota/Adeno Rapid test should be stored at room temperature. (1 ~ $30^0$C)
- Do not store at refrigerator. Do not freeze.
- Do not use it beyond the expiration.
- The shelf-life of the kits is as indicated on the outer package.

*Specimen collection, Preparation, Storage and Precaution*

- Sample collection swab
  - To take a portion of feces (about 50 mg), insert the sterile swab into a stool sample that presents the most secretion under visual inspection.
  - Insert the swab into the specimen tube containing assay diluent.
  - Mix the swab a few times until the sample has been dissolved into the assay diluent, and then discard the swab.
  - Specimen extracted in assay diluent may be stored at 2 ~ 8 $^0$C for up to 1 week prior to testing.

- Specimen transport and storage
    - Specimen should be tested as soon as possible after collection. Do not use any kind of transport media to store or transport specimens
    - Faecal sample may be stored refrigerated (2~8$^0$C) for 72 hours. If longer storage is required, freezing at -20$^0$C is recommended.
- Precaution
- Faecal specimens should be collected as soon as possible following the onset of symptoms. In general, the symptoms begin 1 to 2 days following infection with a virus that causes gastroenteritis and may last for 1 to 10 days, depending on which virus causes the illness (Rotavirus 3 days and Adenovirus 5-8 days).
- Faecal specimens for direct testing should be collected into containers that do not contain media, preservatives, as all of these additives may interfere with SD BIOLINE Rota/Adeno Rapid test.

*Warnings and Precautions*

- Precautions
    - SD BIOLINE Rota/Adeno Rapid test should be stored at room temperature.
    - The test device is sensitive to humidity as well as heat.
    - Perform the test immediately after removing the test device from the foil pouch.
    - Do not use the test kit if the pouch is damaged or the seal is broken.

Warnings

- For in vitro diagnostic use only. DO NOT RE-USE test device.
- The instruction must be followed exactly to get accurate results. Anyone performing an assay with this product must be trained in its use and must be experienced in laboratory procedures.
- Do not eat or smoke while handling specimens.
- Wear protective gloves while handling specimens. Wash hands thoroughly afterwards.
- Avoid splashing or aerosol formation.
- Clean up spills thoroughly using an appropriate disinfectant.
- Decontaminate and dispose of all specimens, reaction kits and potentially contaminated materials, as if they were infectious waste, in a biohazard container.
- Do not mix and interchange different specimen.

*Procedure of the test*

- Extraction Procedure : preparation of extracted sample (Figure)
    - Allow test device and extracted sample to room temperature prior to testing.
    - Take assay diluent up to the Fill Line and then, transfer into the sample collection tube.
    - Repeat the above step for two times
    - Take a portion of feces (about 50mg) from a stool sample with the sample collection swab.

- Insert the swqb into the sample collection tube containing assay diluent.
- Swirl the swab at least 10 times until the sample has been dissolved into the assay diluent and discard the swab while squeezing the swab against the wall of tube.

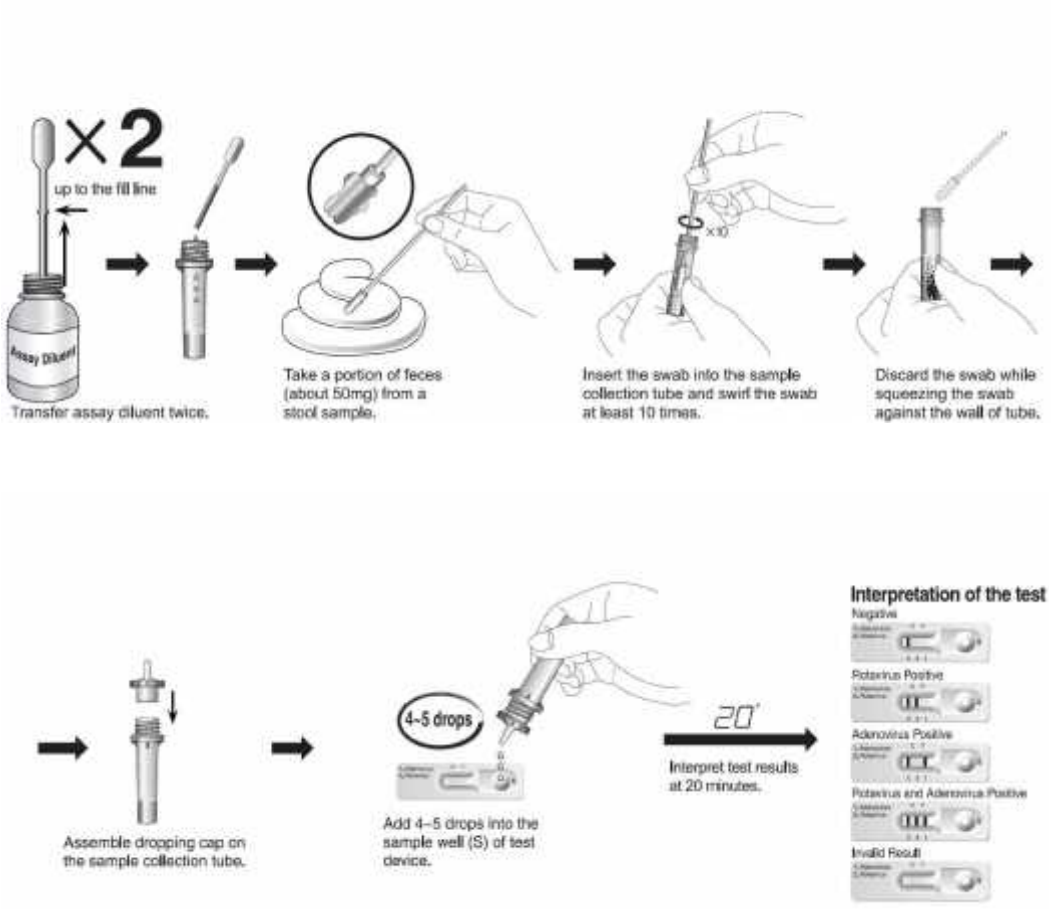



**Figure 6. Procedure of the test**

- **Test Procedure**
  - Remove the test device from the foil pouch, and place it on a flat, dry surface.
  - Assemble dropping cap on the sample collection tube.

- Add 4~5 drops (about 100~125 µL) into the sample well (s) of the test device.
- As the test begins to work, you will see purple color move across the result window in the center of the test device.
- Interpret test results at 20 minutes. Do not interpret test result after 20 minutes.

*Interpretation of the test*

- A color band will appear in the left section of the result window to show that the test is working properly. This band is the Control Band.
- The right section of the result window indicates the test results. If another color band appears in the right section of the result window, this band is the Test Band.

**Negative Result**: The presence of only control band (C) within the result window indicates a negative result.


**Figure 7. Negative result**

**Rotavirus Positive Result:** The presence of two color bands (“T2” band and “C” band) within the result window, no matter which band appears first, indicates a positive result.


**Figure 8. Rotavirus positive result**

**Adenovirus Positive Result :** The presence of two color bands ("T1" band and "C" band) within the result window, no matter which band appears first, indicates a positive result.


**Figure 9. Adenovirus positive result**

**Rotavirus and Adenovirus Positive Result:** All the lines above described could appear at the same time during the test performance due to a simultaneous infection of Rotavirus and Adenovirus.

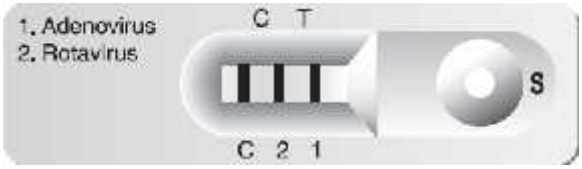



**Figure 10. Rotavirus and Adenovirus Positive Result**

**Invalid Result :** If the purple color band is not visible within the result window after performing the test, the result is considered invalid. Some causes of invalid results are not following the directions correctly or the test may have deteriorated

beyond the expiration date. It is recommended that the specimen be re-tested using a new test kit.


**Figure 11. Invalid result**

**Statistical analysis**

The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test. The continuous data was expressed as mean ± standard deviation (SD) and the comparison was done using student‘t’ test. A probability value (‘p’ value) of less than or equal to 0.05 was considered as statistically significant.

Chapter 5

# Results

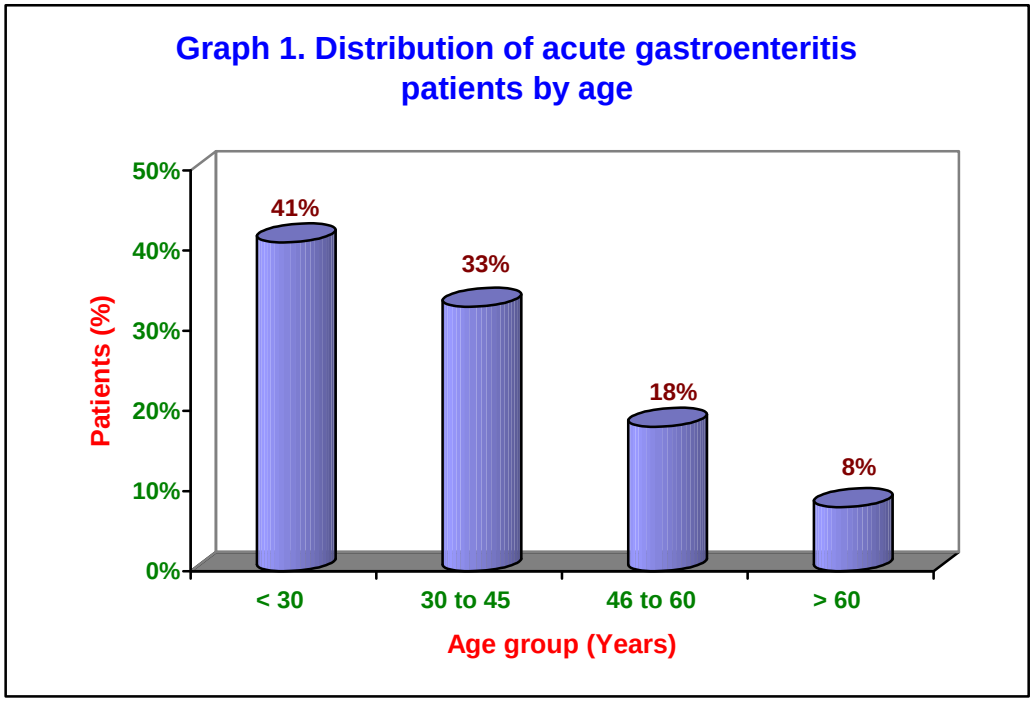
# RESULTS

The present one year hospital based cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2011 to December 2011. A total of 100 patients presenting with passage of more than three stools per day with decrease in stool consistency, increase in stool urgency and/or vomiting and/or abdominal discomfort were studied.

Data obtained was coded and entered into the Microsoft excel spreadsheet. The data was analyzed and final results were tabulated as below.

**Table 1. Distribution of acute gastroenteritis patients by age**

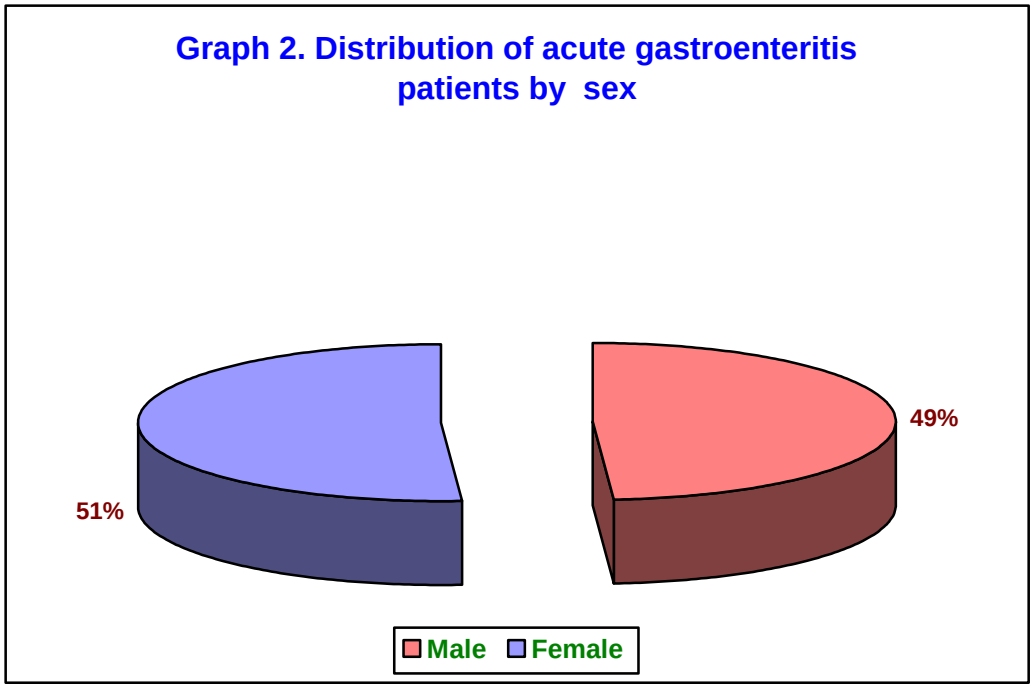
| Age group (Years) | Distribution (n=100) | |
|---|---|---|
| | Number | Percentage |
| < 30 | 41 | 41.00 |
| 30 to 45 | 33 | 33.00 |
| 46 to 60 | 18 | 18.00 |
| > 60 | 8 | 8.00 |
| **Total** | **100** | **100.00** |




In this study 41 patients of age less than 30 years had acute gastroenteritis followed by 33 patients (33%) in 30 to 45 years age group, 18 patients (18%) in 46 to 60 years age group and 8 patients were there in age group of more than 60 years.

**Table 2. Distribution of acute gastroenteritis patients by sex**

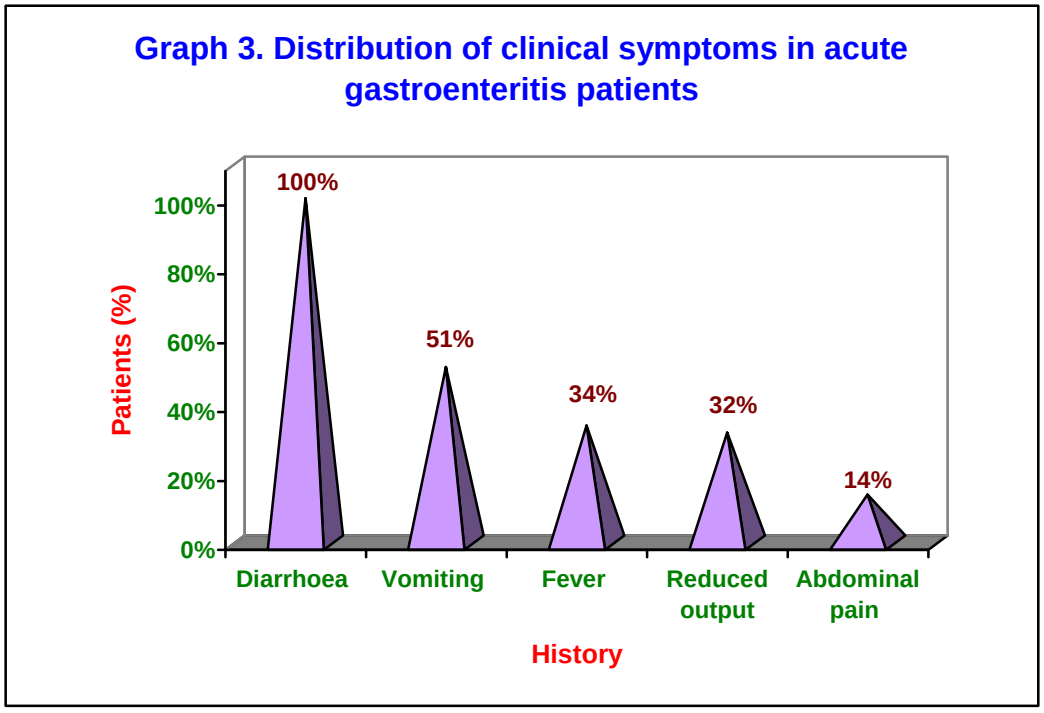
| Sex | Distribution (n=100) | |
|---|---|---|
| | Number | Percentage |
| Male | 49 | 49.00 |
| Female | 51 | 51.00 |
| **Total** | **100** | **100.00** |




In the present study acute gastroenteritis was present in 51 females (51%) and 49 males (49%).

**Table 3. Distribution of clinical symptoms in acute gastroenteritis patients**

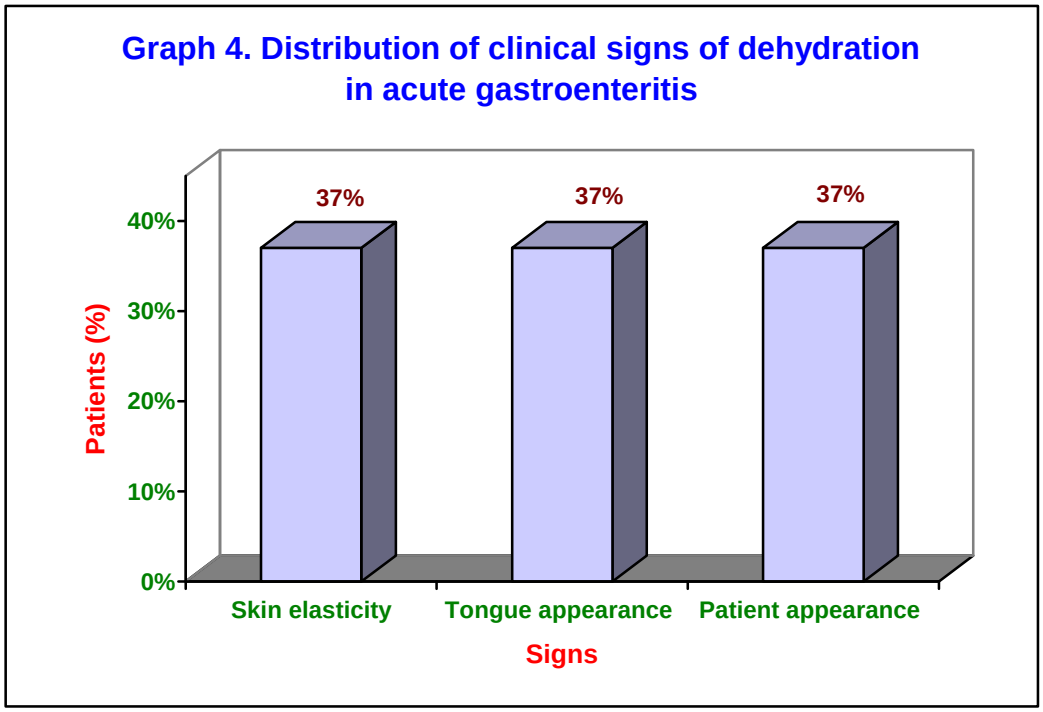
| History | Distribution (n=100) | |
|---|---|---|
| | Number | Percentage |
| Diarrhoea | 100 | 100.00 |
| Vomiting | 51 | 51.00 |
| Fever | 34 | 34.00 |
| Reduced urine output | 32 | 32.00 |
| Abdominal pain | 14 | 14.00 |




In this study all the 100 cases (100%) had diarrhea as defined by inclusion criteria. The next common symptom in our study was vomiting seen in 51 cases (51%) followed by fever seen in 34 (34%) patients, reduced urine output which was reported in 32 cases (32%) and abdominal pain was reported in only in 14 cases (14%).

**Table 4. Distribution of clinical signs of dehydration in acute gastroenteritis**

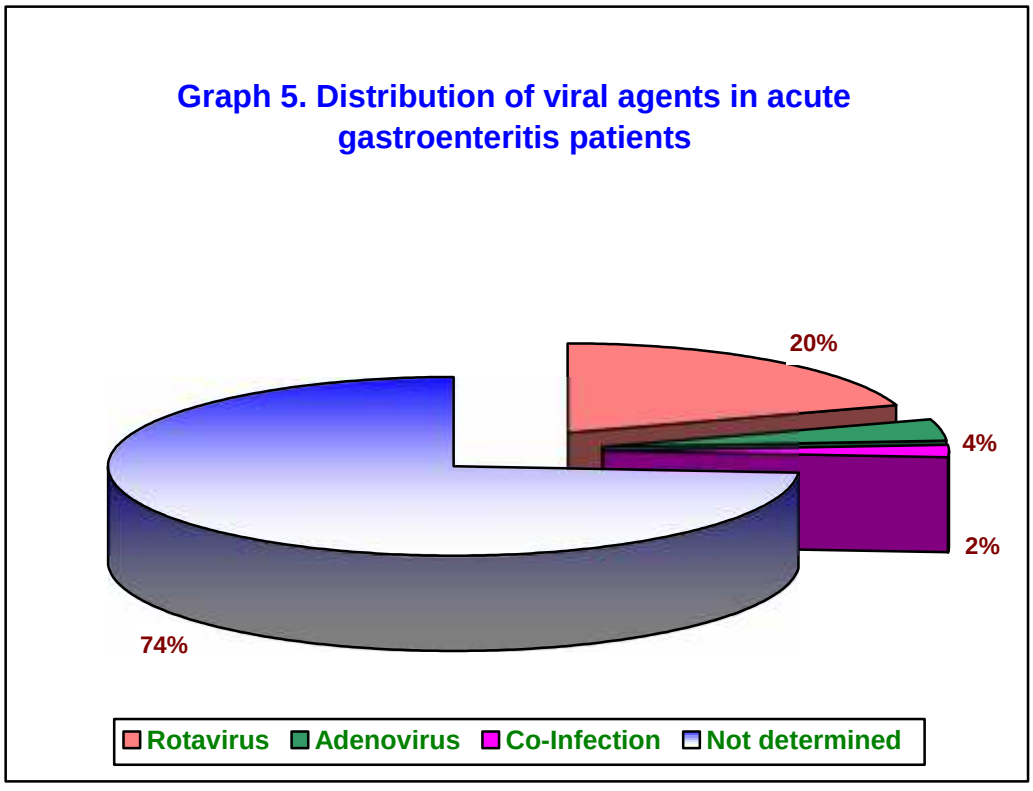
| Signs | Distribution (n=100) | |
|---|---|---|
| | Number | Percentage |
| Skin elasticity | 37 | 37.00 |
| Tongue appearance | 37 | 37.00 |
| Patient appearance | 37 | 37.00 |




In this study 37 cases (37%) had all three signs of dehydration.

**Table 5. Distribution of viral agents in acute gastroenteritis patients**

| Virus | Results | Distribution (n=100) | |
|---|---|---|---|
| | | **Number** | **Percentage** |
| Positive | Adeno | 4 | 4.00 |
| | Rota | 20 | 20.00 |
| | Both | 2 | 2.00 |
| | Prevalence | **26** | **26.00** |
| Not determined | | 74 | 74.00 |
| **Total** | Total | **100** | **100.00** |

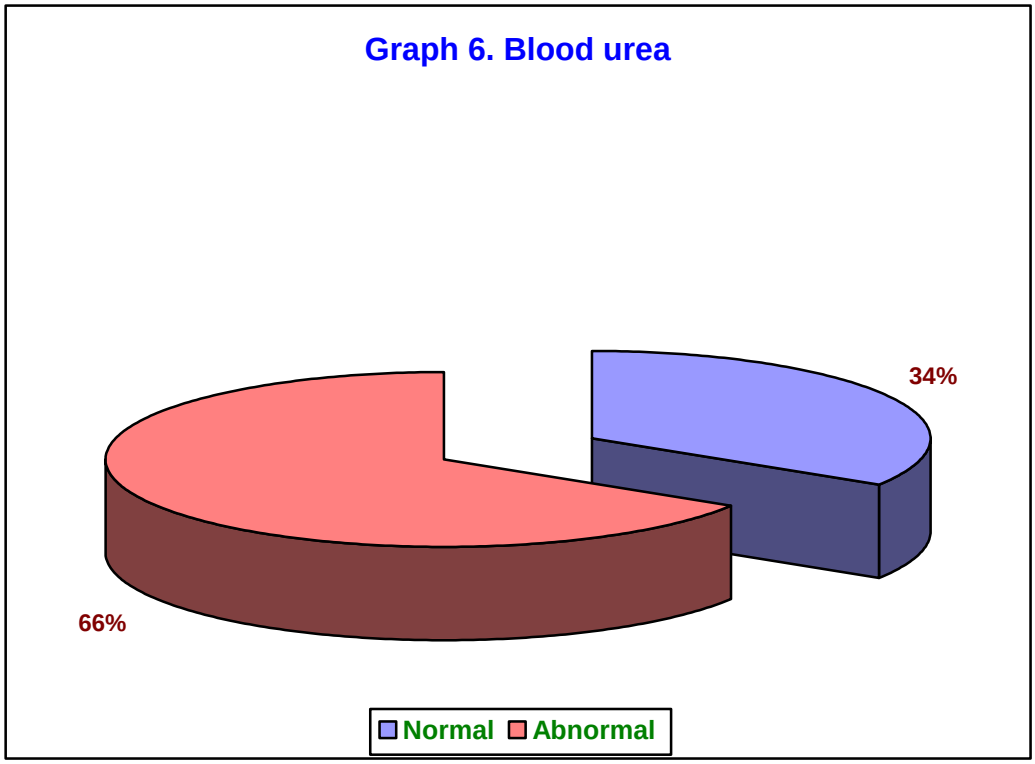



In this study total 26 cases were diagnosed as viral gastroenteritis. Rotavirus infection was seen in 20 cases, 4 cases suffered from Adeno virus infection and co infection of Rotavirus and Adenovirus was noted in 2 cases.

## RESULTS OF BIO-CHEMICAL PARAMETERS IN ACUTE GASTROENTERITIS PATIENTS

**Table 6. Blood urea**

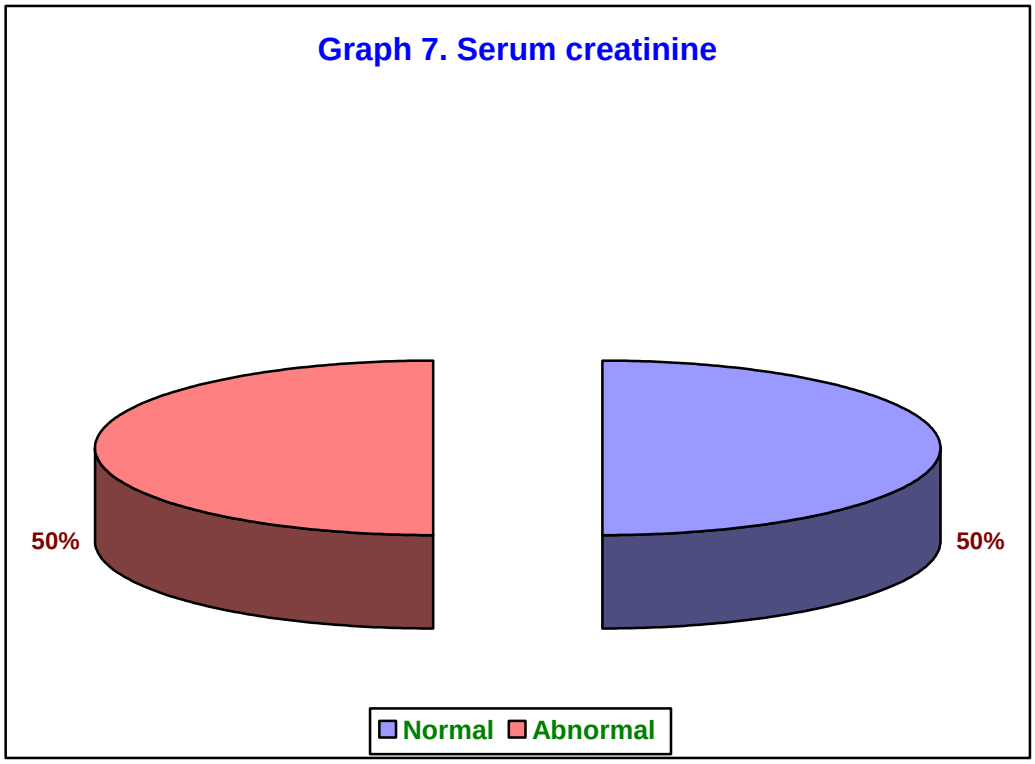
| Blood urea levels (mg/dL) | Distribution (n=100) | |
|---|---|---|
| | Number | Percentage |
| Normal (14 to 36) | 34 | 34.00 |
| Abnormal (> 36 or <14) | 66 | 66.00 |
| **Total** | **100** | **100.00** |




In this study normal blood urea levels was observed in 34 cases (34%) and 66 cases (66%) had abnormal blood urea levels.

**Table 7. Serum creatinine**

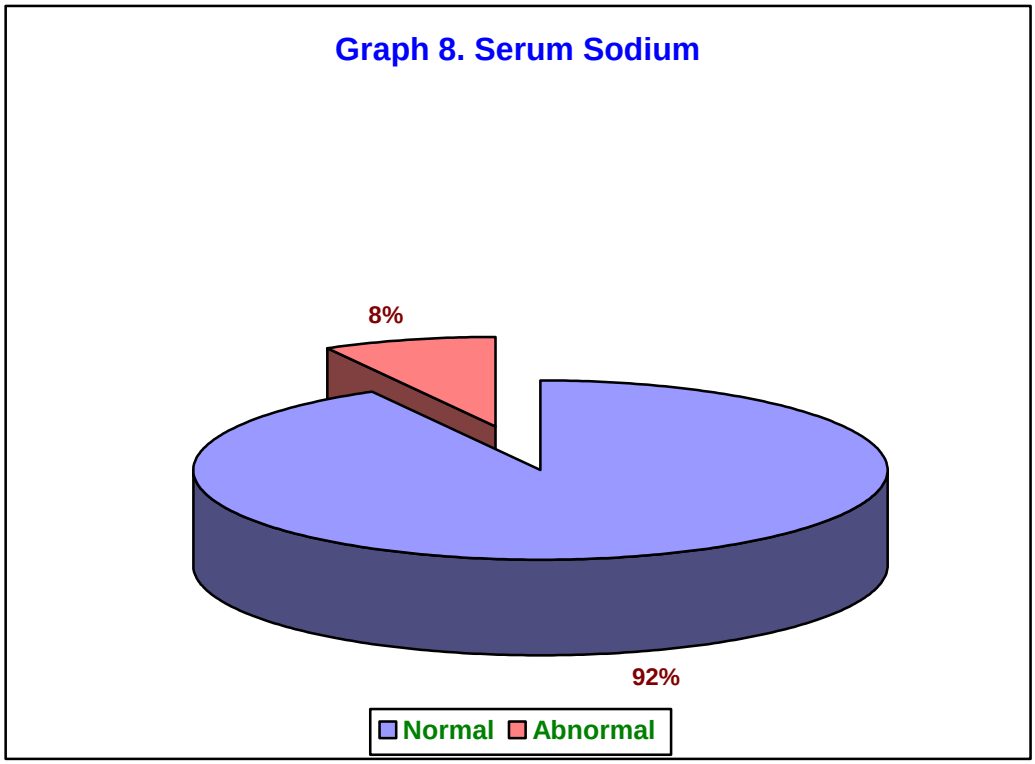
| Serum Creatinine (mg/dL) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (0.8 to 1.3) | 50 | 50.00 |
| Abnormal (> 1.3 or <0.8) | 50 | 50.00 |
| **Total** | **100** | **100.00** |




In this study normal serum creatinine levels was observed in 50 cases (50%) and 50 cases (50%) had abnormal serum creatinine levels.

**Table 8. Serum Sodium**

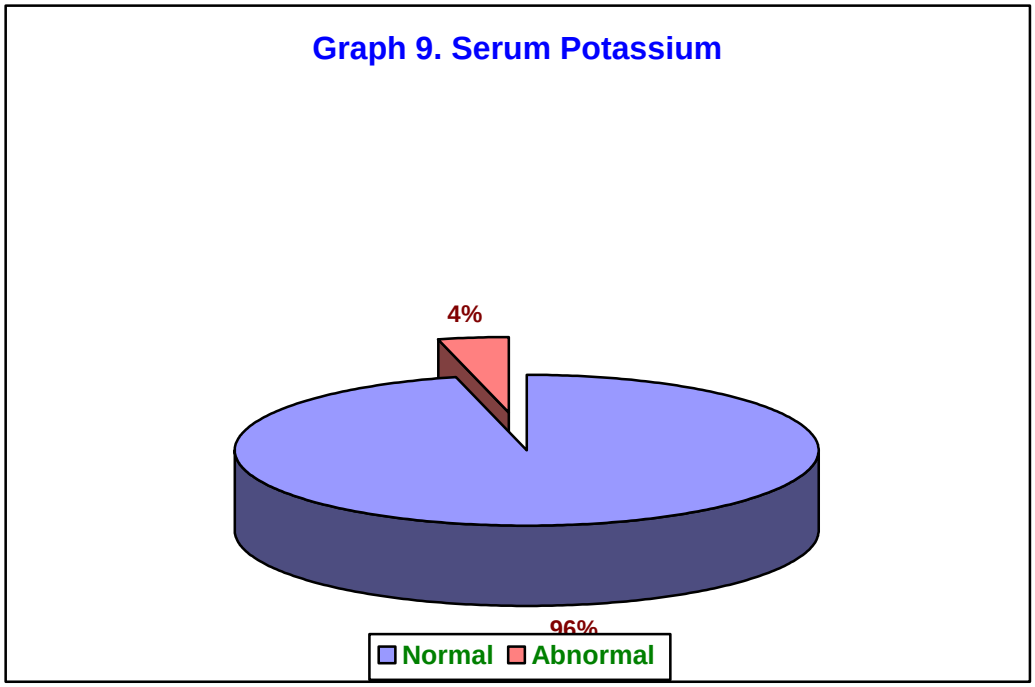
| Serum Sodium (meq/L) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (130 to 145) | 92 | 92.00 |
| Abnormal (> 145 or <130) | 8 | 8.00 |
| **Total** | **100** | **100.00** |




In this study normal serum sodium levels was reported in 92 cases (92%) and 8 cases (8%) had abnormal serum sodium levels.

**Table 9. Serum Potassium**

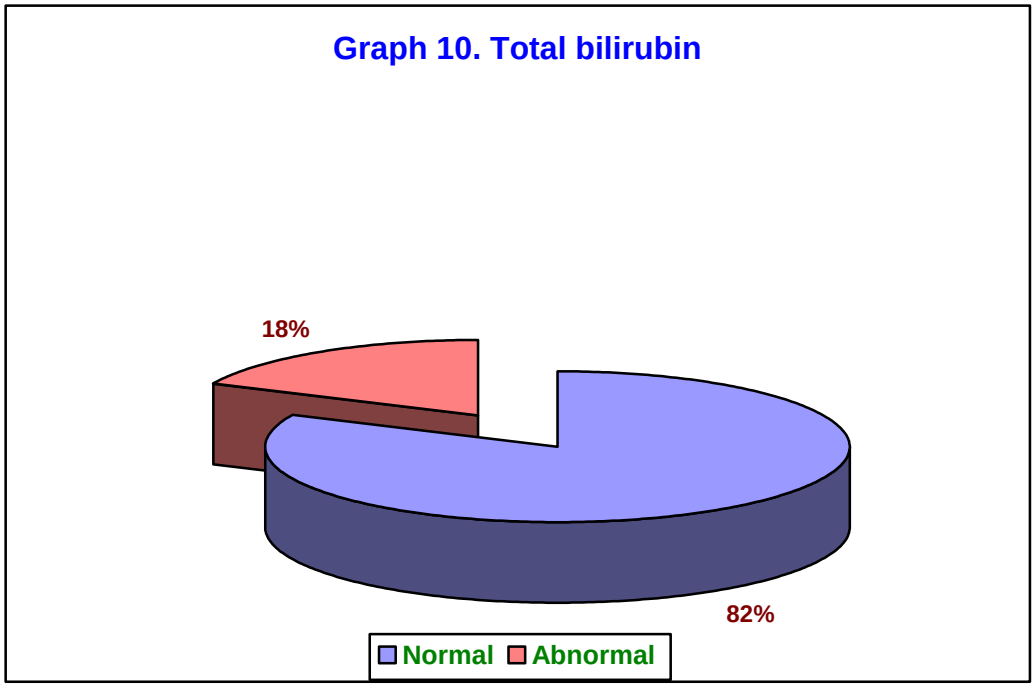
| Serum potassium (meq/L) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (3 to 5) | 96 | 96.00 |
| Abnormal (> 5 or <3) | 4 | 4.00 |
| **Total** | **100** | **100.00** |




In this study normal serum potassium was reported in 96 cases (96%) and 4 cases (4%) had abnormal serum potassium levels.

**Table 10. Total bilirubin**

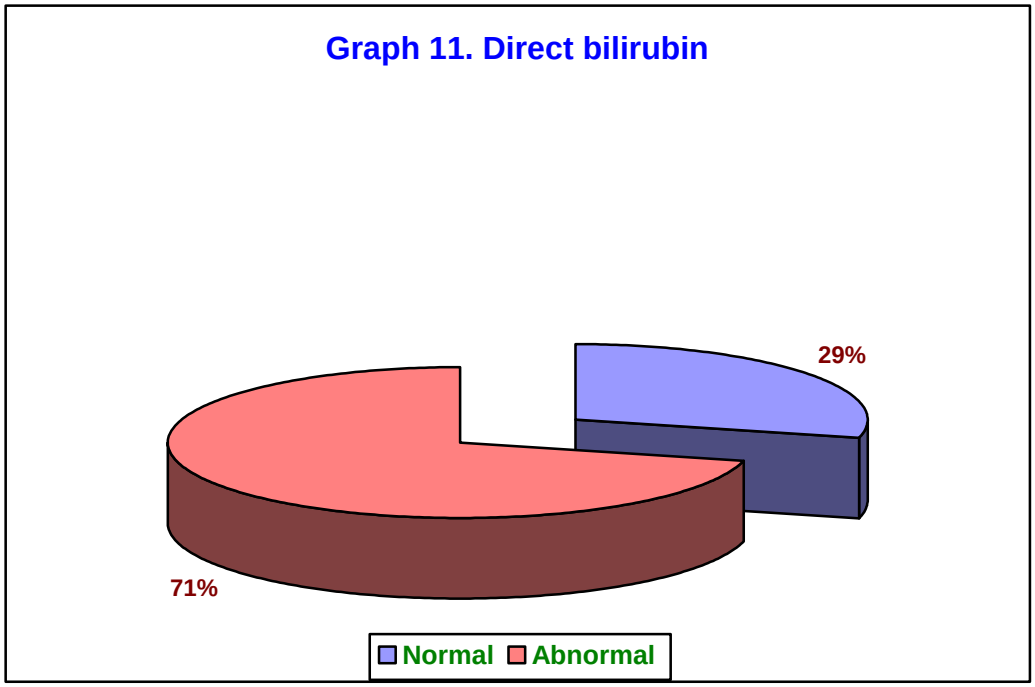
| Total bilirubin (mg/dL) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (0.2 to 1.0) | 82 | 82.00 |
| Abnormal (> 1.0 or <0.2) | 18 | 18.00 |
| **Total** | **100** | **100.00** |




In this study total bilurubin levels were normal in 82 cases (82%) and 18 cases (18%) had abnormal total bilurubin levels.

**Table 11. Direct bilirubin**

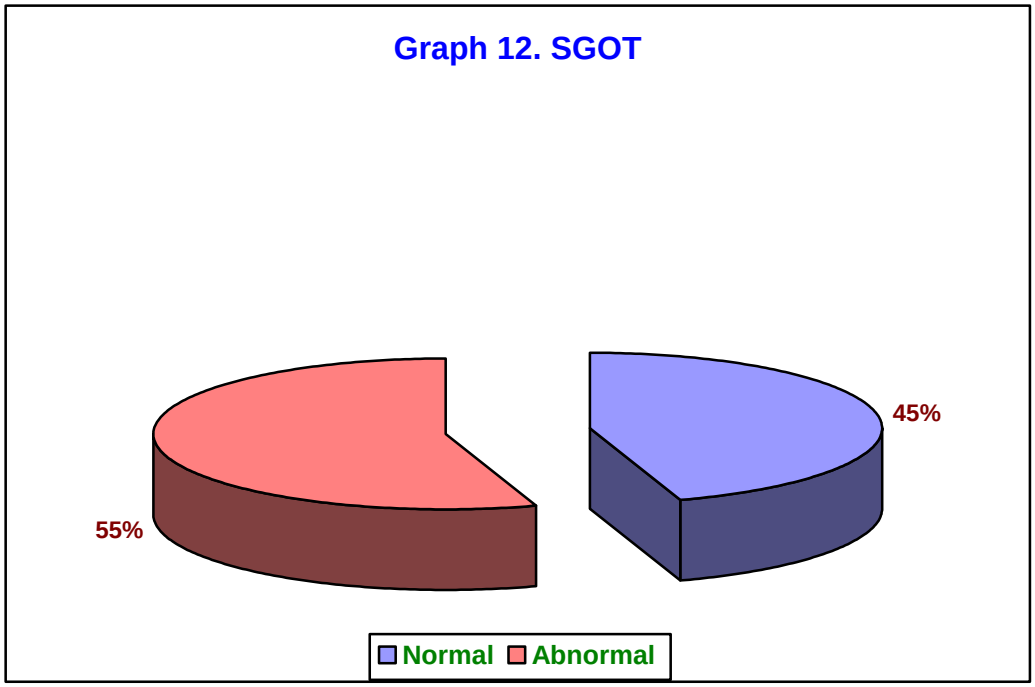
| Direct bilirubin (mg/dL) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (0.0 to 0.2) | 29 | 29.00 |
| Abnormal (>0.2) | 71 | 71.00 |
| **Total** | **100** | **100.00** |




In this study direct bilurubin levels were normal in 29 cases (29%) and 71 cases (71%) had abnormal direct bilurubin levels.

**Table 12. SGOT**

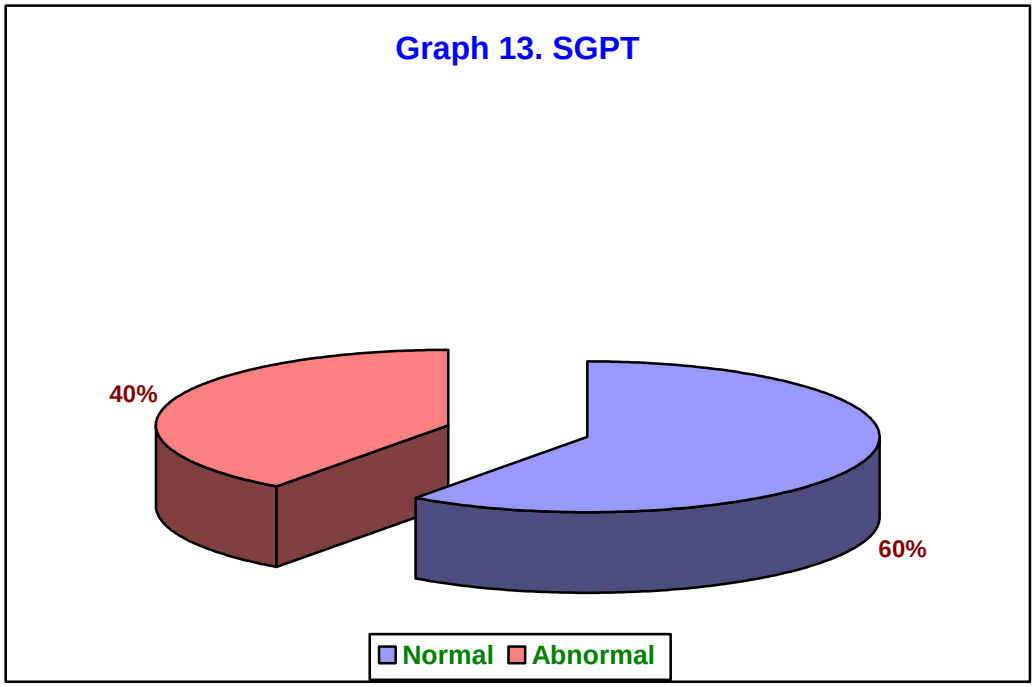
| SGOT (IU/L) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (15.0 to 37.0) | 45 | 45.00 |
| Abnormal (< 15 or >37) | 55 | 55.00 |
| **Total** | **100** | **100.00** |




In this study normal SGOT levels was reported in 45 cases (45%) and 55 cases (55%) had abnormal SGOT levels.

**Table 13. SGPT**

| SGPT (IU/L) | Distribution (n=100) | |
|---|---|---|
| | **Number** | **Percentage** |
| Normal (30.0 to 65.0) | 60 | 60.00 |
| Abnormal (< 30 or >65) | 40 | 40.00 |
| **Total** | **100** | **100.00** |

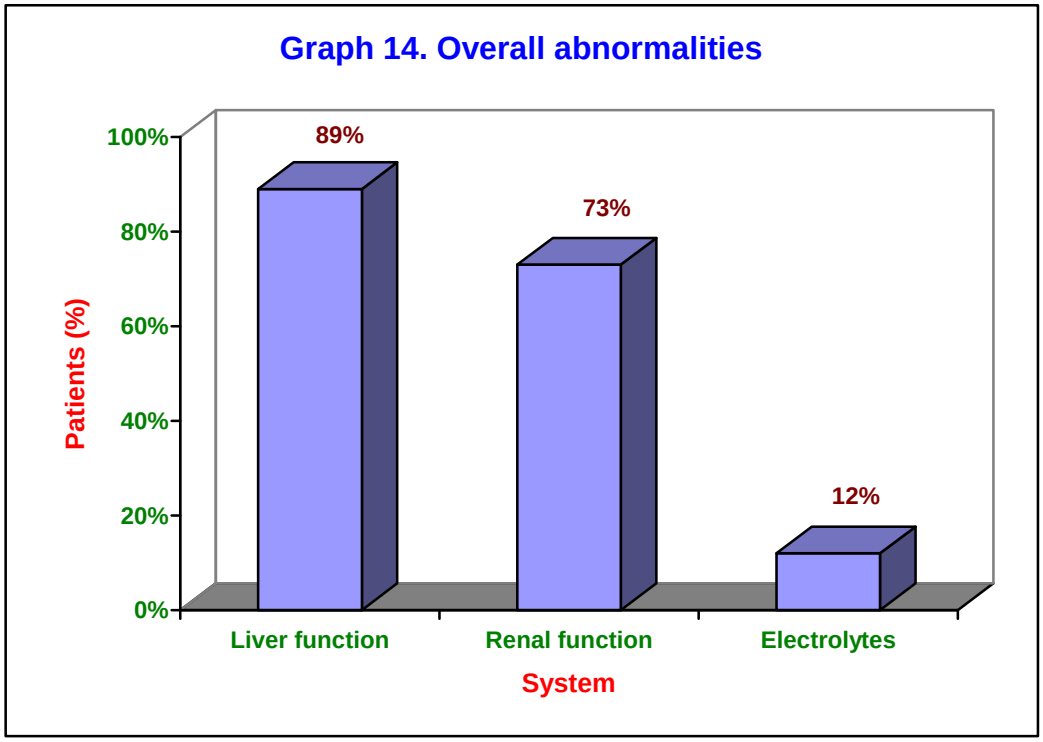



In this study normal SGPT levels was reported in 60 cases (45%) and 40 cases (40%) had abnormal SGPT levels.

## DISTRIBUTION OF BIOCHEMICAL ABNORMALITIES IN ACUTE GASTROENTERITIS PATIENTS

**Table 14. Biochemical abnormalities**

| System | Distribution (n=100) | |
|---|---|---|
| | Number | Percentage |
| Liver function | 89 | 89.00 |
| Renal function | 73 | 73.00 |
| Electrolytes | 12 | 12.00 |

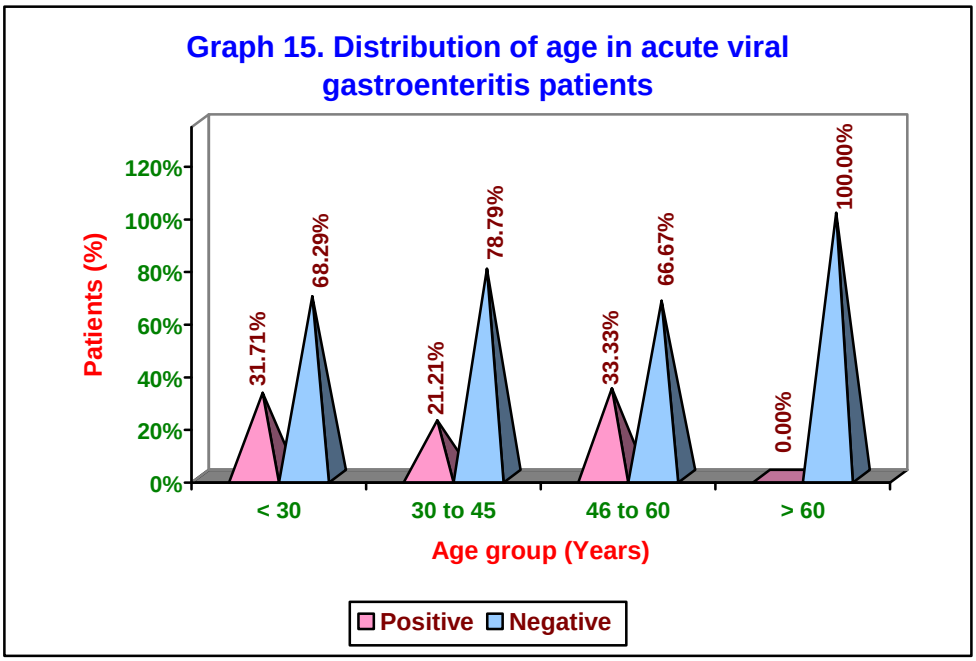



In this study abnormal liver function test was reported in 89 cases (89%) followed by abnormal renal function test in 73 cases (73%) and abnormal electrolytes were reported in 12 cases (12%).

**Table 15. Distribution of age in acute viral gastroenteritis patients**

| Age group (Years) | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| < 30 | 13 | 31.71 | 28 | 68.29 | 41 | 41.00 |
| 30 to 45 | 7 | 21.21 | 26 | 78.79 | 33 | 33.00 |
| 46 to 60 | 6 | 33.33 | 12 | 66.67 | 18 | 18.00 |
| > 60 | 0 | 0.00 | 8 | 100.00 | 8 | 8.00 |

**$x^2$=4.401** **p=0.2213 (NS)**

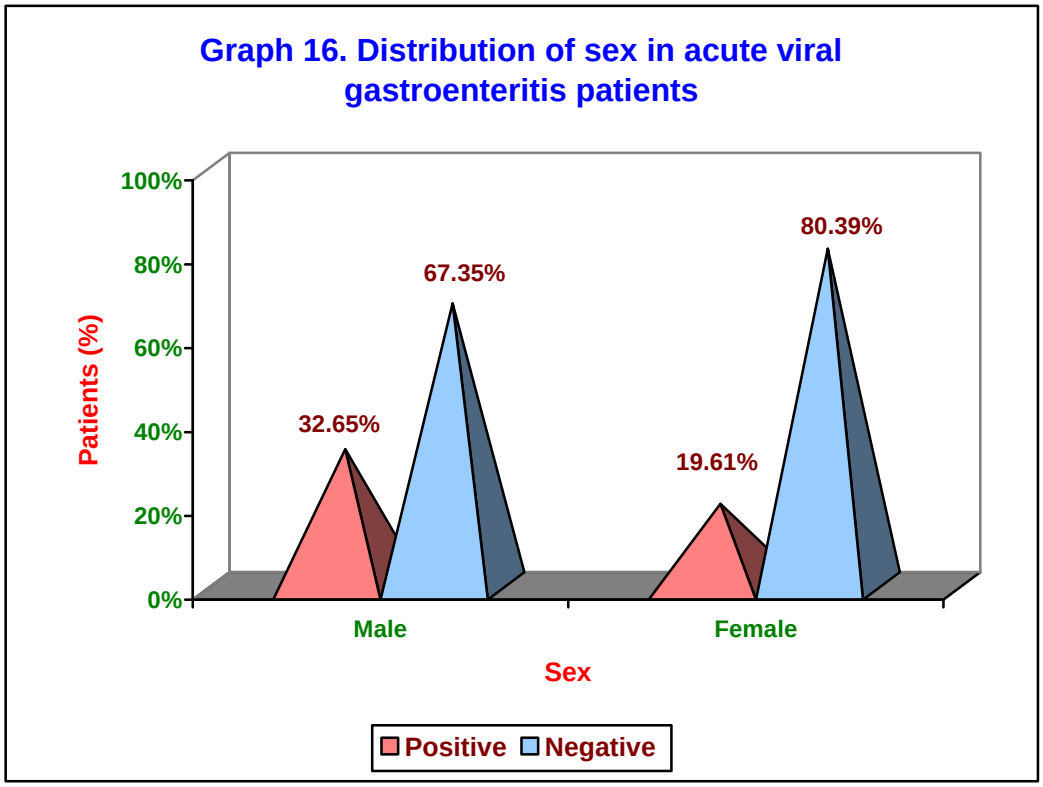



In this study 13 patients (31.71%) out of 41 patients of age below 30 years were found to be suffering from acute viral gastroenteritis followed by 7 patients (21.21%) out of 33 in the age group of 30 to45 years and 6 patients (33.33%) out of 18 in the age group between 46 to 60 years were diagnosed as acute viral gastroenteritis. No etiology was determined in 60 years and above age group. Association of viral etiology as a cause of gastroenteritis with age was found to be statistically non significant (p=0.2213).

**Table 16. Distribution of sex in acute viral gastroenteritis patients**

| Sex | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Male | 16 | 32.65 | 33 | 67.35 | 49 | 49.00 |
| Female | 10 | 19.61 | 41 | 80.39 | 51 | 51.00 |

**$x^2$=2.210** **p=0.137 (NS)**

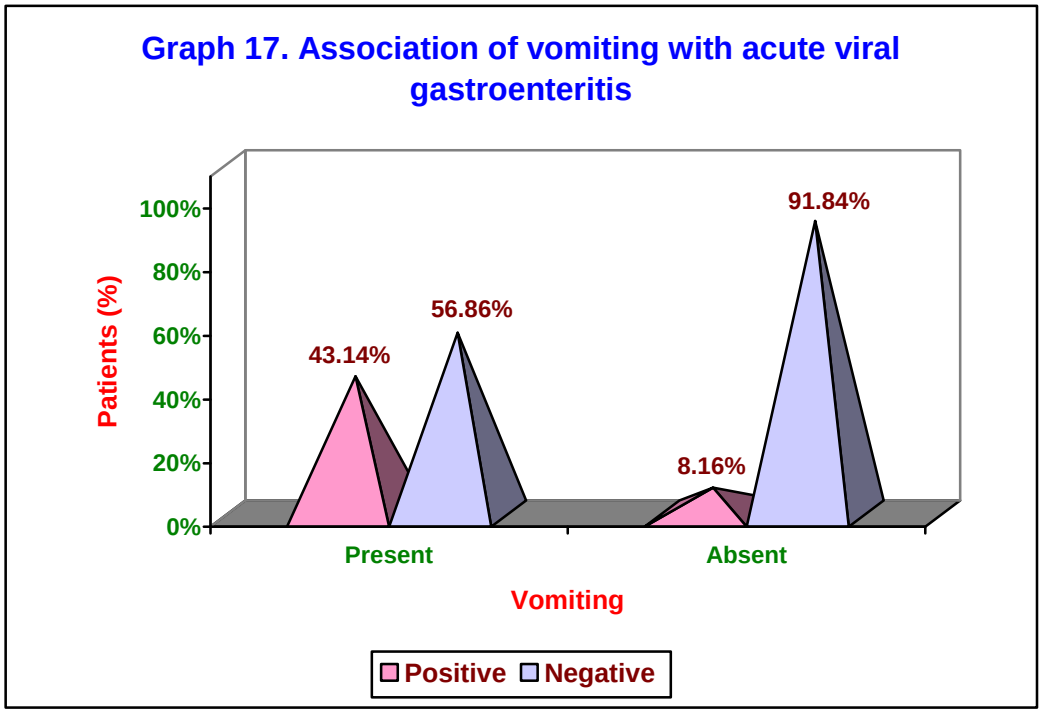



In the present study 16 (32.65%) out of 49 males, were diagnosed as acute viral gastroenteritis and 10(19.61%) out of 51 females, were diagnosed as acute viral gastroenteritis. Association of acute viral gastroenteritis with sex was found to be statistically non significant (p=0.137).

**Table 17. Association of vomiting with acute viral gastroenteritis**

| Vomiting | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Present | 22 | 43.14 | 29 | 56.86 | 51 | 51.00 |
| Absent | 4 | 8.16 | 45 | 91.84 | 49 | 49.00 |

**$x^2$=15.887** **p<0.001 (HS)**

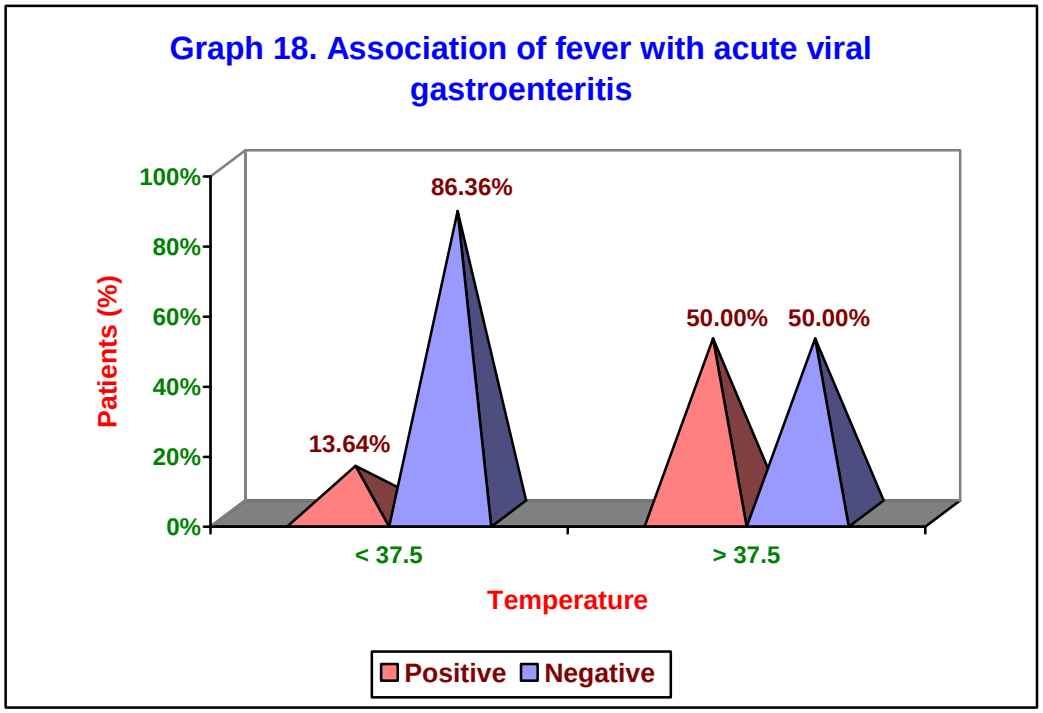



In the studied population, 51 patients gave history of vomiting. Out of 51 patients, 22 (43.14%) were positive for viral etiology, whereas 4 patients (8.16%) of viral etiology gave no history of vomiting. Association of vomiting with viral gastroenteritis was found to be statistically highly significant (p<0.001).

**Table 18. Association of fever with acute viral gastroenteritis**

| Temperature | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| < 37.5 | 9 | 13.64 | 57 | 86.36 | 66 | 66.00 |
| > 37.5 | 17 | 50.00 | 17 | 50.00 | 34 | 34.00 |

**$x^2$=15.422** **p<0.001 (HS)**

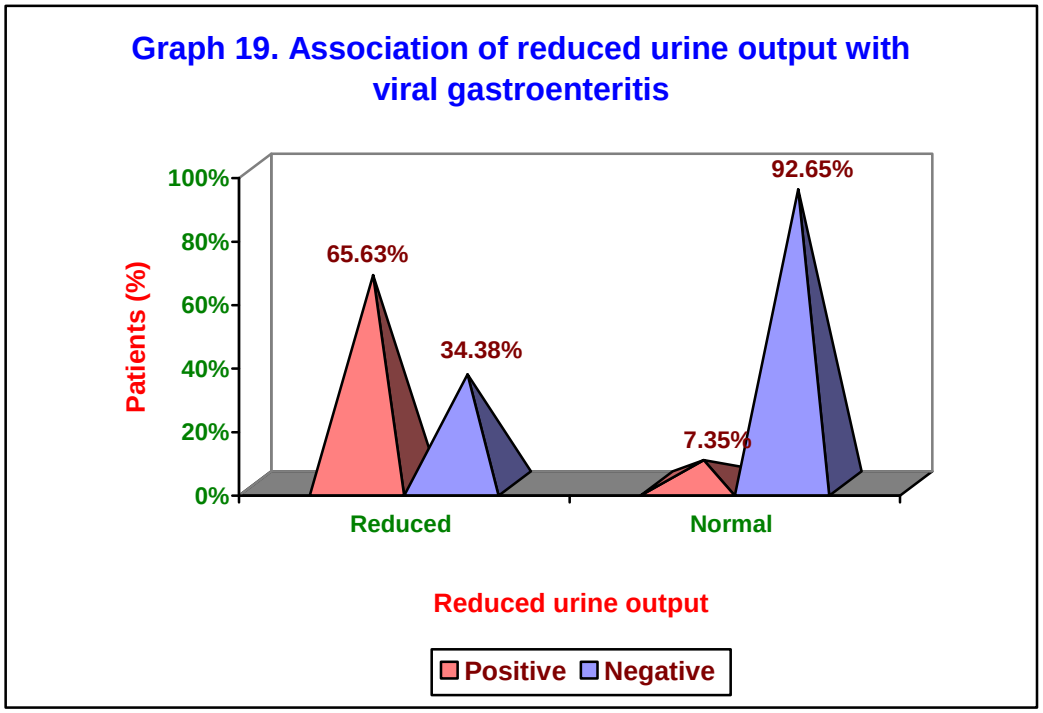



In the studied population, 34 patients gave history of fever. Out of 34 patients, 17 (50%) were positive for viral etiology, whereas 9 patients (13.64%) of viral etiology gave no history of fever. Association of fever with viral gastroenteritis was found to be statistically highly significant (p<0.001).

**Table 19. Association of reduced urine output with acute viral gastroenteritis**

| Urine output | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Reduced | 21 | 65.63 | 11 | 34.38 | 32 | 32.00 |
| Normal | 5 | 7.35 | 63 | 92.65 | 68 | 68.00 |

**$x^2$=38.4** **p<0.001 (HS)**

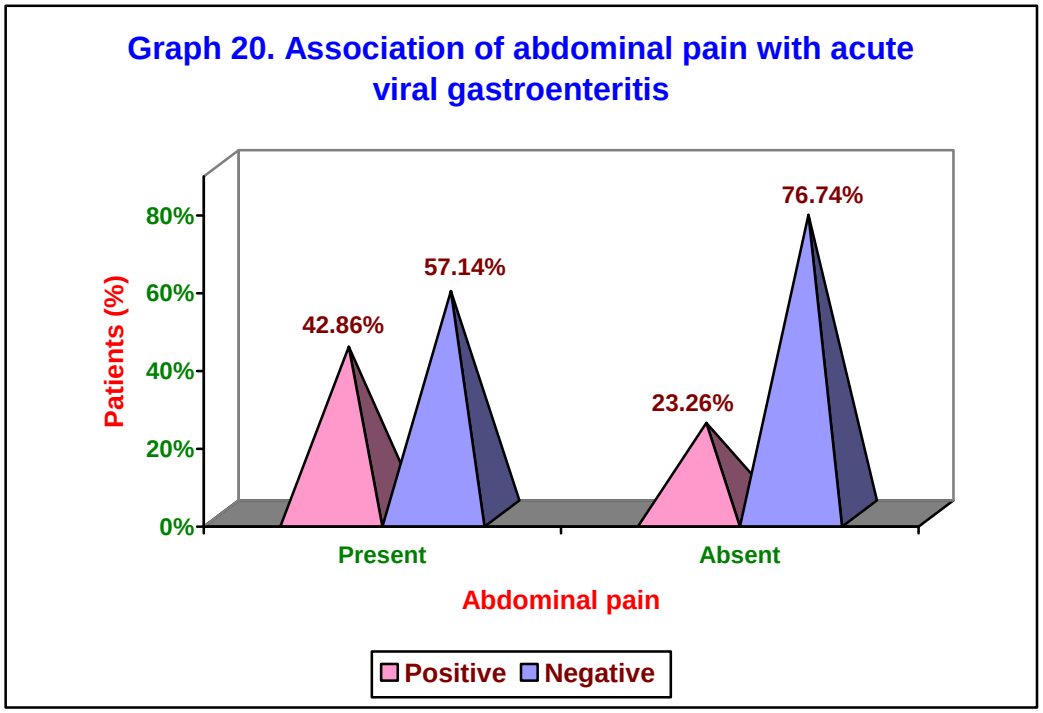



In the studied population, 32 patients gave history of reduced urine output. Out of 32 patients, 21 (65.63%) were positive for viral etiology, whereas 5 patients (7.35%) of viral etiology gave no history reduced urine output. Association of reduced urine output with viral gastroenteritis was found to be statistically highly significant (p<0.001).

**Table 20. Association of abdominal pain with acute viral gastroenteritis**

| Abdominal Pain | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Present | 6 | 42.86 | 8 | 57.14 | 14 | 14.00 |
| Absent | 20 | 23.26 | 66 | 76.74 | 86 | 86.00 |

**$x^2$=2.404** **p=0.121 (NS)**

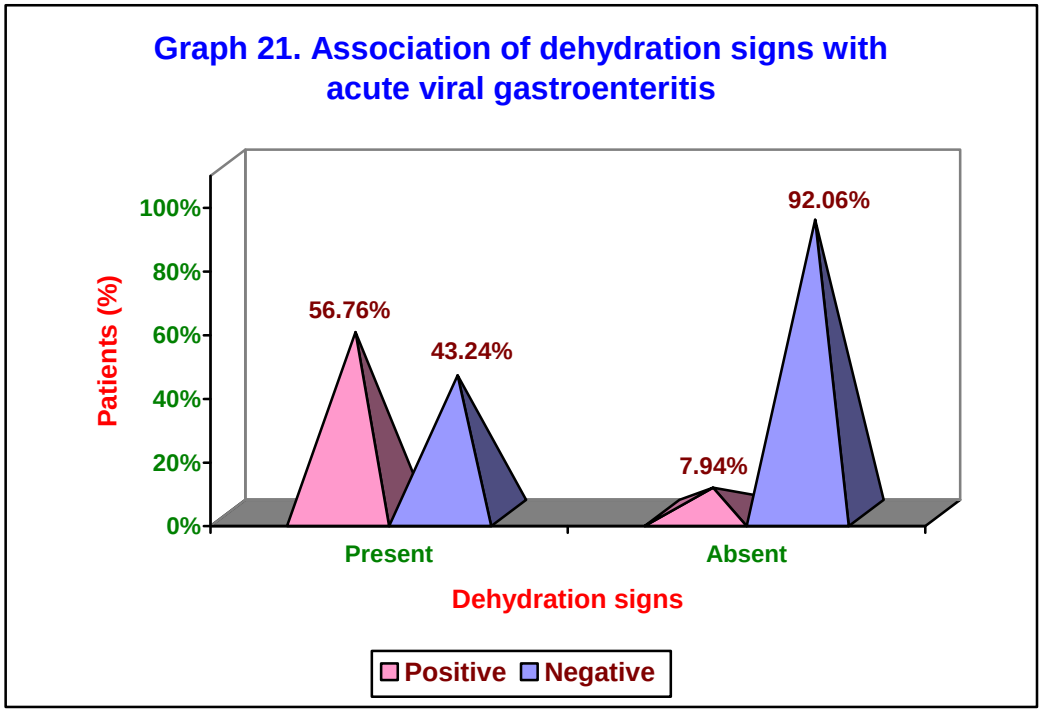



In the studied population, 8 patients gave history of abdominal pain. Out of 8 patients, 6 (42.68%) were positive for viral etiology, whereas 20 patients (23.26%) of viral etiology gave no history of abdominal pain. Association of abdominal pain with viral gastroenteritis was found to be statistically non significant (p=0.121).

**Table 21. Association of dehydration signs with acute viral gastroenteritis**

| Dehydration signs | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Present | 21 | 56.76 | 16 | 43.24 | 37 | 37.00 |
| Absent | 5 | 7.94 | 58 | 92.06 | 63 | 63.00 |

**$x^2$=28.876** **p<0.001 (HS)**

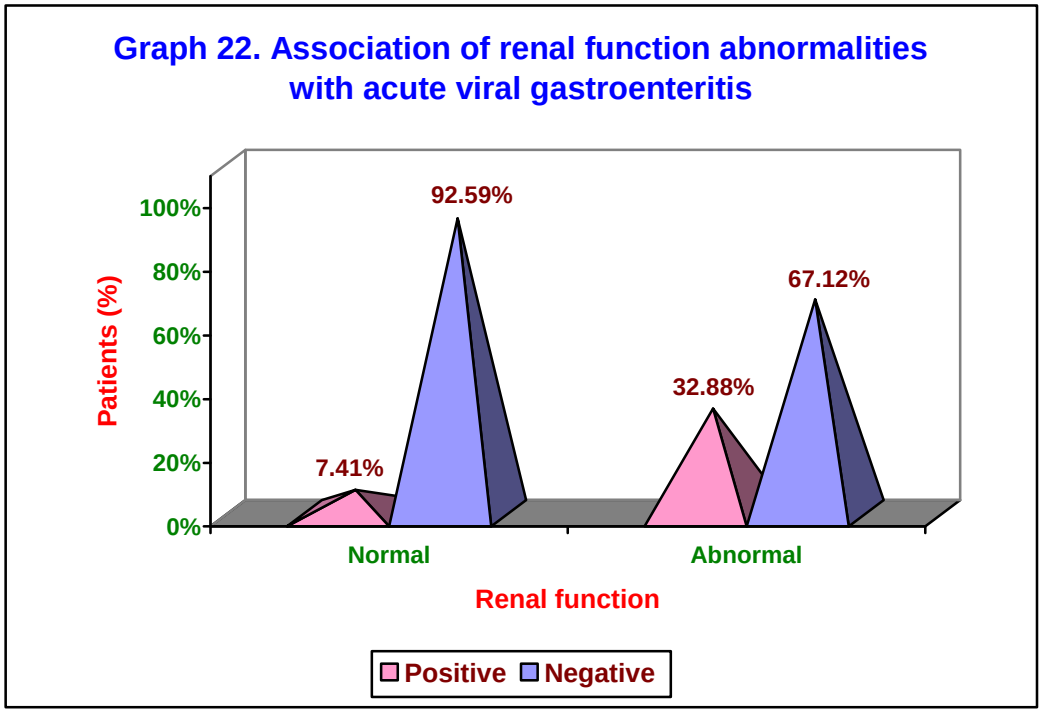



In the studied population, 37 patients presented with all three signs of dehydration. Out of 37 patients, 21 (56.76%) were positive for viral etiology, whereas 5 patients (7.94%) of viral etiology had no signs of dehydration. Association of dehydration signs with viral gastroenteritis was found to be statistically highly significant (p<0.001).

**Table 22. Association of renal function abnormalities with acute viral gastroenteritis**

| Renal function | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Normal | 2 | 7.41 | 25 | 92.59 | 27 | 27.00 |
| Abnormal | 24 | 32.88 | 49 | 67.12 | 73 | 73.00 |

**$x^2$=6.645** **p=0.009 (S)**

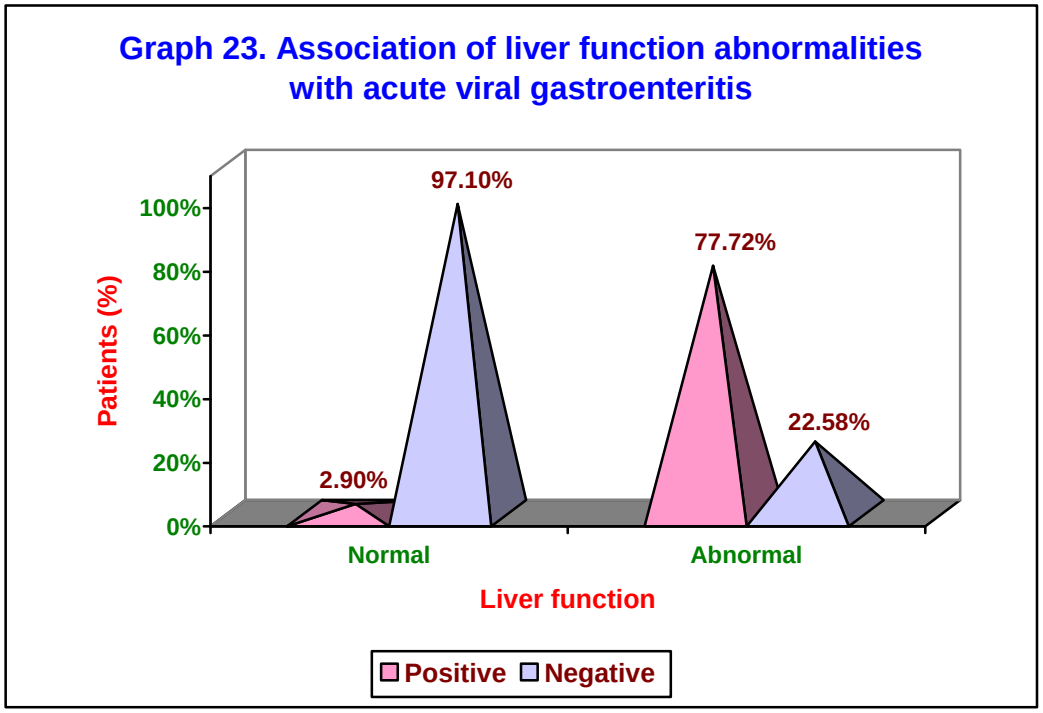



In the studied population, 73 patients had renal function abnormalities. Out of 73 patients, 24 (32.88%) were positive for viral etiology, whereas 2 patients (7.41%) of viral etiology had normal renal function test. Association of renal function test with viral gastroenteritis was found to be statistically significant (p=0.009).

**Table 23. Association of liver function abnormalities with acute viral gastroenteritis**

| Liver function | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Normal | 2 | 2.90 | 67 | 97.10 | 69 | 69.00 |
| Abnormal | 24 | 77.42 | 7 | 22.58 | 31 | 31.00 |

**$x^2$=61.739** **p<0.001 (HS)**

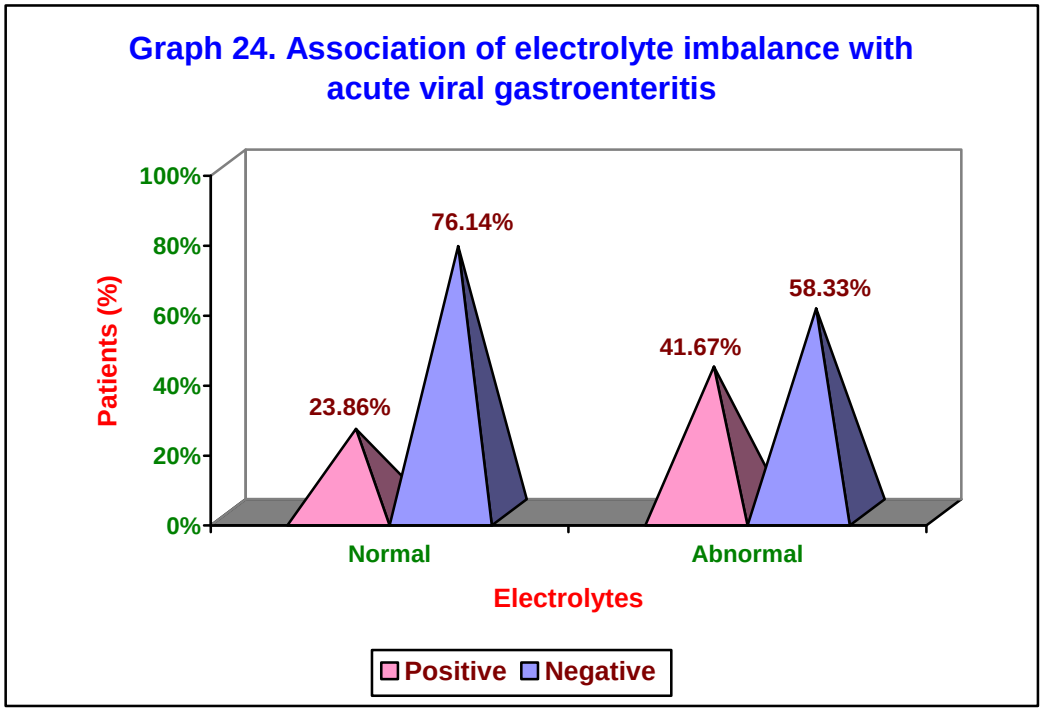



In the studied population, 31 patients had liver function abnormalities. Out of 31 patients, 24 (77.72%) were positive for viral etiology, whereas 2 patients (2.90%) of viral etiology had normal liver function test. Association of liver function test with viral gastroenteritis was found to be statistically highly significant (p<0.001).

**Table 24. Association of electrolyte imbalance with acute viral gastroenteritis**

| Electrolytes | Viral gastroenteritis | | | | Total (n=100) | |
|---|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | | |
| | No. | % | No. | % | No. | % |
| Normal | 21 | 23.86 | 67 | 76.14 | 88 | 88.00 |
| Abnormal | 5 | 41.67 | 7 | 58.33 | 12 | 12.00 |

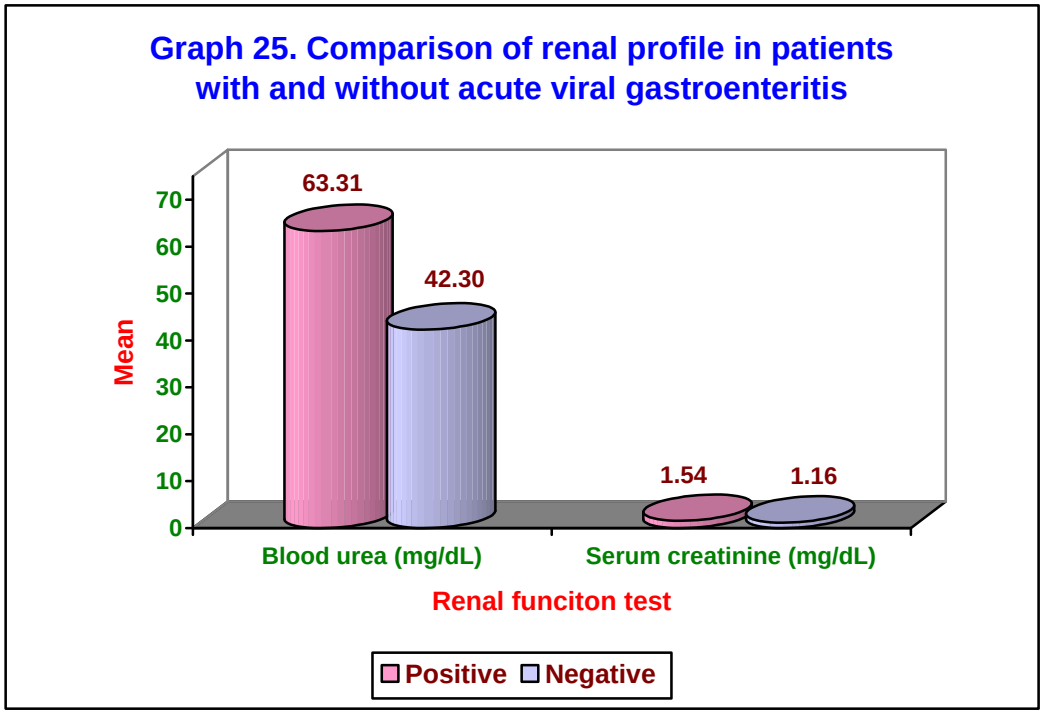
**$x^2$=1.739** **p=0.187 (NS)**




In the studied population, 12 patients had electrolyte abnormalities. Out of 12 patients, 5 (41.67%) were positive for viral etiology, whereas 21 patients (23.86%) of viral etiology had normal electrolytes. Association of viral gastroenteritis and electrolyte disturbance was statistically not significant (p=0.187).

**Table 25. Comparison of renal profile in patients with and without acute viral gastroenteritis**

| Renal function tests | Viral gastroenteritis | | | | 'p' value |
|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | |
| | Mean | SD | Mean | SD | |
| Blood urea (mg/dL) | 63.31 | 16.14 | 42.30 | 23.93 | <0.001 |
| Serum Creatinine (mg/dL) | 1.54 | 0.45 | 1.16 | 0.42 | <0.001 |

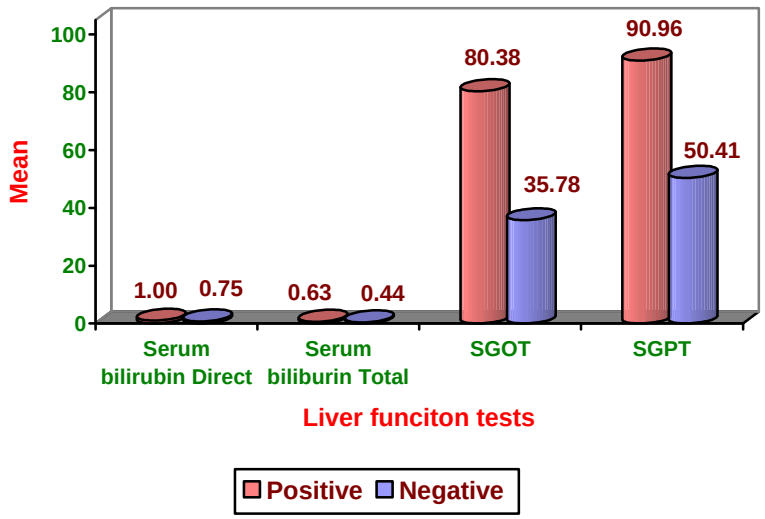



In this study, significant rise was noted in blood urea and serum creatinine levels in patients with positive viral etiology as compared to non determined etiology. (63.31 ± 16.14 mg/dL vs. 42.30 ± 23.93 mg/dL; p<0.001 and 1.54 ± 0.45 mg/dL vs. 1.16 ± 0.42 mg/dL; p<0.001 respectively)

**Table 26. Comparison of liver profile in patients with and without acute viral gastroenteritis**

| Liver function tests | Viral gastroenteritis | | | | 'p' value |
|---|---|---|---|---|---|
| | Positive (n=26) | | Negative (n=74) | | |
| | Mean | SD | Mean | SD | |
| Serum biliburin-Direct (mg/dL) | 1.00 | 0.48 | 0.75 | 0.34 | 0.005 |
| Serum biliburin-Total (mg/dL) | 0.63 | 0.38 | 0.44 | 0.29 | 0.014 |
| SGOT (mg/dL) | 80.38 | 50.38 | 35.78 | 33.57 | <0.001 |
| SGPT (mg/dL) | 90.96 | 48.63 | 50.41 | 49.62 | <0.001 |

**Graph 26. Comparison of liver profile in patients with and without acute viral gastroenteritis**




In this study, significant rise was noted in SGOT and SGPT levels in patients with positive viral etiology as compared to non determined etiology (80.38 ± 50.38 mg/dL vs. 35.78 ± 33.57 mg/dL; p<0.001 and 90.96 ± 48.63 mg/dL vs. 50.41 ± 49.62 mg/dL; p<0.001 respectively). Similarly statistically significant rise in total bilurubin and direct bilurubin levels was (1.00±0.48 mg/dL vs. 0.75±0.34 mg/dL; p = 0.005 and 0.63±0.38 mg/dL vs. 0.44±0.29 mg/dL; p = 0.014 respectively) noted.

Chapter 6

# Discussion

# DISCUSSION

Gastroenteritis is inflammation of the lining of the stomach and small and large intestines. Most cases are infectious, although gastroenteritis may occur after ingestion of drugs and chemical toxins (metals, plant substances). Acquisition may be foodborne, waterborne, or via person-to-person spread. In the US, an estimated 1 in 6 people contracts foodborne illness each year. Symptoms include anorexia, nausea, vomiting, diarrhea, and abdominal discomfort. Diagnosis is clinical or by stool culture, although PCR and immunoassays are increasingly used. Treatment is symptomatic, although some parasitic and some bacterial infections require specific anti-infective therapy.[128]

Gastroenteritis is usually uncomfortable but self-limited. Electrolyte and fluid loss is usually little more than an inconvenience to an otherwise healthy adult but can be grave for people who are very young, elderly, or debilitated or who have serious concomitant illnesses. Worldwide, an estimated 1.5 million children die each year from infectious gastroenteritis; although high, this number represents one half to one quarter of previous mortality. Improvements in water sanitation in many parts of the world and the appropriate use of oral rehydration therapy for infants with diarrhea are likely responsible for this decrease. Infectious gastroenteritis may be caused by viruses, bacteria, or parasites.[128]

The character and severity of symptoms vary. Generally, onset is sudden, with anorexia, nausea, vomiting, borborygmi, abdominal cramps, and diarrhea (with or without blood and mucus). Malaise, myalgias, and prostration may occur. The abdomen may be distended and mildly tender; in severe cases, muscle

guarding may be present. Gas-distended intestinal loops may be palpable. Borborygmi are present even without diarrhea (an important differential feature from paralytic ileus). Persistent vomiting and diarrhea can result in intravascular fluid depletion with hypotension and tachycardia. In severe cases, shock, with vascular collapse and oliguric renal failure, occurs.[128]

If vomiting is the main cause of fluid loss, metabolic alkalosis with hypochloremia can occur. If diarrhea is more prominent, acidosis is more likely. Both vomiting and diarrhea can cause hypokalemia. Hyponatremia may develop, particularly if hypotonic fluids are used in replacement therapy.[128]

In viral infections, watery diarrhea is the most common symptom; stools rarely contain mucus or blood. Rotavirus gastroenteritis in infants and young children may last for 5 to 7 days. Vomiting occurs in 90% of patients, and fever >39° C (>102.2° F) occurs in about 30%. The hallmark of adenovirus gastroenteritis is diarrhea lasting 1 to 2 week. Low-grade fever occurs in about 50% of patients.[128]

The present study was undertaken to investigate the etiology and clinical profile among adults patients with acute viral gastroenteritis and to provide data for recommendations concerning routine testing panel to guide clinicians in the rationale use of diagnostic methods by assessing the systemic manifestations including biochemical parameters.

The present one year hospital based cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2011 to December 2011. A total of 100

patients presenting with passage of more than three stools per day with decrease in stool consistency, increase in stool urgency and/or vomiting and/or abdominal discomfort were studied.

In this study of 100 patients the prevalence of acute viral gastroenteritis was found to be 26%. Rotavirus infection was positive in 20% patients and 4% patients showed positivity for Adeno virus infection. Co-infection of Rotavirus and Adenovirus was observed in 2% cases.

In a study done by U J Deka et al[129] the prevalence of rotavirus infection in adults was 5.6% (6 out of 108 cases). T Krishnan et al[5] studied 53 cases of Rotavirus positive gastroenteritis in Calcutta and he found, 17 (32%) were from adults over 18 years. Hulya Akan et al[3] studied 672 patients in Turkey, and concluded that Rotavirus positivity was 18.7% (n=126). Concomitantly, in 596 cases adenovirus positivity was 8.9% (n=53) and Rota-adenovirus co-infection was 4.4% (n=26). In our study, prevalence of viral etiology was comparable to previous studies.

In this study most of the patients (41%) were less than 30 years followed by 30 to 45 years (33%). However 18% of patients were between 46 to 60 years and 8% patients were aged more than 60 years. Viral etiology associated diarrhea involved cases from 18 to 60 years with maximum in the fourth decades (33.33%).

In a study done by U J Deka et al[129] found that 50% of viral gastroenteritis patients were from third decade of life. Hulya Akan et al[3] observed 13.7% viral infections in 15-64 adult age group and 18% in geriatric age group

which was statistically significant (p=0.048). In our study association of viral etiology as a cause of gastroenteritis with age was found to be statistically non significant (p=0.2213).

The study group included a total of 100 patients. There were 49 males (49%) and 51 females (51%). Viral etiology associated diarrhea was observed in 16 males (32.65%) and 10 females (19.61%).

U J Deka et al[129] reported male dominance (2:1) in rotavirus associated diarrhea from Assam. A study conducted by Hulya Akan et al[3] in Turkey concluded that presence or absence of Rotavirus in the patients did not differ significantly by gender (p=0.785). In our study association of acute viral gastroenteritis with sex was found to be statistically non significant (p=0.137).

In this study all the 100 cases (100%) had diarrhea as defined by inclusion criteria. The next common symptom in this study was vomiting in 51% followed by fever in 34% patients, reduced urine output in 32% and abdominal pain among 14% patients. Of the 51 patients with history of vomiting, 43.14% were positive for viral etiology, whereas 8.16% of patients with viral etiology did not gave history of vomiting.

Hulya Akan et al[3] concluded from a study in Turkey that statistically significant difference was present between the Rotavirus cases and Rotavirus negative cases regarding presence of vomiting (p=0.010). Results in our study showed strong association of vomiting with viral gastroenteritis (p<0.001).

Of the 34 patients with history of fever, 50% were positive for viral etiology, whereas 13.64% of patients with viral etiology gave no history of fever.

Kapikian et al[45] reported fever in 17% of viral etiology associate diarrhea. Another study done by Ward et al[48] observed fever in 19% viral diarrhea. In present study, association of fever with viral gastroenteritis was statistically significant ($p<0.001$).

In the studied population, 32 patients gave history of reduced urine output. Out of 32 patients, 21 (65.63%) were positive for viral etiology, whereas 5 patients (7.35%) of viral etiology gave no history of reduced urine output. Association of reduced urine output with viral gastroenteritis was found to be statistically highly significant ($p<0.001$).

The history suggestive of abdominal pain was noted in 8 patients. Among them 42.68% were positive for viral etiology, but 23.26% of patient with viral etiology gave no history of abdominal pain.

A study conducted by Hulya Akan et al[3] observed no significant difference among rotavirus cases and rotavirus negative cases in respect of presence of pain abdomen. In present study there was no significant association of abdominal pain with viral gastroenteritis ($p=0.121$).

In this study based on skin elasticity, tongue appearance and patient's appearance 37% of patient had signs of dehydration. Among these 56.76% were positive for viral etiology, whereas 7.94% of patients with viral etiology had no signs of dehydration.

A retrospective study[3] in Turkey concluded that statistically highly significant difference was present between the Rotavirus cases and Rotavirus negative cases regarding presence of dehydration ($p<0.001$). In our study association of dehydration signs with viral gastroenteritis was found to be statistically highly significant ($p<0.001$).

Out of 73 patients with renal function abnormalities, 32.88% were positive for viral etiology whereas 7.41% of patients with positive viral etiology had normal renal function test showing statistically significant association of abnormal renal function test with viral gastroenteritis ($p=0.009$).

Among the 31 patients with liver function abnormalities, 77.72% were positive for viral etiology and 2.90% patients with positive viral etiology had normal liver function posing strong association of abnormal liver function with viral gastroenteritis ($p<0.001$).

Teitelbaum et al.[130] demonstrated in their study that 15/75 (20%) children with rotavirus gastroenteritis had associated elevation of their liver transaminases. Our results were similar to the results of the study by Teitelbaum et al.[130]

In those with electrolyte imbalance (n=12), 41.67% were positive for viral etiology, whereas 23.86% of patients with positive viral etiology had normal electrolytes, lacking any statistically significant association of viral gastroenteritis with electrolyte disturbance ($p=0.187$).

David C. A. Candy[131] concluded that the finding of infectious rotavirus in the blood suggests extra-intestinal involvement in rotavirus pathogenesis, though they concede that the impact of rotavirus viremia on clinical manifestations of infection is unknown. In our study, involvement of liver and kidney was statistically significant.

In this study, the qualitative analysis of serum creatinine (1.54 ± 0.45 mg/dL vs. 1.16 ± 0.42 mg/dL; $p<0.001$ respectively) and blood urea (63.31 ± 16.14 mg/dL vs. 42.30 ± 23.93 mg/dL; $p<0.001$) showed statistically significant rise in patients with positive viral etiology as compared to non determined etiology.

Similarly significant rise was noted in SGOT and SGPT levels in patients with positive viral etiology as compared to non determined etiology (80.38 ± 50.38 mg/dL vs. 35.78 ± 33.57 mg/dL; $p<0.001$ and 90.96 ± 48.63 mg/dL vs. 50.41 ± 49.62 mg/dL; $p<0.001$ respectively).

Similarly the statistically significant rise in total bilurubin and direct bilurubin levels was noted in patients with viral etiology as compared to non determined etiology (1.00±0.48 mg/dL vs. 0.75±0.34 mg/dL; $p=0.005$ and 0.63±0.38 mg/dL vs. 0.44±0.29 mg/dL; $p=0.014$ respectively) the difference was statistically not significant.

Chapter 7

# Conclusion

# CONCLUSION

Acute viral gastroenteritis causes significant morbidity in adults. Our study indicates that rotavirus can cause severe gastroenteritis and is an important etiologic agent in hospitalized adult cases whereas Adenovirus represented the second most common etiological agent after rotavirus.

Although there is no clinical gold standard to distinguish viral etiology associated cases from the other gastroenteritis agents, the findings of vomiting, dehydration and reduced urine output may lead clinician to perform rapid antigen test and affect approach to the treatment.

Viral associated gastroenteritis routinely extends beyond the intestine to the blood and have the potential to be widely distributed and cause systemic manifestations. Clinicians should be alert for rare but potentially serious extra intestinal complications of viral gastroenteritis.

The combined cost and stress of hospitalization, diagnostic testing, prompting prolonged medical therapy, appears to justify attempts at prevention. Given the substantial disease related morbidity associated with rotavirus the development of an effective vaccine is a priority.

Further, the findings of this study have to be confirmed involving large sample size and follow up to determine the rotavirus and adenovirus incidence and extra intestinal manifestations.

Chapter 8

# Summary

# SUMMARY

It is now appreciated that viruses are the most common cause of diarrhoeal illness worldwide. Viruses like rotavirus and adenovirus are the most common causative agents of acute viral gastroenteritis. The clinical spectrum of rotavirus disease varies from asymptomatic infection to acute, severe, dehydrating diarrhea with vomiting that can be fatal. The present study was an attempt to investigate the etiology and clinical profile among adult patients with acute viral gastroenteritis.

This one year hospital based cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. A total of 100 patients presenting with passage of more than three stools per day with decrease in stool consistency, increase in stool urgency and/or vomiting and/or abdominal discomfort from January 2011 to December 2011 were studied. The diagnosis of viral etiology (Rota virus, Adeno virus and co-infection) was determined by Rapid kit test.

In this study most of the patients (41%) had age less than 30 years followed by 30 to 45 years (33%). Acute gastroenteritis was present in 51% and 49% males. The most common symptoms were diarrhea (100%) followed by vomiting (51%). Based on skin elasticity, tongue appearance and patient appearance 37% of patient had signs of dehydration. Abnormal blood urea and serum creatinine levels were observed in 66% and 50% of patients. Abnormal liver functions were reported in 89%, abnormal renal function in 73% and electrolyte imbalance was noted in 12%.

The overall prevalence of viral gastroenteritis was 26%. Viral gastroenteritis was significantly associated with symptoms of vomiting, fever, reduced urine output, signs of dehydration, abnormal liver and renal function tests ($p<0.050$).

The combined cost and stress of hospitalization, diagnostic testing, prompting prolonged medical therapy, appears to justify attempts at prevention. Given the substantial disease related morbidity associated with rotavirus the development of an effective vaccine is a priority.

Chapter 9

# Bibliography

# BIBLIOGRAPHY

1. Tidy C. Gastroenteritis in adults and older children. Available from:URL:http://www.patient.co.uk/doctor/Gastroenteritis-in-Adults-and-Older-Children.htm Access Date:18.06.12.

2. Casburn-Jones AC, Farthing MJG. Management of infectious diarrhoea. Gut 2004;53(2):296–305.

3. Akan H, Izbırak G, Gürol Y, Sarıkaya S, Gündüz TS, Yılmaz G, et al. Rotavirus and adenovirus frequency among patients with acute gastroenteritis and their relationship to clinical parameters:a retrospective study in Turkey. Asia Pac Fam Med 2009;8(1):8.

4. Clark B, McKendrick M. A review of viral gastroenteritis. Curr Opin Infect Dis 2004;17(5):461-9.

5. Krishnan T, Sen A, Choudhury JS, Das S, Naik TN, Bhattacharya SK. Emergence of adult diarrhoea rotavirus in Calcutta, India. Lancet 1999;353:380–1.

6. Broor S, Ghosh D, Mathur P. Molecular epidemiology of rotaviruses in India. Indian J Med Res 2003;118:59-67.

7. Gangarosa RE, Glass RI, Lew JF, Boring JR. Hospitalizations involving gastroenteritis in the United States, 1985:the special burden of the disease among the elderly. Am J Epidemiol 1992;135:281-90.

8. Ramani S, Kang G. Viruses causing childhood diarrhoea in the developing world. Curr Opin Infect Dis 2009;22(5):477-82.

9. Scarcella C, Carasi S, Cadoria F, Macchi L, Pavan A, Salamana M, et al. An outbreak of viral gastroenteritis linked to municipal water supply, Lombardy, Italy, June 2009. Euro Surveill 2009;14(29):epub ahead of print.

10. Fischer TK, Ashley D, Kerin T, Reynolds-Hedmann E, Gentsch J, Widdowson MA, et al. Rotavirus antigenemia in patients with acute gastroenteritis. J Infect Dis 2005;192(5):913-9.

11. Kumar ML, Super DM, Lembo RM, Thomas FC, Prokay SL. Diagnostic efficacy of two rapid tests for detection of respiratory syncytial virus antigen. J Clin Microbiol 1987;25:873-5.

12. Jansen A, Stark K, Kunkel J, Schreier E, Ignatius R, Liesenfeld O, et al. Aetiology of community-acquired, acute gastroenteritis in hospitalised adults:a prospective cohort study. BMC Infect Dis. 2008;8:143.

13. Svenungsson B, Lagergren A, Ekwall E, Evengård B, Hedlund KO, Kärnell A, et al. Enteropathogens in adult patients with diarrhea and healthy control subjects:a 1-year prospective study in a Swedish clinic for infectious diseases. Clin Infect Dis 2000;30:770-8.

14. Diskin A, Dronen SC. Gastroenteritis in emergency medicine. 2012. Available from:URL:http://emedicine.medscape.com/article/775277-overview Access Date:15.06.12

15. Diarrhoeal disease. Fact Sheet No. 330. Geneva;World Health Organization:2009. Available from:URL:http://www.who.int/mediacentre/factsheets/fs330/en/index.html Access Date:19.06.12

16. Lamberti LM, Fischer Walker CL, Black RE. Systematic review of diarrhea duration and severity in children and adults in low- and middle-income countries. BMC Public Health 2012;12:276

17. Fischer-Walker CL, Black RE. Diarrhoea morbidity and mortality in older children, adolescents, and adults. Epidemiol Infect 2010;138(9):1215-26.

18. Feldman R, Banatvala N. The frequency of culturing stools from adults with diarrhoea in Great Britain. Epidemiol Infect 1994;113:41-4.

19. Wheeler J, Sethi D, Cowden J, Wall P, Rodrigues L, Tompkins D, et al. Study of infectious intestinal disease in England:rates in the community, presenting to general practice, and reported to national surveillance. BMJ 1999;318:1046-50.

20. De Wit MA, Kortbeek LM, Koopmans MP, de Jager CJ, Wannet WJ, Bartelds A, et al. A comparison of gastroenteritis in a general practice-based study. Epidemiol Infect 2001;127:389-97.

21. Hall AJ, Curns AT, McDonald LC, Parashar UD, Lopman BA. The Roles of Clostridium difficile and Norovirus Among Gastroenteritis-Associated Deaths in the United States, 1999-2007. Clin Infect Dis 2012;55(2):216-23.

22. Lal P, Bansal AK, Aggarwal CS, Taneja DK, Gogia V. Incidence of diarrhoea and some related environmental and behavioural factors in Jhuggis of Delhi. Indian J Public Health 1996;40(2):35-7.

23. Glass RI, Noel J, Ando T, Fankhauser R, Belliot G, Mounts A, Parashar UD, et al. The epidemiology of enteric caliciviruses from humans:a reassessment using new diagnostics. J Infect Dis 2000;181(2):S254-61.

24. CDC research shows outbreaks linked to imported foods increasing. Available from:URL: http://www.cdc.gov/media/releases/2012/p0314 _foodborne.html. Access Date:14.03.2012.

25. Gonzalez GG, Liprandi F, Ludert JE. Molecular epidemiology of enteric viruses in children with sporadic gastroenteritis in Valencia, Venezuela. J Med Virol. 2011;83:1972-82.

26. Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. Bull World Health Organ 2003;81:197-204.

27. Guandalini S, Cuffari C. Diarrhea. Available from:URL:http:// emedicine.medscape.com/article/928598-overview#a0104 Access Date:10.06.12.

28. Farthing M, Lindberg G, Dite P, Khalif I, Salazar-Lindo E, Ramakrishna BS, et al. Acute Diarrhoea. USA:World Gastroenterology Organisation practice guideline:2008.

29. Anderson EJ, Weber SG. Rotavirus infection in adults. Lancet Infect Dis. 2004;4(2):91-9.

30. Bishop RF, Davidson GP, Holmes IH, Ruck BJ. Virus particles in epithelial cells of duodenal mucosa from children with acute non-bacterial gastroenteritis. Lancet 1973;2:1281–83.

31. Estes MK. Rotaviruses and their replication. In:Knipe DM, Howley PM, eds. Fields' virology, 4th edn., Philadelphia:Lippincott Williams and Wilkins;2001:1747–85.

32. Lundgren O, Svensson L. Pathogenesis of rotavirus diarrhea. Microbes Infect 2001;3:1145–56.

33. Barnes GL, Townley RR. Duodenal mucosal damage in 31 infants with gastroenteritis. Arch Dis Child 1973;48:343–9.

34. Davidson GP, Barnes GL. Structural and functional abnormalities of the small intestine in infants and young children with rotavirus enteritis. Acta Paediatr Scand 1979;68:181–6.

35. Offit PA. Host factors associated with protection against rotavirus disease:the skies are clearing. J Infect Dis 1996;174:S59–64.

36. Bernstein DI, McNeal MM, Schiff GM, Ward RL. Induction and persistence of local rotavirus antibodies in relation to serum antibodies. J Med Virology 1989;28:90–5.

37. De Boissieu D, Lebon P, Badoual J, Bompard Y, Dupont C. Rotavirus induces alpha-interferon release in children with gastroenteritis. J Pediatr Gastroenterol Nutr 1993;16:29–32.

38. Bishop RF, Barnes GL, Cipriani E, Lund JS. Clinical immunity after neonatal rotavirus infection:a prospective longitudinal study in young children. N Engl J Med 1983;309:72–6.

39. Jiang B, Gentsch JR, Glass RI. The role of serum antibodies in the protection against rotavirus disease:an overview. Clin Infect Dis 2002;34:1351–61.

40. Coulson BS, Grimwood K, Hudson IL, Barnes GL, Bishop RF. Role of coproantibody in clinical protection of children during reinfection with rotavirus. J Clin Microbiol 1992;30:1678–84.

41. Sharma R, Hudak ML, Premachandra BR, Stevens G, Monteiro CB, Bradshaw JA, et al. Clinical manifestations of rotavirus infection in the neonatal intensive care unit. Pediatr Infect Dis J 2002;21:1099–105.

42. Crawley JM, Bishop RF, Barnes GL. Rotavirus gastroenteritis in infants aged 0-6 months in Melbourne, Australia: Implications for vaccination. J Paediatr Child Health 1993;29:219–21.

43. Grimwood K, Lund JC, Coulson BS, Hudson IL, Bishop RF, Barnes GL. Comparison of serum and mucosal antibody responses following severe acute rotavirus gastroenteritis in young children. J Clin Microbiol 1988;26:732–8.

44. Velazquez FR, Matson DO, Calva JJ, Guerrero L, Morrow AL, Carter-Campbell S, et al. Rotavirus infections in infants as protection against subsequent infections. N Engl J Med 1996;335:1022–8.

45. Kapikian AZ, Wyatt RG, Levine MM, Yolken RH, VanKirk DH, Dolin R, et al. Oral administration of human rotavirus to volunteers:induction of illness and correlates of resistance. J Infect Dis 1983;147:95–106.

46. Ward RL, Bernstein DI, Shukla R, Young EC, Sherwood JR, McNeal MM, et al. Effects of antibody to rotavirus on protection of adults challenged with a human rotavirus. J Infect Dis 1989;159:79–88.

47. Ward RL, Bernstein DI, Shukla R, McNeal MM, Sherwood JR, Young EC, et al. Protection of adults rechallenged with a human rotavirus. J Infect Dis 1990;161:440–5.

48. Ward RL, Bernstein DI, Young EC, Sherwood JR, Knowlton DR, Schiff GM. Human rotavirus studies in volunteers: Determination of infectious dose and serological response to infection. J Infect Dis 1986;154:871–80.

49. Middleton PJ, Szymanski MT, Abbott GD, Bortolussi R. Orbivirus acute gastroenteritis of infancy. Lancet 1974;1:1241–4.

50. Wenman WM, Hinde D, Feltham S, Gurwith M. Rotavirus infection in adults. Results of a prospective family study. N Engl J Med 1979;301:303–6.

51. Kapikian AZ, Kim HW, Wyatt RG, Cline WL, Arrobio JO, Brandt CD, et al. Human reovirus-like agent as the major pathogen associated with "winter" gastroenteritis in hospitalized infants and young children. N Engl J Med 1976;294:965–72.

52. Grimwood K, Abbott GD, Fergusson DM, Jennings LC, Allan JM. Spread of rotavirus within families: A community based study. BMJ 1983;287:575–7.

53. Foodborne outbreak of Group A rotavirus gastroenteritis among college students:District of Columbia, March–April 2000. MMWR Morb Mortal Wkly Rep 2000;49:1131–3.

54. Saulsbury FT, Winkelstein JA, Yolken RH. Chronic rotavirus infection in immunodeficiency. J Pediatr 1980;97:61–5.

55. Adams WR, Kraft LM. Epizootic diarrhea of infant mice:identification of the etiologic agent. Science 1963;141:359–60.

56. Gilger MA, Matson DO, Conner ME, Rosenblatt HM, Finegold MJ, Estes MK. Extraintestinal rotavirus infections in children with immunodeficiency. J Pediatr 1992;120:912–7.

57. Bolivar R. Rotavirus screening in adult cancer patients. South Med J 1983;76:418.

58. Troussard X, Bauduer F, Gallet E, Freymuth F, Boutard P, Ballet JJ, et al. Virus recovery from stools of patients undergoing bone marrow transplantation. Bone Marrow Transplant 1993;12:573–6.

59. Albrecht H, Stellbrink HJ, Fenske S, Ermer M, Raedler A, Greten H. Rotavirus antigen detection in patients with HIV infection and diarrhea. Scand J Gastroenterol 1993;28:307–10.

60. Thomas PD, Pollok RC, Gazzard BG. Enteric viral infections as a cause of diarrhoea in the acquired immunodeficiency syndrome. HIV Med 1999;1:19–24.

61. Iturriza-Gomara M, Green J, Brown DW, Ramsay M, Desselberger U, Gray JJ. Molecular epidemiology of human group A rotavirus infections in the United Kingdom between 1995 and 1998. J Clin Microbiol 2000;38:4394–401.

62. Cox MJ, Medley GF. Serological survey of antigroup A rotavirus IgM in UK adults. Epidemiol Infect 2003;131:719–26.

63. Nakajima H, Nakagomi T, Kamisawa T, Sakaki N, Muramoto K, Mikami T, et al. Winter seasonality and rotavirus diarrhoea in adults. Lancet 2001;357:1950.

64. Pryor WM, Bye WA, Curran DH, Grohmann GS. Acute diarrhoea in adults:a prospective study. Med J Aust 1987;147:490–3.

65. Oyofo BA, Subekti D, Tjaniadi P, Machpud N, Komalarini S, Setiawan B, et al. Enteropathogens associated with acute diarrhea in community and hospital patients in Jakarta, Indonesia. FEMS Immunol Med Microbiol 2002;34:139–46.

66. del Refugio Gonzalez-Losa M, Polanco-Marin GG, Manzano-Cabrera L, Puerto-Solis M. Acute gastroenteritis associated with rotavirus in adults. Arch Med Res 2001;32:164–7.

67. James VL, Lambden PR, Caul EO, Cooke SJ, Clarke IN. Seroepidemiology of human group C rotavirus in the UK. J Med Virol 1997;52:86–91.

68. von Bonsdorff CH, Hovi T, Makela P, Morttinen A. Rotavirus infections in adults in association with acute gastroenteritis. J Med Virol 1978;2:21–8.

69. Foster SO, Palmer EL, Gary GW Jr, Martin ML, Herrmann KL, Beasley P, et al. Gastroenteritis due to rotavirus in an isolated Pacific island group:an epidemic of 3,439 cases. J Infect Dis 1980;141:32–9.

70. Meurman OH, Laine MJ. Rotavirus epidemic in adults. N Engl J Med 1977;296:1298–9.

71. Friedman MG, Galil A, Sarov B, Margalith M, Katzir G, Midthun K, et al. Two sequential outbreaks of rotavirus gastroenteritis:evidence for symptomatic and asymptomatic reinfections. J Infect Dis 1988;158:814–22.

72. Marrie TJ, Lee SH, Faulkner RS, Ethier J, Young CH. Rotavirus infection in a geriatric population. Arch Intern Med 1982;142:313–6.

73. Cubitt WD, Holzel H. An outbreak of rotavirus infection in a long-stay ward of a geriatric hospital. J Clin Pathol 1980;33:306–8.

74. Dupuis P, Beby A, Bourgoin A, Lussier-Bonneau MD, Agius G. Epidemic of viral gastroenteritis in an elderly community. Presse Med 1995;24:356–8.

75. Abbas AM, Denton MD. An outbreak of rotavirus infection in a geriatric hospital. J Hosp Infect 1987;9:76–80.

76. Lewis DC, Lightfoot NF, Cubitt WD, Wilson SA. Outbreaks of astrovirus type 1 and rotavirus gastroenteritis in a geriatric inpatient population. J Hosp Infect 1989;14:9–14.

77. Halvorsrud J, Orstavik I. An epidemic of rotavirusassociated gastroenteritis in a nursing home for the elderly. Scand J Infect Dis 1980;12:161–4.

78. Ryan MJ, Wall PG, Adak GK, Evans HS, Cowden JM. Outbreaks of infectious intestinal disease in residential institutions in England and Wales 1992–1994. J Infect 1997;34:49–54.

79. Hopkins RS, Gaspard GB, Williams FP, Karlin RJ, Cukor G, Blacklow NR. A community waterborne gastroenteritis outbreak:evidence for rotavirus as the agent. Am J Public Health 1984;74:263–5.

80. Griffin DD, Fletcher M, Levy ME, Ching-Lee M, Nogami R, Edwards L, et al. Outbreaks of adult gastroenteritis traced to a single genotype of rotavirus. J Infect Dis 2002;185:1502–5.

81. Fang ZY, Ye Q, Ho MS, Dong H, Qing S, Penaranda ME, et al. Investigation of an outbreak of adult diarrhea rotavirus in China. J Infect Dis 1989;160:948–53.

82. Halasz P, Holloway G, Coulson BS. Death mechanisms in epithelial cells folowing rotavirus infection, exposure to inactivated rotavirus or genome transfection. J Gen Virol 2010;91:2007-18.

83. Yolken RH, Wilde J. Assays for detecting human rotavirus. In:Kapikian AZ, ed. Viral infections of the gastrointestinal tract, 2nd edn. New York:M Dekker, 1994:251–78.

84. Wilde J, Yolken R, Willoughby R, Eiden J. Improved detection of rotavirus shedding by polymerase chain reaction. Lancet 1991;337:323–6.

85. Hrdy DB. Epidemiology of rotaviral infection in adults. Rev Infect Dis 1987;9:461–9.

86. Rao GG. Control of outbreaks of viral diarrhoea in hospitals:a practical approach. J Hosp Infect 1995;30:1–6.

87. Duerkson-Hughes P, Wold WS, Gooding LR. Adenovirus E1A renders infected cells sensitive to cytolysis by tumor necrosis factor. J Immunol 1989;143:4193-4200.

88. Richardson S, Grimwood K, Gorrell R, Palombo E, Barnes G, Bishop R. Extended excretion of rotavirus after severe diarrhoea in young children. Lancet 1998;351:1844–8.

89. Vollet JJ, Ericsson CD, Gibson G, Pickering LK, DuPont HL, Kohl S, et al. Human rotavirus in an adult population with travelers' diarrhea and its relationship to the location of food consumption. J Med Virol 1979;4:81–7.

90. Steffen R, Collard F, Tornieporth N, Campbell-Forrester S, Ashley D, Thompson S, et al. Epidemiology, etiology, and impact of traveler's diarrhea in Jamaica. JAMA 1999;281:811–7.

91. Bolivar R, Conklin RH, Vollet JJ, Pickering LK, DuPont HL, Walters DL, et al. Rotavirus in travelers' diarrhea:study of an adult student population in Mexico. J Infect Dis 1978;137:324–7.

92. Keswick BH, Blacklow NR, Cukor GC, DuPont HL, Vollet JL. Norwalk virus and rotavirus in travellers' diarrhoea in Mexico. Lancet 1982;1:109–10.

93. Ryder RW, Oquist CA, Greenberg H, Taylor DN, Orskov F, Orskov I, et al. Travelers' diarrhea in panamanian tourists in Mexico. J Infect Dis 1981;144:442–8.

94. Sheridan JF, Aurelian L, Barbour G, Santosham M, Sack RB, Ryder RW. Traveler's diarrhea associated with rotavirus infection:analysis of virus-specific immunoglobulin classes. Infect Immun 1981;31:419–29.

95. Kim HW, Brandt CD, Kapikian AZ, Wyatt RG, Arrobio JO, Rodriguez WJ, et al. Human reovirus-like agent infection:occurrence in adult contacts of pediatric patients with gastroenteritis. JAMA 1977;238:404–7.

96. Rodriguez WJ, Kim HW, Brandt CD, Yolken RH, Richard M, Arrobio JO, et al. Common exposure outbreak of gastroenteritis due to type 2 rotavirus with high secondary attack rate within families. J Infect Dis 1979;140:353–7.

97. von Bonsdorff CH, Hovi T, Makela P, Hovi T, Tevalvoto-Aarnio M. Rotavirus associated with acute gastroenteritis in adults. Lancet 1976;2:423.

98. Orstavik I, Haug KW, Sovde A. Rotavirus-associated gastroenteritis in two adults probably caused by virus reinfection. Scand J Infect Dis 1976;8:277–8.

99. Guarino A, Canani RB, Spagnuolo MI, Albano F, Di Benedetto L. Oral bacterial therapy reduces the duration of symptoms and of viral excretion in children with mild diarrhea. J Pediatr Gastroenterol Nutr 1997; 25: 516–9.

100. Sattar SA, Lloyd-Evans N, Springthorpe VS, Nair RC. Institutional outbreaks of rotavirus diarrhoea:potential role of fomites and environmental surfaces as vehicles for virus transmission. J Hyg 1986;96:277–89.

101. Murphy BR, Morens DM, Simonsen L, Chanock RM, La Montagne JR, Kapikian AZ. Reappraisal of the association of intussusception with the licensed live rotavirus vaccine challenges initial conclusions. J Infect Dis 2003;187:1301–8.

102. Murphy TV, Smith PJ, Gargiullo PM, Schwartz B. The first rotavirus vaccine and intussusception:epidemiological studies and policy decisions. J Infect Dis 2003;187:1309–13.

103. Gompf SG, Cunha BA. Adenoviruses. Available from: URL: http ://emedicine.medscape.com/article/211738-overview Access Date: 20.06.12

104. Kopecky-Bromberg SA, Palese P. Recombinant vectors as influenza vaccines. Curr Top Microbiol Immunol. 2009;333:243-67.

105. Harvey AR, Hellström M, Rodger J. Gene therapy and transplantation in the retinofugal pathway. Prog Brain Res. 2009;175:151-61.

106. Limbach KJ, Richie TL. Viral vectors in malaria vaccine development. Parasite Immunol. Sep 2009;31(9):501-19.

107. Vora GJ, Lin B, Gratwick K, Meador C, Hansen C, Tibbetts C et al. Co-infections of adenovirus species in previously vaccinated patients. Emerg Infect Dis. June 2006;12:921-30.

108. Echavarría M. Adenoviruses in immunocompromised hosts. Clin Microbiol Rev. Oct 2008;21(4):704-15.

109. Shah KV. SV40 and human cancer: A review of recent data. Int J Cancer. Jan 15 2007;120(2):215-23.

110. Martini F, Corallini A, Balatti V, Sabbioni S, Pancaldi C, Tognon M. Simian virus 40 in humans. Infect Agent Cancer. 2007;2:13.

111. Tabain I, Ljubin-Sternak S, Cepin-Bogovic J, Markovinovic L, Knezovic I, Mlinaric-Galinovic G. Adenovirus Respiratory Infections in Hospitalized Children:Clinical Findings in Relation to Species and Serotypes. Pediatr Infect Dis J. 2012;31(7):680-4

112. Faden H, Wynn RJ, Campagna L, Ryan RM. Outbreak of adenovirus type 30 in a neonatal intensive care unit. J Pediatr. Apr 2005;146(4):523-7.

113. Kajon AE, Moseley JM, Metzgar D, Huong HS, Wadleigh A, Ryan MA. Molecular epidemiology of adenovirus type 4 infections in US military recruits in the postvaccination era (1997-2003). J Infect Dis. Jul 1 2007;196(1):67-75.

114. Russell KL, Hawksworth AW, Ryan MA, Strickler J, Irvine M, Hansen CJ, et al. Vaccine-preventable adenoviral respiratory illness in US military recruits,1999-2004. Vaccine. April 2006;15:2835-42.

115. Wirsing von König CH, Rott H, Bogaerts H, Schmitt HJ. A serologic study of organisms possibly associated with pertussis-like coughing. Pediatr Infect Dis J 1998;17(7):645-9.

116. Versteegh FG, Mooi-Kokenberg EA, Schellekens JF, Roord JJ. Bordetella pertussis and mixed infections. Minerva Pediatr. 2006;58(2):131-7.

117. Dart JK, El-Amir AN, Maddison T, Desai P, Verma S, Hughes A, et al. Identification and control of nosocomial adenovirus keratoconjunctivitis in an ophthalmic department. Br J Ophthalmol. 2009;93(1):18-20.

118. Bruno B, Zager RA, Boeckh MJ, Gooley TA, Myerson DH, Huang ML, et al. Adenovirus nephritis in hematopoietic stem-cell transplantation. Transplantation. 2004;77(7): 1049-57.

119. Nakamura Y, Ohashi K, Nakano N, Nemoto T, Funada N, Ando M. [Acute necrotizing tubulointerstitial nephritis due to adenoviral infection following hematopoietic stem cell transplantation:clinical findings obtained from 4 autopsy cases]. Nippon Jinzo Gakkai Shi 2008;50(8): 1036-43.

120. Jalal H, Bibby DF, Tang JW, Bennett J, Kyriakou C, Peggs K. First reported outbreak of diarrhea due to adenovirus infection in a hematology unit for adults. J Clin Microbiol 2005;43(6):2575-80.

121. Ison MG. Adenovirus infections in transplant recipients. Clin Infect Dis 2006;43(3):331-9.

122. Hedderwick SA, Greenson JK, McGaughy VR, Clark NM. Adenovirus cholecystitis in a patient with AIDS. Clin Infect Dis. 1998;26(4):997-9.

123. Liu M, Worley S, Arrigain S, Aurora P, Ballmann M, Boyer D, et al. Respiratory viral infections within one year after pediatric lung transplant. Transpl Infect Dis 2009;11(4):304-12.

124. Echavarria M, Sanchez JL, Kolavic-Gray SA, Polyak CS, Mitchell-Raymundo F, Innis BL, et al. Rapid detection of adenovirus in throat swab specimens by PCR during respiratory disease outbreaks among military recruits. J Clin Microbiol 2003;41(2):810-2.

125. Comparison of a Rotavirus Latex Agglutination Test with Two Rapid Immunochromatographic Test Devices for Detection of Rotavirus in Human Feces. Switzerland; Dep. Medicine Microbiology: 2000.

126. Epidemiological Features of Rotavirus Infection in Goiania, goias, Brazil, From 1986 to 2000. Rio de Janeiro 2003. p. 25-29.

127. Evaluation of Latex Agglutination Kit (Virogen Rotatest) for Detection of Bovine Rotavirus in Fecal Samples. Am Soc Microbiol 2001;496-8.

128. Boyce TG. Overview of Gastroenteritis. Available from:URL:http://www.merckmanuals.com/professional/gastrointestinal_disorders/gastroenteritis/overview_of_gastroenteritis.html Access Date:19.08.12

129. Deka UJ, Dutta PK, Phukan AC, Kakati S, Doley B. Acute Diarrhoeal Diseases in Adults with Special Reference to Rotavirus Diarrhoea. JAPI 2005;53:242.

130. Teitelbaum JE, Daghistani R. Rotavirus causes hepatic transaminase elevation. Dig Dis Sci 2007;52:3396-8.

131. Candy DCA. Rotavirus Infection:A Systemic Illness? PLoS Med. 2007 April;4(4):e117.

# Annexures

## Annexure I

# ANNEXURE I – CONSENT FORM

## "CLINICAL PROFILE OF ACUTE VIRAL GASTROENTERITIS – A ONE YEAR CROSS-SECTIONAL STUDY"

**Objective and purpose of the study:**

This research is intended to study the frequency and the clinical manifestations of acute gastroenteritis. The principal investigator of the study is Dr. ***** ****** under the guidance of Dr. ****** *******. My co-operation will be of great help to patients with gastroenteritis by helping them in detecting the etiology of infection and thus in guiding the institute in the treatment and prevention of gastroenteritis.

**Procedure:**

If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood, urine and stool samples for the necessary investigations

**Risk and Benefits:**

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

**Alternatives**

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part now, you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study any time. If you choose not to take part in the study you will receive the standard treatment for patients with your condition.

**Privacy and Confidentiality**

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

**Institution / Sponsor's policy**

Does not apply to this research

**Financial incentives for participation**

You will not be paid / offered any gifts /incentives for participating in the study.

**Authorization to publish the results**

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

If I have any questions about your rights as a participant you may call Principal and Chairman, J.N.M.C Ethical Committee for Human Research phone number **** *******.

**Consent Statement**

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

In case of the queries during study or in future you may contact following person

Principal investigator : Dr. ***** *******

Guide : Dr. ****** *******

Name of the Participant: _____

Signature / Thumb print _____

Name of the Witness _____

Signature _____

Name of the investigator _____

Signature _____

Date: Place:

Annexures

# Annexure II

# ANNEXURE II – PROFORMA

**Name:**

**Age**

**Sex:**

**IP No.**

**History**

Diarrhoea :

Vomiting :

Abdominal pain and discomfort:

Reduced urine output :

Past history

Drug intake :

Associated conditions :

Family history

**General physical examination**

| | | | | | |
|---|---|---|---|---|---|
| Weight (Kg) | : | Temperature ($^0$F) | : | Pallor | : |
| Cyanosis | : | Pedal oedema | : | Clubbing: | |
| PR | : | BP | : | RR | : |

**Signs of dehydration**

Skin elasticity :

Tongue appearance :

Patients appearance :

**Systemic examination**

| | | | |
|---|---|---|---|
| RS | : | CNS | : |
| CVS | : | GIT | : |

**Investigations**

Rapid kit test of adeno and rota virus

| | | | |
|---|---|---|---|
| Hb% | : | Urine routine | : |
| Blood urea | : | Serum creatinine: | |
| FBS | : | CXR | : |
| LFT | : | | |

**Diagnosis**

**Treatment**

**Outcome**

Annexures

# Annexure III

# ANNEXURE III – KEY TO MASTER CHART

| | |
|---|---|
| GPE | - General physical examination |
| LFT | - Liver function test |
| gm | - Gram |
| meq | - Milli equivalent |
| L | - Liter |
| mg | - Milli gram |
| dL | - Deci litre |
| Sr. | - Serum |
| Bili | - Bilirubin |
| SGOT | - Serum glutamic oxaloacetic transaminase |
| SGPT | - Serum glutamic pyruvic transaminase |
| ROTA | - Rotavirus |
| ADENO | - Adenovirus |
| M | - Male |
| F | - Female |
| D | - Positive dehydration sign |
| N | - Normal |
| - | - Absent |
| + | - Present |
| BOTH | - Co-infection (Rota and Adeno) |

## ANNEXURE III - MASTER CHART

| Case Number | Sex | Age (Years) | History | | | | GPE | | | | Investigations | | | | | | | | | | | | Diagnosis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Dehydration | | | | | | | | | | LFT | | | | | |
| | | | | | | | | | | | | | | | | | | Sr. Bili | | | | | |
| | | | Diarrhoea | Vomiting | Adbominal pain | Reduced urine output | Temperature | Skin elasticity | Tongue appearance | Patient appearance | Adeno and rotavirus test | Haemoglobin (gm%) | Urine routine | Blood urea (mg/dL) | Serum creatinine (mg/dL) | Serum sodium (meq/L) | Serum potassium (meq/L) | Total (mg/dL) | Direct (mg/dL) | SGOT | SGPT | |
| 1 | F | 44 | + | + | - | - | - | N | N | N | - | 13.8 | N | 78 | 1.9 | 138 | 4.6 | 0.4 | 0.2 | 60 | 72 | - |
| 2 | F | 38 | + | - | - | - | - | N | N | N | - | 11.3 | N | 53 | 1.7 | 144 | 3.9 | 0.5 | 0.3 | 31 | 36 | - |
| 3 | M | 24 | + | + | - | - | + | D | D | D | + | 14.5 | N | 53 | 1.4 | 132 | 4.1 | 1.6 | 1.2 | 36 | 48 | ROTA |
| 4 | F | 55 | + | + | - | - | + | D | D | D | - | 14.1 | N | 56 | 1.9 | 134 | 4.4 | 0.3 | 0.1 | 48 | 54 | - |
| 5 | M | 22 | + | + | + | - | + | D | D | D | + | 9.3 | N | 78 | 0.9 | 131 | 4.6 | 0.9 | 0.3 | 39 | 65 | BOTH |
| 6 | M | 24 | + | - | + | - | - | N | N | N | - | 12.3 | N | 53 | 1.7 | 138 | 4.3 | 0.4 | 0.2 | 52 | 43 | - |
| 7 | M | 28 | + | + | - | + | - | N | N | N | - | 13.8 | N | 54 | 1.8 | 148 | 4.5 | 0.6 | 0.4 | 46 | 48 | - |
| 8 | F | 50 | + | - | - | - | - | N | N | N | - | 13.4 | N | 41 | 1.5 | 134 | 3.6 | 0.3 | 0.1 | 64 | 76 | - |
| 9 | F | 25 | + | + | + | + | + | D | D | D | + | 10.4 | N | 79 | 2.9 | 143 | 3.8 | 0.8 | 0.9 | 39 | 32 | ROTA |
| 10 | M | 60 | + | + | + | - | + | D | D | D | + | 13.0 | N | 35 | 1.3 | 133 | 4.2 | 2.6 | 1.0 | 61 | 86 | ROTA |
| 11 | F | 32 | + | - | - | - | - | N | N | N | - | 11.4 | N | 36 | 1.3 | 134 | 4.6 | 0.4 | 0.3 | 36 | 38 | - |
| 12 | M | 25 | + | + | - | - | - | N | N | N | - | 12.8 | N | 48 | 1.4 | 136 | 4.2 | 0.5 | 0.3 | 38 | 42 | - |
| 13 | M | 55 | + | - | - | - | - | N | N | N | - | 12.0 | N | 34 | 1.2 | 132 | 3.8 | 0.8 | 0.5 | 32 | 30 | - |
| 14 | M | 22 | + | + | + | + | + | D | D | D | + | 12.7 | N | 48 | 1.6 | 130 | 4.1 | 0.9 | 0.4 | 55 | 68 | ADENO |
| 15 | M | 20 | + | + | - | + | + | D | D | D | + | 11.2 | N | 73 | 2.7 | 138 | 3.4 | 0.9 | 0.2 | 220 | 100 | ROTA |
| 16 | M | 40 | + | - | - | - | - | N | N | N | - | 11.0 | N | 40 | 0.9 | 138 | 4.2 | 1.0 | 0.6 | 22 | 30 | - |
| 17 | F | 56 | + | + | - | - | - | N | N | N | - | 11.9 | N | 26 | 1.3 | 137 | 4.6 | 0.4 | 0.2 | 26 | 90 | - |
| 18 | F | 22 | + | + | - | + | - | N | N | N | - | 14.2 | N | 58 | 1.7 | 144 | 4.5 | 0.3 | 0.1 | 20 | 36 | - |
| 19 | M | 58 | + | - | - | - | + | N | N | N | - | 12.6 | N | 54 | 1.5 | 134 | 4.2 | 0.4 | 0.2 | 40 | 36 | - |
| 20 | F | 48 | + | + | - | - | - | N | N | N | - | 12.8 | N | 53 | 1.5 | 136 | 4.1 | 0.2 | 0.0 | 22 | 46 | - |
| 21 | F | 30 | + | - | - | - | - | N | N | N | - | 12.7 | N | 48 | 1.4 | 132 | 3.5 | 1.8 | 0.4 | 48 | 56 | - |
| 22 | F | 25 | + | + | - | - | + | N | N | N | - | 13.8 | N | 76 | 1.6 | 134 | 4.2 | 0.6 | 0.4 | 48 | 58 | - |
| 23 | F | 30 | + | + | - | - | + | D | D | D | + | 14.8 | N | 45 | 1.5 | 128 | 3.9 | 0.6 | 0.1 | 55 | 62 | ROTA |
| 24 | M | 24 | + | + | - | + | + | D | D | D | + | 10.4 | N | 78 | 1.9 | 134 | 3.2 | 0.5 | 0.3 | 75 | 88 | ROTA |
| 25 | M | 18 | + | + | + | + | + | D | D | D | + | 13.7 | N | 75 | 1.4 | 136 | 4.2 | 0.9 | 0.3 | 108 | 138 | ROTA |
| 26 | M | 36 | + | - | + | + | - | N | N | N | - | 13.8 | N | 61 | 1.8 | 142 | 3.9 | 0.9 | 0.2 | 42 | 64 | - |
| 27 | M | 47 | + | - | - | - | - | N | N | N | - | 13.4 | N | 58 | 1.3 | 140 | 3.8 | 0.6 | 0.4 | 44 | 68 | - |
| 28 | M | 24 | + | + | - | - | - | N | N | N | - | 12.6 | N | 56 | 1.7 | 138 | 4.4 | 0.5 | 0.3 | 48 | 56 | - |
| 29 | M | 45 | + | - | - | - | - | N | N | N | - | 12.4 | N | 52 | 1.2 | 134 | 4.2 | 0.8 | 0.6 | 36 | 44 | - |
| 30 | F | 35 | + | + | - | + | + | D | D | D | + | 12.6 | N | 43 | 1.7 | 134 | 3.3 | 0.8 | 0.5 | 59 | 69 | BOTH |
| 31 | M | 68 | + | - | - | - | + | N | N | N | - | 13.8 | N | 48 | 1.3 | 132 | 3.7 | 0.4 | 0.2 | 36 | 47 | - |
| 32 | F | 35 | + | + | + | + | + | D | D | D | + | 10.4 | N | 66 | 1.3 | 141 | 4.1 | 0.8 | 0.5 | 100 | 146 | ADENO |
| 33 | F | 29 | + | + | - | + | + | D | D | D | + | 14.0 | N | 72 | 1.5 | 142 | 4.1 | 1.0 | 0.8 | 84 | 98 | ROTA |
| 34 | M | 32 | + | + | - | + | + | D | D | D | + | 11.6 | N | 78 | 1.4 | 129 | 4 | 1.5 | 1.2 | 160 | 196 | ROTA |
| 35 | F | 20 | + | - | - | + | + | D | D | D | - | 14.2 | N | 62 | 1.4 | 139 | 4.2 | 0.2 | 0.0 | 46 | 50 | - |
| 36 | F | 25 | + | + | - | - | - | N | N | N | - | 13.1 | N | 60 | 1.2 | 136 | 4.2 | 0.2 | 0.1 | 40 | 48 | - |
| 37 | M | 45 | + | - | - | - | - | N | N | N | - | 12.1 | N | 42 | 1.3 | 134 | 3.8 | 0.4 | 0.2 | 36 | 38 | - |
| 38 | M | 49 | + | + | - | - | - | N | N | N | - | 11.4 | N | 68 | 0.9 | 139 | 4.1 | 0.3 | 0.0 | 28 | 32 | - |
| 39 | M | 32 | + | - | - | - | + | N | N | N | - | 11.3 | N | 62 | 1.7 | 136 | 4.2 | 0.4 | 0.1 | 38 | 41 | - |
| 40 | M | 65 | + | + | - | - | - | N | N | N | - | 11.2 | N | 55 | 1.6 | 136 | 3.6 | 0.7 | 0.5 | 39 | 38 | - |
| 41 | M | 31 | + | + | - | - | - | N | N | N | - | 13.9 | N | 26 | 1.1 | 132 | 3.3 | 0.5 | 0.3 | 24 | 36 | - |
| 42 | F | 56 | + | - | - | - | - | D | D | D | - | 11.1 | N | 44 | 1.4 | 134 | 4.1 | 0.7 | 0.5 | 32 | 36 | - |
| 43 | F | 22 | + | + | - | - | - | N | N | N | - | 12.8 | N | 26 | 0.7 | 139 | 3.6 | 0.6 | 0.4 | 26 | 19 | - |
| 44 | M | 30 | + | + | - | + | + | N | N | N | + | 13.6 | N | 82 | 1.9 | 143 | 9.1 | 1.1 | 0.9 | 88 | 96 | ADENO |
| 45 | M | 38 | + | - | - | - | - | N | N | N | - | 9.0 | N | 16 | 0.7 | 133 | 4.8 | 0.7 | 0.2 | 46 | 48 | - |
| 46 | M | 42 | + | - | - | - | - | N | N | N | - | 12.1 | N | 27 | 0.8 | 136 | 4.1 | 0.8 | 0.3 | 22 | 49 | - |

## ANNEXURE III - MASTER CHART

| Case Number | Sex | Age (Years) | History | | | | GPE | | | | Investigations | | | | | | | | | | | | Diagnosis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Dehydration | | | | | | | | | | LFT | | | | | |
| | | | | | | | | | | | | | | | | | | Sr. Bili | | | | | |
| | | | Diarrhoea | Vomiting | Adbominal pain | Reduced urine output | Temperature | Skin elasticity | Tongue appearance | Patient appearance | Adeno and rotavirus test | Haemoglobin (gm%) | Urine routine | Blood urea (mg/dL) | Serum creatinine (mg/dL) | Serum sodium (meq/L) | Serum potassium (meq/L) | Total (mg/dL) | Direct (mg/dL) | SGOT | SGPT | |
| 47 | M | 27 | + | + | - | - | + | D | D | D | - | 14.2 | N | 74 | 0.9 | 142 | 3.9 | 1.0 | 0.9 | 18 | 27 | - |
| 48 | F | 27 | + | + | - | - | + | D | D | D | - | 14.0 | N | 96 | 1.9 | 144 | 4.6 | 0.7 | 0.5 | 20 | 40 | - |
| 49 | F | 21 | + | - | - | - | - | N | N | N | - | 14.0 | N | 19 | 0.9 | 140 | 4.1 | 0.9 | 0.7 | 20 | 41 | - |
| 50 | F | 51 | + | - | - | - | - | N | N | N | - | 13.0 | N | 24 | 0.4 | 140 | 3.8 | 1.0 | 0.9 | 18 | 26 | - |
| 51 | F | 33 | + | + | + | + | + | N | N | N | - | 13.2 | N | 22 | 0.8 | 148 | 4.2 | 1.1 | 0.8 | 17 | 27 | - |
| 52 | F | 18 | + | + | - | + | + | N | N | N | + | 11.4 | N | 69 | 1.3 | 139 | 4.2 | 0.8 | 0.6 | 62 | 76 | ROTA |
| 53 | M | 50 | + | + | - | + | + | D | D | D | + | 12.8 | N | 56 | 1.4 | 138 | 4.3 | 0.8 | 0.4 | 94 | 108 | ROTA |
| 54 | M | 23 | + | - | + | - | + | D | D | D | - | 15.0 | N | 17 | 0.8 | 130 | 4 | 1.9 | 0.3 | 10 | 18 | - |
| 55 | M | 40 | + | - | + | - | - | N | N | N | - | 13.0 | N | 28 | 1.1 | 134 | 4.6 | 0.9 | 0.2 | 20 | 31 | - |
| 56 | F | 30 | + | - | - | - | - | N | N | N | - | 18.0 | N | 18 | 0.9 | 130 | 4.5 | 0.9 | 0.3 | 48 | 52 | - |
| 57 | F | 20 | + | - | - | + | - | N | N | N | + | 14.1 | N | 74 | 1.3 | 138 | 3.8 | 1.6 | 1.3 | 74 | 52 | ROTA |
| 58 | F | 65 | + | - | - | - | - | N | N | N | - | 14.0 | N | 18 | 0.8 | 130 | 4 | 0.8 | 0.6 | 16 | 18 | - |
| 59 | M | 75 | + | + | - | - | - | D | D | D | - | 12.0 | N | 90 | 0.9 | 138 | 4 | 0.9 | 0.6 | 48 | 52 | - |
| 60 | F | 30 | + | - | - | - | - | N | N | N | - | 10.0 | N | 19 | 0.3 | 138 | 2.9 | 0.8 | 0.7 | 14 | 18 | - |
| 61 | M | 31 | + | - | + | - | - | N | N | N | - | 11.0 | N | 19 | 0.7 | 130 | 4 | 0.9 | 0.2 | 40 | 45 | - |
| 62 | M | 24 | + | + | - | + | - | D | D | D | + | 11.9 | N | 88 | 1.4 | 146 | 4.8 | 0.7 | 0.5 | 151 | 146 | ADENO |
| 63 | M | 21 | + | + | - | + | - | D | D | D | + | 12.4 | N | 30 | 1.2 | 131 | 4 | 0.4 | 0.1 | 28 | 40 | ROTA |
| 64 | M | 21 | + | - | - | - | - | N | N | N | - | 15.0 | N | 10 | 0.9 | 130 | 2.8 | 0.8 | 0.4 | 30 | 48 | - |
| 65 | F | 22 | + | + | + | - | - | D | D | D | - | 13.6 | N | 49 | 1.4 | 131 | 3.8 | 1.1 | 0.7 | 28 | 36 | - |
| 66 | M | 40 | + | - | - | - | - | N | N | N | - | 13.8 | N | 34 | 1.1 | 136 | 4.2 | 1.2 | 0.8 | 42 | 58 | - |
| 67 | M | 46 | + | - | + | - | + | D | D | D | - | 14.1 | N | 82 | 1.6 | 132 | 4.1 | 0.7 | 0.4 | 46 | 68 | - |
| 68 | M | 41 | + | - | - | - | - | N | N | N | - | 14.0 | N | 19 | 0.9 | 131 | 3.8 | 0.8 | 0.6 | 10 | 14 | - |
| 69 | M | 22 | + | + | - | + | - | D | D | D | - | 13.2 | N | 82 | 2.1 | 138 | 3.4 | 1.8 | 1.6 | 300 | 446 | - |
| 70 | F | 18 | + | - | - | + | - | D | D | D | - | 12.7 | N | 57 | 1.3 | 135 | 3.7 | 1.2 | 1.0 | 38 | 44 | - |
| 71 | F | 30 | + | + | - | - | + | N | N | N | - | 12.0 | N | 10 | 0.4 | 131 | 4 | 1.0 | 0.8 | 30 | 88 | - |
| 72 | F | 40 | + | - | - | - | - | N | N | N | - | 13.0 | N | 14 | 0.9 | 130 | 4.2 | 0.6 | 0.2 | 40 | 68 | - |
| 73 | M | 55 | + | + | - | - | - | D | D | D | + | 11.8 | N | 46 | 1.1 | 143 | 4.4 | 0.4 | 0.2 | 27 | 38 | ROTA |
| 74 | F | 90 | + | - | - | - | - | N | N | N | - | 13.0 | N | 14 | 0.9 | 130 | 4.2 | 0.8 | 0.2 | 40 | 68 | - |
| 75 | F | 75 | + | + | - | + | + | D | D | D | - | 13.1 | N | 48 | 0.9 | 140 | 4.1 | 0.8 | 0.6 | 32 | 48 | - |
| 76 | M | 72 | + | - | - | - | - | N | N | N | - | 12.0 | N | 18 | 0.8 | 130 | 3.8 | 1.0 | 0.9 | 30 | 44 | - |
| 77 | F | 35 | + | - | - | - | - | N | N | N | - | 12.8 | N | 17 | 0.8 | 129 | 3.6 | 1.0 | 0.8 | 26 | 54 | - |
| 78 | F | 60 | + | + | - | + | + | D | D | D | + | 11.2 | N | 80 | 1.6 | 140 | 4.8 | 1.4 | 1.2 | 71 | 94 | ROTA |
| 79 | M | 20 | + | + | - | + | - | D | D | D | + | 14.2 | N | 72 | 1.7 | 135 | 4.4 | 1.1 | 0.9 | 22 | 36 | ROTA |
| 80 | F | 40 | + | - | - | + | - | N | N | N | + | 12.6 | N | 62 | 1.9 | 148 | 4.6 | 1.2 | 1.0 | 28 | 39 | ROTA |
| 81 | F | 34 | + | + | - | + | - | D | D | D | - | 11.0 | N | 98 | 1.6 | 132 | 3.6 | 0.8 | 0.1 | 20 | 41 | - |
| 82 | F | 21 | + | - | - | - | - | N | N | N | - | 10.0 | N | 18 | 0.6 | 140 | 4.2 | 0.6 | 0.1 | 42 | 48 | - |
| 83 | M | 35 | + | - | - | + | - | D | D | D | + | 13.7 | N | 48 | 1.2 | 138 | 4.7 | 0.4 | 0.1 | 60 | 72 | ROTA |
| 84 | M | 50 | + | - | - | + | - | N | N | N | + | 14.6 | N | 68 | 1.0 | 141 | 3.8 | 1.2 | 0.8 | 114 | 176 | ROTA |
| 85 | M | 43 | + | + | - | - | - | N | N | N | - | 13.4 | N | 18 | 0.8 | 139 | 3.8 | 0.7 | 0.4 | 44 | 51 | - |
| 86 | M | 55 | + | - | - | - | - | N | N | N | - | 15.0 | N | 10 | 0.9 | 130 | 4.5 | 0.8 | 0.6 | 15 | 18 | - |
| 87 | F | 68 | + | - | - | - | - | N | N | N | - | 14.0 | N | 28 | 1.0 | 136 | 4.1 | 0.8 | 0.7 | 26 | 42 | - |
| 88 | F | 49 | + | + | - | + | - | D | D | D | + | 12.7 | N | 48 | 1.6 | 138 | 4.2 | 1.2 | 0.8 | 180 | 196 | ROTA |
| 89 | F | 27 | + | - | - | - | - | N | N | N | - | 13.0 | N | 19 | 0.4 | 128 | 3.8 | 1.0 | 0.8 | 10 | 14 | - |
| 90 | F | 29 | + | + | - | - | - | N | N | N | - | 13.2 | N | 13 | 0.8 | 130 | 3.5 | 0.9 | 0.6 | 15 | 20 | - |
| 91 | F | 32 | + | - | - | - | - | N | N | N | - | 13.4 | N | 27 | 0.8 | 140 | 3.9 | 1.1 | 0.8 | 20 | 48 | - |
| 92 | F | 20 | + | + | - | + | + | D | D | D | - | 14.6 | N | 76 | 1.4 | 142 | 3.9 | 0.9 | 0.8 | 48 | 61 | - |

## ANNEXURE III - MASTER CHART

| Case Number | Sex | Age (Years) | History | | | | GPE | | | | Investigations | | | | | | | | | | | | Diagnosis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Dehydration | | | | | | | | | | LFT | | | | | |
| | | | | | | | | | | | | | | | | | | Sr. Bili | | | | | |
| | | | Diarrhoea | Vomiting | Adbominal pain | Reduced urine output | Temperature | Skin elasticity | Tongue appearance | Patient appearance | Adeno and rotavirus test | Haemoglobin (gm%) | Urine routine | Blood urea (mg/dL) | Serum creatinine (mg/dL) | Serum sodium (meq/L) | Serum potassium (meq/L) | Total (mg/dL) | Direct (mg/dL) | SGOT | SGPT | |
| 93 | F | 26 | + | - | - | - | - | N | N | N | - | 14.0 | N | 18 | 0.8 | 140 | 4.2 | 0.7 | 0.5 | 20 | 40 | - |
| 94 | M | 38 | + | + | - | - | + | N | N | N | - | 13.2 | N | 20 | 0.9 | 136 | 4.8 | 0.2 | 0.1 | 21 | 37 | - |
| 95 | F | 25 | + | - | - | - | - | N | N | N | - | 12.6 | N | 27 | 0.8 | 133 | 4.9 | 0.8 | 0.3 | 22 | 49 | - |
| 96 | F | 25 | + | - | - | - | - | N | N | N | - | 13.9 | N | 76 | 0.8 | 140 | 3.6 | 0.8 | 0.7 | 20 | 58 | - |
| 97 | F | 25 | + | - | - | - | - | N | N | N | - | 14.7 | N | 22 | 0.9 | 136 | 0.8 | 0.9 | 0.7 | 36 | 67 | - |
| 98 | M | 22 | + | + | - | + | + | D | D | D | - | 13.2 | N | 90 | 1.9 | 136 | 4.8 | 0.7 | 0.2 | 21 | 37 | - |
| 99 | F | 26 | + | + | - | - | + | D | D | D | - | 13.0 | N | 66 | 1.2 | 130 | 4.4 | 0.8 | 0.3 | 24 | 26 | - |
| 100 | F | 23 | + | - | - | - | - | N | N | N | - | 11.7 | N | 35 | 1.3 | 140 | 3.2 | 0.8 | 0.6 | 47 | 89 | - |