RESEARCH ARTICLE

A PROSPECTIVE STUDY ON ANTIBIOTIC TRENDS IN ACUTE FEBRILE ILLNESS.

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Manuscript Info	*Abstract*
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	Aims And Objectives: The present study aims to document the antibiotics used in Acute febrile illness. 1. To identify the different antibiotics used in acute febrile illness. 2. To find out the epidemiology of antibiotics and their combination in diagnosed condition. 3. To find out the epidemiology of co morbid condition. 4. Patient knowledge after counseling. **Method:**An observational, prospective cohort study was conducted at a tertiary care teaching hospital in Hyderabad, T.S, India. A total of 200 patients from the inpatient department of general medicine in Aware Global Hospital, who were prescribed antibiotics and those who fulfilled the exclusion and inclusion criteria were selected for the study which was conducted for 6 months. All information significant to the study was collected from the case records and discussions conducted with the in-patients and bystanders during ward rounds, with the support of a physician, which were analyzed by SPSS and Chi-square method. Moreover, daily follow-ups were conducted to assemble data on amendment in therapy, add-on therapy, and clinical improvement. **Results:**The mean age was 41years and standard deviation was 18years of this population. 57% were males and 43% were females. The main demographic characteristics, co-morbidities, diagnosis and treatment are taken. The most common treatment used is Monocef (ceftriaxone) -34% and Magnex forte (cefperazone+sulbactam) -28%. They belongs to the class of 3rd generation Cephalosporin. Combination of antibiotics like Magnex forte + Azee 6% and Monocef + Azee 12% were most commonly used combinations. In the population 19.5% with hypertension(htn), 3.5% with diabetes mellitus(dm), 6%with hypertension and diabetes mellitus, 11.5% with combinations and 59.5% with no comorbidities were observed. **Conclusion**:The study was conducted to review and analyze different trends of antibiotics used in individuals suffering from AFI(Acute Febrile Illness). During our study, it was observed that Dengue and Respiratory tract infections were most commonly cause of AFI (Acute Febrile Illness). Monocef (ceftriaxone) and Magnex forte (cefperazone+sulbactam) belonging to the class of 3rd generation Cephalosporin weremost commonly used antibiotics. During the study it was found that majority of the patients were without co-morbidities and were within the age limit of 15-30years. In the patients who were

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suffering from AFI with comorbidities majority of them had hypertension and DM-type 2.

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Introduction:-

"Acute febrile illness", or "acute fever" or "short febrile illness" is traditionally defined as any illness associated with fever of two weeks or shorter in duration, rapid in onset, caused by diverse pathogens.

The clinical signs and symptoms of most of these infections are very similar and the correct diagnosis is only possible by using pathogen specific diagnostic tests . Several studies have documented the etiology of acute febrile illness in tropical countries like India as Dengue, Malaria,Typhoid fever,Rickettsial infection.leptospirosis, enteric fever, chikungunya, and Japanese encephalitis.Further confounding this is the fact that a majority of the patients present with non-descript symptoms (e.g., low-grade fever, general malaise, headache, and myalgia) and usually no focal point of infection.(1)

The following infectious diseases are considered for the study :

1. Malaria is a mosquito-borne disease caused by a parasite. People with malaria often experience fever, chills, and flu-like illness. Left untreated, they may develop severe complications and die.In 2016 an estimated 216 million cases of malaria occurred worldwide and 445,000 people died, mostly children in the African Region. About 1,700 cases of malaria are diagnosed in the United States each year. The vast majority of cases in the United States are in travelers and immigrants returning from countries where malaria transmission occurs, many from sub-Saharan Africa and South Asia. (2)

2. Upper respiratory tract infections (URI or URTI) are illnesses caused by an acute infection which involves the upper respiratory tract including the nose, sinuses, pharynx or larynx. (3) This commonly includes nasal obstruction, sore throat, tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, and the common cold.Most infections are viral in nature and in other instances the cause is bacterial.In 2015, 17.2 billion cases of upper respiratory infections occurred. As of 2014, upper respiratory infections caused about 3,000 deaths down from 4,000 in 1990.

3. Lower respiratory tract infection (LRTI), while often used as a synonym for pneumonia, can also be applied to other types of infection including lung abscess and acute bronchitis. Symptoms include shortness of breath, weakness, fever, coughing and fatigue. There are a number of symptoms that are characteristic of lower respiratory tract infections. The two most common are bronchitis and edema. Influenza affects both the upper and lower respiratory tracts. In 2015 there were about 291 million cases. These resulted in 2.74 million deaths down from 3.4 million deaths in 1990. This was 4.8% of all deaths in 2013. Lower respiratory infectious disease is the fifth-leading cause of death and the combined leading infectious cause of death, being responsible for 2·74 million deaths worldwide. This is generally similar to estimates in the 2010 Global Burden of Disease study. This total only accounts for streptococcus pneumoniae and Haemophilus Influenzae infections and does not account for atypical or nosocomial causes of lower respiratory disease, therefore underestimating total disease burden.(4)

4. Urinary tract infection (UTI) is defined as the presence of microorganisms in the urine that cannot be accounted for by contamination. The organisms have the potential to invade the tissues of the urinary tract and adjacent structures. Lower tract infections include cystitis (bladder), urethritis (urethra), prostatitis (prostate gland), and epididymitis. Upper tract infections (such as pyelonephritis) involve the kidney and are referred to as pyelonephritis(3) Urinary tract infections (UTIs) are considered to be the most common bacterial infection. According to the 1997 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, UTI accounted for nearly 7 million office visits and 1 million emergency department visits, resulting in 100,000 hospitalizations. Women are significantly more likely to experience UTI than men. Almost half of all women will experience atleast one UTI during their lifetime. Specific subpopulations at increased risk of UTI include infants, pregnant women, the elderly, patients with spinal cord injuries and/or catheters, patients with diabetes or multiple sclerosis, patients with acquired immunodeficiency disease syndrome or human immunodeficiency virus, and patients with underlying urologic abnormalities.(5)

5. Viral hepatitis refers to the clinically important hepatotropic viruses responsible for hepatitis A (HAV), hepatitis B (HBV), delta hepatitis, hepatitis C (HCV), and hepatitis E. Worldwide in 2015, hepatitis A occurred in about 114 million people, chronic hepatitis B affected about 343 million people and chronic hepatitis C about 142 million people. In the United States, NASH affects about 11 million people and alcoholic hepatitis affects about 5 million people. Hepatitis results in more than a million deaths a year, most of which occur indirectly from

liver scarring or liver cancer. In the United States, hepatitis A is estimated to occur in about 2,500 people a year and results in about 75 deaths.(6)

6. Gastroenteritis is defined as the inflammation of the mucus membranes of the gastrointestinal tract and is characterized by diarrhea or vomiting. Worldwide, gastroenteritis affects 3 to 5 billion children each year, and accounts for 1.5 to 2.5 million deaths per year. In developed countries, such as the United States, acute gastroenteritis seldom causes deaths, however, it still accounts for 300 deaths per year. Moreover, it puts a heavy burden on the health care system. Acute gastroenteritis causes 1.5 million visits to primary care providers each year and 220,000 hospital admissions for children under the age of 5 years; that is 10% of all the hospital admissions of children in the United States. In general, developing countries have a higher rate of hospital admissions as compared to developed countries. In the United States, the admission rate is 9 per 1000, per annum, for children younger than 5 years old. When compared to the United Kingdom and Australia, the admission rates are around 12 to 15 per 1000 per annum. However, the rate increases dramatically to 26 per 1000 per annum in China. This may be due to the facts that children in developed countries have a better nutrition status and better primary care. The difference can also be explained by the fact that, the incidence of acute gastroenteritis is significantly higher in developing countries than the industrialized countries.(7)

7. Fever of unknown origin (FUO) was defined as (1) temperatures of >38.3°C (>101°F) on several occasions; (2) a duration of fever of >3 weeks; and (3) failure to reach a diagnosis despite 1 week of inpatient investigation. In general, infection accounts for about 20–25% of cases of FUO in Western countries; next in frequency are neoplasms and noninfectious inflammatory diseases (NIIDs), the latter including "collagen or rheumatic diseases," vasculitis syndromes, and granulomatous disorders. In geographic areas outside the West,infections are a much more common cause of FUO (43% vs 22%), while the proportions of cases due to NIIDs and neoplasms are similar.(8)

8. Dengue is a debilitating viral disease of the tropics, transmitted by mosquitoes, and causing sudden fever and acute pains in the joints. The actual numbers of dengue cases are underreported and many cases are misclassified. One recent (2013) estimate indicates that 390 million dengue infections occur every year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease).Another (2012) study, of the prevalence of dengue, estimates that 3.9 billion people in 128 countries are at risk of infection with dengue viruses.(9)

9. Meningitis is an inflammation of the membranes (meninges) surrounding your brain and spinal cord.The swelling from meningitis typically triggers symptoms such as headache, fever and a stiff neck.Most cases of meningitis in the U.S. are caused by a viral infection, but bacterial and fungal infections are other causes.Worldwide, the incidence of meningitis due to N. meningitidis is highest in a region of sub-Saharan African known as the "meningitis belt". This is characterized by seasonal epidemics during the dry season (incidence rate: 10- 100 cases per 100,000 population), punctuated by explosive epidemics in 8-12 year cycles (incidence rates can be greater than 1,000 cases per 100,000 population). Across the meningitis belt, at least 350 million people are at risk for meningitis during these annual epidemics. Meningitis epidemics are generally caused by serogroup A, although outbreaks have also been caused by serogroups C. (10)

10. Chikungunya is an acute viral disease characterised by fever and painful arthralgia. The arthritic symptoms associated with chikungunya can be debilitating and may persist for months or even years in some patients. Severe neurological complications such as encephalitis have also been reported during recent large outbreaks. The disease is caused by chikungunya virus (CHIKV), a mosquito-borne alphavirus from the Togaviridae family, which has recently emerged to become one of the most important exotic viral threats worldwide. Chikungunya is endemic throughout Africa, and over the past decade, it has also spread throughout the Indian Ocean, Asia, the South Pacific, southern Europe, the Caribbean and Central America. The rapid emergence of CHIKV has been linked to expansion of the mosquito vector species, Aedes aegypti and Ae. albopictus, throughout most tropical and subtropical regions of the world. Furthermore, mutations in some strains of CHIKV have been associated with increased transmissibility of the virus. The lack of a commercial vaccine and the failure of vector control strategies to limit the expansion of chikungunya have prompted the need for further options to prevent the spread of this disease.(11)

11. Rickettsial infections are caused by various bacterial species from the genera Rickettsia, Orientia, Ehrlichia, Neorickettsia, Neoehrlichiaand Anaplasma. Rickettsia spp. are classically divided into the typhus group and spotted fever group (SFG). Orientia spp. make up the scrub typhus group. The rickettsial pathogens most likely to be encountered during travel outside the United States include R. africae (African tick-bite fever), R.conorii(Mediterranean spotted fever), R. rickettsii (known as both Rocky Mountain spotted fever and Brazilian spotted fever), O. tsutsugamushi (scrub typhus), and R. typhi (murine or fleaborne typhus) all age groups are at risk for rickettsial infections during travel to endemic areas. Both short and long-term travelers are

at risk for infection. Transmission is increased during outdoor activities in the spring and summer months.Because of the 5- to 14-day incubation period for most rickettsial diseases, tourists often do not experience symptoms during their trip, and disease onset may coincide with their return home or develop within a week after returning. Although the most commonly diagnosed rickettsial diseases in travelers are usually in the spotted fever or typhus groups, travelers may acquire a wide range of rickettsioses, including emerging and newly recognized species(12) Undifferentiated febrile illnesses (UFIs) are a common clinical problem in south Asia.1,2 Defined as a fever without a focus of infection on initial physical examination or in basic laboratory tests, UFIs represent a considerable burden of disease with diagnostic and therapeutic challenges. Empirical broad-spectrum antimicrobials are generally prescribed but with little evidence-based guidance on likely etiologies or potential treatment responses.(13) The aim of this prospective, observational study was to evaluate the clinical use of antibiotics in acute febrile illness in aware global hospital, situated at Hyderabad, T.S. Our working hypothesis is to evaluate the clinical use of antibiotics in acute febrile illness prescribed by the physician.

Definition:
Acute febrile illness was defined as a patient with fever of 38°C or higher at presentation to ED or history of fever that persisted for 2–7 days with no localizing source.(14) "Acute febrile illness", or "acute fever" or "short febrile illness" is traditionally defined as any illness associated with fever of two weeks or shorter in duration, rapid in onset, caused by diverse pathogens. The clinical signs and symptoms of most of these infections are very similar & the correct diagnosis is only possible by using pathogen specific diagnostic tests (1)

Epidemiology :
Acute febrile illness is a common cause of hospital admission, and although it is not recognized as a disease state by the World Health Organization (WHO), its associated infectious causes contribute to substantial morbidity and death among children worldwide. Studies among adults with febrile illness who required hospital admission documented case fatality ratios that ranged from 5% to 24%.(15) The etiologies of human febrile illness can vary region wise in India suggesting that diagnosis, treatment, and control programs need to be based on a methodical evaluation of area specific etiologies. Knowledge of local prevalence of infections is critical in order to target clinical work up and treatment. The various common causes of acute febrile illness in tropical countries have similar clinical presentation. A large number of patients present to Indian hospitals with acute febrile illness and multisystem involvement. There may be overlapping clinical, presentation in various acute febrile illnesses and it is important to diagnose the specific etiology so that appropriate treatment can be initiated. Disease burden of infectious etiologies of acute febrile illness is under reported in various parts of India due to lack of laboratory confirmation. Undifferentiated febrile illnesses are common in tropical areas of Asia. Common causes include dengue, malaria, leptospirosis, enteric fever, chikungunya, rickettsia and Japanese encephalitis.(1) Drug use studies using aggregate data indicate that there is over or under consumption of medicines. The data on utilization may provide useful information for promoting appropriate use of medicines. Antimicrobial agents are among the most frequently prescribed drugs. Inappropriate use of these agents is associated with allergic reactions, toxicity, super infection, and more importantly the development of antimicrobial resistance. In addition, the excessive and inappropriate use of antimicrobials can cause an unnecessary economic burden to health care system and the patients as well. Antimicrobial resistance is more prevalent in hospital settings than in the community. Studies have shown that patients with drug-resistant organisms require longer hospitalization and have increased risk of mortality.(16).

Risk factors :
The causes of human febrile illness can vary region wise in India suggesting that diagnosis, treatment, and control programs need to be based on a methodical evaluation of area specific etiologies. Knowledge of local prevalence of infections is critical in order to target clinical work up and treatment. The various common causes of acute febrile illness in tropical countries have similar clinical presentation. A large number of patients present to Indian hospitals with acute febrile illness and multisystem involvement. There may be overlapping clinical presentation in various acute febrile illnesses and it is important to diagnose the specific etiology so that appropriate treatment can be initiated. Disease burden of infectious etiologies of acute febrile illness is under reported in various parts of India due to lack of laboratory confirmation. Undifferentiated febrile illnesses are common in tropical areas of Asia. Common causes include dengue, malaria, leptospirosis, enteric fever, chikungunya, rickettsia and Japanese encephalitis.(17)

Pathophysiology:
Temperature is ultimately regulated in the hypothalamus. A trigger of the fever, called a pyrogen, causes a release of prostaglandin E2 (PGE2). PGE2 then in turn acts on the hypothalamus, which generates a systemic response back to the rest of the body, causing heat creating effects to match a new temperature level. In many respects, the hypothalamus works like a thermostat.(18) When the set point is raised, the body increases its temperature through both active generation of heat and retention of heat. Peripheral vasoconstriction both reduces heat loss through the skin and causes the person to feel cold. Nor epinephrine increases thermo genesis in brown adipose tissue, and acetylcholine stimulates muscle to raise metabolic rate.(19) If these measures are insufficient to make the blood temperature in the brain match the new set point in the hypothalamus, then shivering begins in order to use muscle movements to produce more heat. When the hypothalamic set point moves back to baseline either spontaneously or with medication, the reverse of these processes (vasodilation, end of shivering and non shivering heat production) and sweating are used to cool the body to the new, lower setting.

This contrasts with hyperthermia, in which the normal setting remains, and the body overheats through undesirable retention of excess heat or over-production of heat.(18) Hyperthermia is usually the result of an excessively hot environment (heat stroke) or an adverse reaction to drugs. Fever can be differentiated from hyperthermia by the circumstances surrounding it and its response to anti-pyretic medications.

Pyrogens :
The term pyrogen (Greek pyro, "fire") is used to describe any substance that causes fever. Exogenous pyrogens are derived from outside the patient; most are microbial products, microbial toxins, or whole microorganisms (including viruses). The classic example of an exogenous pyrogen is the lipopolysaccharide (endotoxin) produced by all gram-negative bacteria. Pyrogenic products of gram-positive organisms include the enterotoxins of Staphylococcus aureus and the groups A and B streptococcal toxins, also called super antigens. One staphylococcal toxin of clinical importance is that associated with isolates of S. aureus from patients with toxic shock syndrome.

Pyrogenic cytokines :
Cytokines are small proteins (molecular mass, 10,000–20,000 Da) that regulate immune, inflammatory, and hematopoietic processes. For example, the elevated leukocytosis seen in several infections with an absolute neutrophilia is attributable to the cytokines interleukin (IL) 1 and IL-6. Some cytokines also cause fever; formerly referred to as endogenous pyrogens, they are now called pyrogenic cytokines. The pyrogenic cytokines include IL-1, IL-6, tumor necrosis factor (TNF), and ciliary neurotropic factor, a member of the IL-6 family. Interferons (IFNs), particularly IFN-α, also are pyrogenic cytokines; fever is a prominent side effect of IFN-α used in the treatment of hepatitis. Each pyrogenic cytokine is encoded by a separate gene, and each has been shown to cause fever in laboratory animals and in humans. When injected into humans at low doses (10–100 ng/kg), IL-1 and TNF produce fever; in contrast, for IL-6, a dose of 1–10 μg/kg is required for fever production. A wide spectrum of bacterial and fungal products induce the synthesis and release of pyrogenic cytokines. However, fever can be a manifestation of disease in the absence of microbial infection.

Elevation of the hypothalamic set point by cytokines :
During fever, levels of prostaglandin E2 (PGE2) are elevated in hypothalamic tissue and the third cerebral ventricle. The concentrations of PGE2 are highest near the circumventricular vascular organs (organum vasculosum of lamina terminalis)—networks of enlarged capillaries surrounding the hypothalamic regulatory centers. Destruction of these organs reduces the ability of pyrogens to produce fever. Most studies in animals have failed to show, however, that pyrogenic cytokines pass from the circulation into the brain itself. Thus, it appears that both exogenous pyrogens and pyrogenic cytokines interact with the endothelium of these capillaries and that this interaction is the first step in initiating fever—i.e., in raising the set point to febrile levels. The key events in the production of fever are illustrated in. Myeloid and endothelial cells are the primary cell types that produce pyrogenic cytokines. Pyrogenic cytokines such as IL-1, IL-6, and TNF are released from these cells and enter the systemic circulation. Although these circulating cytokines lead to fever by inducing the synthesis of PGE2, they also induce PGE2 in peripheral tissues. The increase in PGE2 in the periphery accounts for the nonspecific myalgias and arthralgias that often accompany fever. It is thought that some systemic PGE2 escapes destruction by the lung and gains access to the hypothalamus via the internal carotid. However, it is the elevation of PGE2 in the brain that starts the process of raising the hypothalamic set point for core temperature. There are four receptors for PGE2, and each signals the cell in different ways. Of the four receptors, the third (EP-3) is essential for fever: when the gene for this receptor is deleted in mice, no fever follows the injection of IL-1 or endotoxin. Deletion of the other PGE2 receptor genes leaves the fever

mechanism intact. Although PGE2 is essential for fever, it is not a neurotransmitter. Rather, the release of PGE2 from the brain side of the hypothalamic endothelium triggers the PGE2 receptor on glial cells, and this stimulation results in the rapid release of cyclic adenosine 5′-monophosphate (cAMP), which is a neurotransmitter, the release of cAMP from glial cells activates neuronal endings from the thermoregulatory center that extend into the area. The elevation of cAMP is thought to account for changes in the hypothalamic set point either directly or indirectly (by inducing the release of neurotransmitters). Distinct receptors for microbial products are located on the hypothalamic endothelium.

Production Of Cytokines In The Cns :
Cytokines produced in the brain may account for the hyperpyrexia of CNS hemorrhage, trauma, or infection. Viral infections of the CNS induce microglial and possibly neuronal production of IL-1, TNF, and IL-6. In experimental animals, the concentration of a cytokine required to cause fever is several orders of magnitude lower with direct injection into the brain substance or brain ventricles than with systemic injection. Therefore, cytokines produced in the CNS can raise the hypothalamic set point, bypassing the circumventricular organs. CNS cytokines likely account for the hyperpyrexia of CNS hemorrhage, trauma, or infection.(18)

Clinical presentations:
Before the history is elicited and a physical examination is performed, an immediate assessment of the patient's general appearance can yield valuable information. The perceptive physician's subjective sense that a patient is septic or toxic often proves accurate. Visible agitation or anxiety in a febrile patient can be a harbinger of critical illness. Presenting symptoms are frequently nonspecific. Detailed questions should be asked about the onset and duration of symptoms and about changes in severity or rate of progression over time. Host factors and co morbid conditions may increase the risk of infection with certain organisms or of a more fulminant course than is usually seen. Lack of splenic function, alcoholism with significant liver disease, IV drug use, HIV infection, diabetes, malignancy, organ transplantation, and chemotherapy all predispose to specific infections and frequently to increased severity. The patient should be questioned about factors that might help identify a nidus for invasive infection, such as recent upper respiratory tract infections, influenza, or varicella; prior trauma; disruption of cutaneous barriers due to lacerations, burns, surgery, body piercing, or decubiti; and the presence of foreign bodies, such as nasal packing after rhinoplasty, tampons, or prosthetic joints. Travel, contact with pets or other animals, or activities that might result in tick or mosquito exposure can lead to diagnoses that would not otherwise be considered. Recent dietary intake, medication use, social or occupational contact with ill individuals, vaccination history, recent sexual contacts, and menstrual history may be relevant. A review of systems should focus on any neurologic signs or sensorium alterations, rashes or skin lesions, and focal pain or tenderness and should also include a general review of respiratory, gastrointestinal, or genitourinary symptoms.

Diagnostic tests:
Physical examination:
A complete physical examination should be performed, with special attention to several areas that are sometimes given short shrift in routine examinations. Assessment of the patient's general appearance and vital signs, skin and soft tissue examination, and the neurologic evaluation are of particular importance. The patient may appear either anxious and agitated or lethargic and apathetic. Fever is usually present, although elderly patients and compromised hosts (e.g., patients who are uremic or cirrhotic and those who are taking glucocorticoids or nonsteroidal anti-inflammatory drugs) may be afebrile despite serious underlying infection. Measurement of blood pressure, heart rate, and respiratory rate helps determine the degree of hemodynamic and metabolic compromise. The patient's airway must be evaluated to rule out the risk of obstruction from an invasive oropharyngeal infection. The etiologic diagnosis may become evident in the context of a thorough skin examination. Petechial rashes are 147 typically seen with meningococcemia or Rocky Mountain spotted fever (RMSF;erythroderma is associated with toxic shock syndrome (TSS) and drug fever. The soft tissue and muscle examination is critical. Areas of erythema or duskiness, edema, and tenderness may indicate underlying necrotizing fasciitis, myositis, or myonecrosis. The neurologic examination must include a careful assessment of mental status for signs of early encephalopathy. Evidence of nuchal rigidity or focal neurologic findings should be sought. (20)

After a quick clinical assessment, diagnostic material should be obtained rapidly and antibiotic and supportive treatment begun.Blood (for cultures; baseline complete blood count with differential; measurement of serum electrolytes, blood urea nitrogen, serum creatinine, and serum glucose; and liver function tests) can be obtained at the time an IV line is placed and before antibiotics are administered. The blood lactate concentration also should be

measured. Three sets of blood cultures should be performed for patients with possible acute endocarditis. Asplenic patients should have a buffy coat examined for bacteria; these patients can have >106 organisms per milliliter of blood (compared with 104/mL in patients with an intact spleen). Blood smears from patients at risk for severe parasitic disease, such as malaria or babesiosis , must be examined for the diagnosis and quantitation of parasitemia. Blood smears may also be diagnostic in ehrlichiosis and anaplasmosis. Patients with possible meningitis should have cerebrospinal fluid (CSF) drawn before the initiation of antibiotic therapy. Focal findings, depressed mental status, or papilledema should be evaluated by brain imaging prior to lumbar puncture, which, in this setting, could initiate herniation. Antibiotics should be administered before imaging but after blood for cultures has been drawn. If CSF cultures are negative, blood cultures will provide the diagnosis in 50–70% of cases. Molecular diagnostic techniques (e.g., broad-range 16S Rrna gene polymerase chain reaction testing for bacterial meningitis pathogens) are of increasing importance in the rapid diagnosis of life-threatening infections.

Focal abscesses necessitate immediate CT or MRI as part of an evaluation for surgical intervention. Other diagnostic procedures, such as wound cultures, should not delay the initiation of treatment for more than minutes. Once emergent evaluation, diagnostic procedures, and (if appropriate) surgical consultation have been completed, other laboratory tests can be conducted. Appropriate radiography, computed axial tomography, MRI, urinalysis, erythrocyte sedimentation rate and C-reactive protein determination, and transthoracic or transesophageal echocardiography all may prove important.(20) If the clinical features do not suggest a specific infection, then initial investigations should include : Complete blood picture: A full blood count (FBC) with differential, including eosinophil count, urea and electrolytes, liver function tests (LFTs), blood glucose and muscle enzymes, inflammatory markers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), chest X-ray and electrocardiogram (ECG) The laboratory diagnosis of infection requires the demonstration—either direct or indirect—of viral, bacterial, fungal, or parasitic agents in tissues, fluids, or excreta of the host.
1. Cultures
2. Nucleic acid detection
3. Immunological tests
4. Serological tests for connective tissue disorders Autoantibody screen Complement level, Immunoglobulins Cryoglobulins
5. Echocardiography
6. Ultrasound of abdomen
7. CT/MRI of thorax, abdomen and/or brain
8. Imaging of the skeletal system Plain X-rays CT/MRI spine

Assessment:
Assessment of fever : The pattern of temperature changes may occasionally hint at the diagnosis: Continuous fever: Temperature remains above normal throughout the day and does not fluctuate more than 1 °C in 24 hours, e.g. lobar pneumonia, typhoid, meningitis, urinary tract infection, or typhus. Typhoid fever may show a specific fever pattern (Wunderlich curve of typhoid fever), with a slow stepwise increase and a high plateau. (Drops due to fever-reducing drugs are excluded.) Intermittent fever: The temperature elevation is present only for a certain period, later cycling back to normal, e.g. malaria, kala-azar, pyaemia, or septicemia Remittent fever: Temperature remains above normal throughout the day and fluctuates more than 1 °C in 24 hours, e.g., infective endocarditis, brucellosis.

Pel-Ebstein fever:
A specific kind of fever associated with Hodgkin's lymphoma, being high for one week and low for the next week and so on. However, there is some debate as to whether this pattern truly exists.[23]

Assessment of accompanying symptoms :
Rigors:
Shivering (followed by excessive sweating) occurs with a rapid rise in body temperature from any cause.

Night sweats:
These are associated with particular infections (e.g. tuberculosis, infective endocarditis), but sweating from any cause is worse at night.

Excessive sweating. Alcohol, anxiety, thyrotoxicosis, diabetes mellitus, acromegaly, lymphoma and excessive environmental heat all cause sweating without temperature elevation.

Recurrent fever. There are various causes, e.g. Borrelia recurrentis, bacterial abscess.
Accompanying features.

Headache:
Severe headache and photophobia, although characteristic of meningitis, may accompany other infections.

Delirium :
Mental confusion during fever is more common in young children or the elderly.

Muscle pain :
Myalgia may occur with viral infections, such as influenza, and with septicemia, including meningococcal sepsis.

Shock :
Shock may accompany severe infections and sepsis [24]

Assessment of patient history:
History: A meticulous history is essential, with particular attention to the chronology of events (e.g., in the case of rash: the site of onset and the direction and rate of spread; see below) and the relation of symptoms to medications, pet exposure, sick contacts, sexual contacts, travel, trauma, and the presence of prosthetic materials.[25]

Treatment :
Emperical therapy:
In the acutely ill patient, empirical antibiotic therapy is critical and should be administered without undue delay. Increased prevalence of antibiotic resistance in community-acquired bacteria must be considered when antibiotics are selected. In addition to the rapid initiation of antibiotic therapy, several of these infections require urgent surgical attention. Neurosurgical evaluation for subdural empyema, otolaryngologic surgery for possible mucormycosis, and cardiothoracic surgery for critically ill patients with acute endocarditis are as important as antibiotic therapy. For infections such as necrotizing fasciitis and clostridial myonecrosis,rapid surgical intervention supersedes other diagnostic or therapeutic maneuvers.

Adjunctive therapy:
Adjunctive treatments may reduce morbidity and mortality rates and include dexamethasone for bacterial meningitis or IV immunoglobulin for TSS and necrotizing fasciitis caused by group A Streptococcus. Adjunctive therapies should usually be initiated within the first hours of treatment; however, dexamethasone for bacterial meningitis must be given before or at the time of the first 781 dose of antibiotic. Glucocorticoids can also be harmful, sometimes resulting in worse outcomes—e.g., when given in the setting of cerebral malaria or viral hepatitis.[20]

Pharmacological therapy:
Antimicrobial agents:
1. Antimicrobial agents are among the most frequently prescribed drugs. Inappropriate use of these agents is associated with allergic reactions, toxicity, super infection, and more importantly the development of antimicrobial resistance. In addition, the excessive and inappropriate use of antimicrobials can cause an unnecessary economic burden to health care system and the patients as well. Antimicrobial resistance is more prevalent in hospital settings than in the community.[1]
2. For those with fever from a life threatening cause, the guideline recommends assessment of temperature and blood pressure and quick establishment of intravenous access, so that fluids and antimicrobial agents can be given if the patient is in shock or if sepsis is suspected.[26]
3. The ability to eradicate bacteria from the urinary tract is directly related to the sensitivity of the organism and the achievable concentration of the antimicrobial agent in the urine.
4. In patients who have frequent symptomatic infections, long-term prophylactic antimicrobial therapy may be instituted . Therapy is generally given for 6 months, with urine cultures followed periodically. [27]
5. Antimicrobial agents may be useful both in effecting symptomatic improvement and in eliminating faecal carriage of pathogens and therefore reducing the risk of transmitting infection to others.[28]

Antibiotics :
1. First level health facility guidelines recommend antimalarials for those with a positive malaria diagnostic test, antibacterials for those with signs of severe illness or specific bacterial infections, and hospital referral of those with severe illness or no apparent diagnosis. For patients with life threatening febrile illness, such as severe sepsis as a result of bacteraemia and meningitis, the guidelines recommend administering parenteral antibacterials, antimalarials, and glucose; patients should then be urgently referred to hospital.6 Selection of the parenteral antibacterial agent should ideally be based on knowledge of patterns of antimicrobial susceptibility among relevant organisms in the area. However, because of widespread resistance to traditional first line antimicrobials, such as penicillins, and invasive Salmonella making amino glycoside monotherapy a poor choice in many areas, extended spectrum cephalosporins such as ceftriaxone are commonly used. [26]
2. In non-specific gastroenteritis, antibiotics have been shown to shorten symptoms by only 1 day in an illness usually lasting 1–3 days.[29]
3. The use of antimicrobials has been controversial, although antibiotics are an important component of treatment. Selection of antibiotics should consider that up to 30% to 40% of H.Influenza and 95% of M. pneumonia Are β-lactamase producers, and up to 30% of S. pneumonia are at least moderately penicillin resistant.[30]
4. In seriously ill pyelonephritis patients, the traditional initial therapy has included an IV fluoroquinolone, an aminoglycoside with or without ampicillin, or an extended-spectrum cephalosporin with or without an aminoglycoside.[27]
5. Empirical antibiotic therapy for suspected meningococcal disease consists of a third-generation cephalosporin such as ceftriaxone or cefotaxime to provide coverage both for meningococci and for other, potentially penicillin-resistant organisms that may produce an indistinguishable clinical syndrome.[31]
6. The antimicrobial therapy of meningitis requires attainment of adequate levels of bactericidal agents within the CSF. The passage of antibiotics into CSF is dependent on the degree of meningeal inflammation and integrity of the blood–brain barrier created by capillary endothelial cells. Antimicrobials fall into three categories according to their ability to penetrate the CSF:
1. those that penetrate even when the meninges are not inflamed, for example chloramphenicol, metronidazole, isoniazid and pyrazinamide
2. those that generally penetrate only when the meninges are inflamed, and used in high doses, for example most β-lactam antibiotics, the quinolones and rifampicin
3. those that penetrate poorly under all circumstances, including the aminoglycosides, vancomycin and erythromycin.[32]
7. Otitis media(URTI) : The benefit of antibiotic treatment may be greater in children under two than in older children , but in any case about 80% of cases treated without antibiotics will resolve spontaneously within 3 days.[33]
8. Antibiotics are generally not recommended in diarrhoea associated with acute infective gastroenteritis. Inappropriate use will only contribute further to the problem of resistant organisms.[34]

Antipyretics :
1. Fever and its associated systemic symptoms can be treated with paracetamol, and by tepid sponging to cool the skin. [24]
2. Most fevers are associated with self-limited infections, such as common viral diseases. The use of antipyretics is not contraindicated in these infections: no significant clinical evidence indicates either that antipyretics delay the resolution of viral or bacterial infections or that fever facilitates recovery from infection or acts as an adjuvant to the immune system. In short, treatment of fever and its symptoms with routine antipyretics does no harm and does not slow the resolution of common viral and bacterial infections.
3. However, in bacterial infections, the withholding of antipyretic therapy can be helpful in evaluating the effectiveness of a particular antibiotic, especially in the absence of positive cultures of the infecting organism, and the routine use of antipyretics can mask an inadequately treated bacterial infection.[23]
4. The treatment of acute bronchitis is symptomatic and supportive in nature. Reassurance and antipyretics alone are often sufficient. Bed rest and mild analgesic-antipyretic therapy are often helpful in relieving the associated lethargy, malaise, and fever.[30]

Adjunctive therapy :
Fluid replacement :
1. Replacement of salt and water is important in patients with drenching sweats. Further management is focused on the underlying cause.[24]

2. Vomiting and diarrhea, two commonly encountered complaints, usually are self-limiting, but severe cases can result in serious complications (e.g., dehydration, metabolic disturbances, and even death). Vomiting associated with gastroenteritis usually resolves in 24 to 48 hours. Few people are particularly susceptible to the development of fluid and electrolyte abnormalities; therefore, fluid and electrolyte replacements are critically important. [35]

3. The clinical course of dengue includes febrile, critical and recovery phases , and there are different challenges for fluid management at each stage.1 In the initial febrile stage, the aim is to treat dehydration. The majority (70%) of non-shocked dengue patients can be treated as outpatients with oral rehydration regimens; however, the remaining 30% of these patients and all DSS patients require intravenous (IV) fluid therapy.[36]

4. All patients with acute, potentially infective diarrhea should be appropriately isolated to minimize person to-person spread of infection. Replacement of fluid losses in diarrheal illness is crucial and may be life-saving. The fluid lost in diarrhea is isotonic, so both water and electrolytes need to be replaced. Absorption of electrolytes from the gut is an active process requiring energy. Infected mucosa is capable of very rapid fluid and electrolyte transport if carbohydrate is available as an energy source. Oral rehydration solutions (ORS) therefore contain sugars, as well as water and electrolytes.[29]

5. Oral fluid and electrolyte replacement is the cornerstone of treatment. Oral Lactobacillus therapy may reduce the duration of diarrhea and or viral excretion in gastroenteritis in infective diseases.[37]

6. The treatment of acute bronchitis is symptomatic and supportive in nature Patients should be encouraged to drink fluids to prevent dehydration and possibly decrease the viscosity of respiratory secretions.[30]

7. Gastroenteritis : Most patients can be managed with oral rehydration regimens, but severely dehydrated patients require rapid volume expansion with intravenous fluids.[38]

Analgesics :

1. the use of nonsteroidal antiinflammatory drugs (e.g., diclofenac and ibuprofen) has not been associated with dengue complications. However, these analgesics are not widely recommended because of the risk of gastrointestinal bleeding. Therefore, paracetamol (acetaminophen) appears to be the safest medication to control symptoms such as fever, malaise, and ache.[39]

2. Chikungunya is usually characterized by an acute febrile and sometimes eruptive polyarthritis, commonly followed by persistent rheumatologic and general disabling symptoms.

3. Simple analgesics and/or non-steroidal anti-inflammatory drugs(NSAIDs) provide relief in most patients ,but better-targeted drugs are clearly needed to treat inflammatory rheumatic disorders.[40]

4. Acetaminophen or a non steroidal anti-inflammatory agent, such as ibuprofen, can be used to relieve pain and malaise in acute otitis media

5. In pharyngitis, as pain is often the primary reason for visiting a physician, emphasis on analgesics such as acetaminophen and non steroidal anti-inflammatory drugs to aid in pain relief is strongly recommended. However, acetaminophen is a better option because there is some concern that non steroidal anti inflammatory drugs may increase the risk for necrotizing fasciitis or toxic shock syndrome. Either systemic or topical analgesics can be used. [41]

Bronchodilators :

In chronic bronchitis , Oral or aerosolized bronchodilators (e.g., Albuterol aerosol) may be of benefit to some patients during acute pulmonary exacerbations. For patients who consistently demonstrate limitations in airflow, a therapeutic change of bronchodilators should be considered.

Oxygen therapy:

The supportive care of the patient with pneumonia includes the use of humidified oxygen for hypoxemia, fluid resuscitation, administration of bronchodilators when bronchospasm is present, and chest physiotherapy with postural drainage if there is evidence of retained secretions.[30]

Corticosteroids :

Meningitis : In pharmacological doses, corticosteroids, and in particular dexamethasone, regulate many components of the inflammatory response and also lower CSF hydrostatic pressure.[32]

Antiemetics :

In acute diarrhea, antimotility agents such as loperamide, diphenoxylate and codeine are occasionally useful for symptomatic control in adults who have mild to-moderate diarrhea and require relief from associated abdominal cramps. Antimotility agents are not recommended for use in children.

Probiotics :
In acute diarrhea, antimotility agents such as loperamide, diphenoxylate and codeine are occasionally useful for symptomatic control in adults who have mild to- moderate diarrhea and require relief from associated abdominal cramps. Antimotility agents are not recommended for use in children.[34]

Antimalarial drugs :
1. Artesunate, artemether, or quinine is suggested for treatment of severe malaria.[42]
2. There are a variety of antimalarial drugs. Treatment often depends on the species of malaria parasite, the part of the world where it was acquired, and the severity of the disease.
3. Oral or intravenous medications may be used, depending on severity.
4. Severe cases of malaria will require hospitalization for supportive treatment and care to manage high fever, seizures, and respiratory complications.[43]

Others:
1. Decongestants, antihistamines, topical corticosteroids, or expectorants have not been proven effective for acute otitis media.
2. In pharyngitis, Either systemic or topical analgesics can be used, as well as antipyretics and other supportive care including rest, fluids, lozenges, and saltwater gargles.
3. Nasal decongestant sprays such as phenylephrine and oxymetazoline that reduce inflammation by vasoconstriction are often used in sinusitis. Antihistamines should not be used for acute bacterial sinusitis in view of their anticholinergic effects that can dry mucosa and disturb clearance of mucosal secretions.[41]
4. Symptomatic treatment with antiemetics and antimotility (antidiarrhoeal) agents is sometimes used, especially as self-medication.[38]
5. Bronchiolitis(LRTI) is characterized by a prodrome of fever and coryzal symptoms which progresses to wheezing, respiratory distress and hypoxia of varying degrees. The treatment of bronchiolitis is mainly supportive and consists of oxygen, adequate hydration and ventilatory assistance if required. [33]

Surgical intervention :
Surgical insertion of tympanostomy tubes (T tubes) is an effective method for the prevention of recurrent otitis media.[41]

Vaccination :
1. Vaccination against influenza and pneumococcus may decrease risk of acute otitis media, especially in those with recurrent episodes. Immunization with the influenza vaccine reduces the incidence of acute otitis media by 36%.[30]
2. Immunization should be considered for individuals with chronic hepatitis B or C infections. Immediate protection can be provided by immune serum globulin if this is given soon after exposure to the virus.[44]

Management of febrile illness :
1. WHO guidelines for managing febrile adolescents and adults in resource limited settings are available for first level health facilities and are forthcoming for district hospitals.
2. First level health facility guidelines recommend antimalarials for those with a positive malaria diagnostic test, antibacterials for those with signs of severe illness or specific bacterial infections, and hospital referral of those with severe illness or no apparent diagnosis.
3. Management guidelines should be validated, locally adapted, and improved on the basis of local or national surveillance data and sentinel hospital studies.
4. Malaria, tuberculosis, and HIV diagnostic tests can enhance management by ruling out a specific illness or by directing towards a particular diagnosis.
5. Clinical trials of empirical treatment strategies and advocacy for better clinical laboratory services could help improve management guidelines and patient outcomes.[42]

Fever management :
1. For those with fever from a life threatening cause, the guideline recommends assessment of temperature and blood pressure and quick establishment of intravenous access, so that fluids and antimicrobial agents can be given if the patient is in shock or if sepsis is suspected.

2. Fever from a life threatening cause is defined as fever that is associated with neck stiffness, extreme weakness or inability to stand, lethargy, unconsciousness, convulsions, severe abdominal pain, or respiratory distress.
3. For patients with life threatening febrile illness, such as severe sepsis as a result of bacteraemia and meningitis, the guidelines recommend administering parenteral antibacterials, antimalarials, and glucose; patients should then be urgently referred to hospital.
4. When clinical and laboratory evaluations do not identify a specific cause for fever, healthcare providers may treat empirically according to the "syndrome" of clinical features that the patient presents with, often guided by management guidelines that recommend approaches to treatment based on syndromes.

Emergency management:
1. The WHO acute care guideline on integrated management of adolescent and adult illness (IMAI) recommends that the patient be rapidly assessed for the presence of emergency signs. Patients with airway obstruction, central cyanosis, severe respiratory distress, or circulatory failure (weak or fast pulse, or slow capillary refill) require urgent management, and referral to a hospital is recommended.
2. For patients who give a history of fever in the past 48 hours, feel hot, or have an axillary temperature of 37.5ºC or more, the history and physical examination focus on trying to identify a source for the fever and on stratifying their malaria risk. Risk of malaria is based on age, malaria transmission in the area of residence, travel history, pregnancy, and HIV infection status. A malaria rapid diagnostic test or malaria smear is indicated if the patient is considered to be at high risk of malaria, or if no obvious source of the fever can be found in a patient at low risk of malaria. Further management depends on the presence or absence of specific signs of illness.
3. Among those without severe disease, especially if the malaria test is negative, other causes of fever should be considered. Other causes include upper respiratory tract infections such as sinusitis, pneumonia, gastroenteritis, urinary tract infection, pelvic inflammatory disease, tuberculosis, HIV related illness, antiretroviral drug reactions, and severe soft tissue or muscle infection.
4. However, when illness persists for at least seven days, it is recommended that the apparent cause be treated, that tuberculosis and other HIV related conditions be considered, and that patients with no apparent cause be referred for assessment. Very severe illness in patients not at risk for malaria is managed with parenteral antibacterials and glucose.c
5. Simple fevers in patients with no malaria risk are managed by treating the apparent cause and evaluating after one week.[42]

Rehydration therapy :
1. Initial assessment of fluid loss is essential for rehydration and should include acute weight loss as it is the most reliable means of determining the extent of water loss. However, if accurate baseline weight is not available, clinical signs are helpful in determining approximate deficits. Physical assessment generally is more reliable in young children and infants than in adults.
2. Fluid replacement is the cornerstone of therapy for diarrhea regardless of etiology. Oral rehydration therapy (ORT) reverses dehydration in nearly all patients with mild to moderate diarrhea; treatment failure with ORT is infrequent (3% to 6%).9 ORT offers the advantages of being inexpensive and noninvasive and does not require hospitalization for administration. In those who are able to take oral fluids, ORT is superior to administration of intravenous (IV) fluids. Moreover, thirst drives use of ORT and provides a safeguard against over hydration.

Antimicrobial therapy:
1. Antibiotics are not essential in the treatment of most mild diarrheas, and empirical therapy for acute GI infections may result in courses of unnecessary antibiotics. However, appropriate antibiotic therapy shortens the duration of illness and reduces morbidity in some bacterial (cholera, enterotoxigenic E. coli, shigellosis, campylobacteriosis, yersiniosis) infections and can be lifesaving in invasive infections (C. difficile, salmonellosis). Antibiotic treatment also reduces the duration and shedding of organisms in infections with susceptible Shigella species and possibly in infection with susceptible Campylobacter species.
2. It is also important to note that outcomes of some bacterial diarrheal illnesses may be worsened by the use of antibiotics. use of an antimicrobial agent may worsen the risk of hemolytic uremic syndrome (HUS), which is defined by the triad of acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia, by increasing the production of shiga-like toxin

Antimotility Agents :
Ant peristaltic drugs such as diphenoxylate and loperamide offer symptomatic relief in patients with mild diarrhea. However, these agents are contraindicated in most toxin-mediated diarrheal illnesses (enterohemorrhagic E. coli, pseudomembranous colitis, shigellosis) and thus should be avoided in patients with high fever and bloody diarrhea. Slowing of fecal transit time is thought to result in extended toxin-associated damage.[45]

Non-pharmocological therapy and preventive measures :
Urinary tract infections (UTI):
1. Women with RUTIs should be educated about the characteristics of reinfection and relapse; the proper way to practice post-coital voiding; the importance of avoiding skin allergens, tight clothing and bubble baths; ways to ensure personal hygiene, and the choice of alternative forms of contraception rather than spermicides.
2. Patients should be advised and encouraged to drink plenty of fluids (two to three liters per day) and to urinate frequently to help flush bacteria from the bladder. Holding urine for a long time allows bacteria to multiply within the urinary tract, resulting in cystitis.
3. Avoiding multiple sexual partners will reduce the risk of both UTIs and sexually transmitted infections.
4. Women are encouraged to avoid spermicidal contraceptives, diaphragms and vaginal douching, which may irritate the vagina and urethra and facilitate the entry and colonization of bacteria within the urinary tract.
5. Skin allergens introduced to the genital area, such as bubble bath liquids, bath oils, vaginal creams and lotions, deodorant sprays or soaps are better avoided as they could alter vaginal flora and ultimately result in UTIs.
6. Probiotics are beneficial microorganisms that could protect against UTIs.[46]

Respiratory tract infections (RTI) :
1. Acetaminophen or a nonsteroidal anti-inflammatory drug (NSAID) such as ibuprofen should be offered early to relieve pain and malaise in acute otitis media regardless of the use of antibiotics.11 Decongestants, antihistamines, topical corticosteroids, and expectorants have not been proven effective for acute otitis media,10,26 and side effects associated with these treatments may be unpleasant.
2. Surgical insertion of tympanostomy tubes (T tubes) is an effective method for the prevention of recurrent otitis media. These small tubes are placed through the inferior portion of the tympanic membrane under general anesthesia and aerate the middle ear. Children with recurrent otitis who have more than three episodes in 6 months or four or more episodes (one of which is recent) in a year should be considered for T-tube placement.[47]

Gastroenteritis:
1. Because rotavirus infects nearly all children in both industrialized and developing countries early in life, good hygiene and sanitation alone are considered inadequate for prevention.[45]
2. Public health measures of improved water supply and sanitation facilities and the quality control of commercial products are important for the control of the majority of enteric infections. In addition, many diarrheal diseases can be prevented by following simple rules of personal hygiene and safe food preparation. Hand washing with soap is instrumental in preventing the spread of illness and should. be emphasized for caregivers and persons with diarrheal illnesses. Safe food handling and preparation practices can significantly decrease the incidence of certain types of enteric infections.[45]

Dengue :
Steps for prevention include:
1. Disease notification: In dengue endemic regions, suspected, probable, and confirmed cases of dengue fever should be reported to the relevant authorities as soon as possible so that measures can be instituted to prevent transmission.
2. Screening : Screening is not applicable as dengue fever is a communicable disease. However, populations may be screened for epidemiological purposes or to check for previous exposure to DENV.
3. Primary prevention : The WHO recommends strategies for the prevention and control of dengue infection. Communities in dengue endemic regions should be educated to recognize symptoms and prevent transmission.
4. Regular removal of all sources of stagnant water to prevent mosquito breeding grounds.
5. Appropriate clothing to cover exposed skin, especially during the day, and the use of insecticides, mosquito repellents, mosquito coils, and mosquito nets.
6. Mosquito nets and coils should be placed around sick patients to prevent transmission.

7. Secondary prevention : Recurrence is possible with different serotypes leading to a secondary infection. The usual primary prevention measures should therefore be followed after recovery from an initial infection.[48]
8. Community based programs involving local authorities to participate in eliminating breeding places of dengue mosquitoes are the only cost effective and sustainable way of ensuring control in any dengue-affected country and countries deficient in resources.
9. Measurement of variable "practices for control" was based on data collected on 11 statements. These statements included, cleaning water storage containers after seven days, examining mosquito larvae in water containers, cleaning roofs in rainy seasons, Using bed nets/mosquito repellants, Using insecticides, examining discarded utensils, wear cloth to fully cover body, using larvacides, installing window nets, using apple juice during fever and using herbal tea and cardamom during fever.[49]

Malaria:
Mosquito control:
Mosquito nets help keep mosquitoes away from people and reduce infection rates and transmission of malaria. Nets are not a perfect barrier and are often treated with an insecticide designed to kill the mosquito before it has time to find a way past the net. Insecticide-treated nets are estimated to be twice as effective as untreated nets and offer greater than 70% protection compared with no net.[50]

Other methods :
1. Community participation and health education strategies promoting awareness of malaria and the importance of control measures have been successfully used to reduce the incidence of malaria in some areas of the developing world.[51]
2. Education can also inform people to cover over areas of stagnant, still water, such as water tanks that are ideal breeding grounds for the parasite and mosquito, thus cutting down the risk of the transmission between people. This is generally used in urban areas where there are large centers of population in a confined space and transmission would be most likely in these areas.[52]

Medications :
1. There are a number of medications that can help prevent or interrupt malaria in travelers to places where infection is common. Many of these medications are also used in treatment. In places where Plasmodium is resistant to one or more medications, three medications—mefloquine, doxycycline , or the combination of atovaquone/proguanil (Malarone)—are frequently used for prevention. Doxycycline and the atovaquone/proguanil are better tolerated while mefloquine is taken once a week.[53]
2. The protective effect does not begin immediately, and people visiting areas where malaria exists usually start taking the drugs one to two weeks before arriving and continue taking them for four weeks after leaving (except for atovaquone/proguanil, which only needs to be started two days before and continued for seven days afterward)[54]

Assessment of acute febrile illness severity :
1. assessment of the acute illness should focus on classifying the patient's health problem on the basis of the presenting symptoms. For patients who give a history of fever in the past 48 hours, feel hot, or have an axillary temperature of 37.5ºC or more, the history and physical examination focus on trying to identify a source for the fever.[42]
2. Acute febrile illnesses lead to a significant level of morbidity among the population. The major groups of these fever patients are the ones suffering from malaria, leptospirosis, dengue, chickungunya, scrub typhus, infectious mononucleosis, typhoid fever, acute human immunodeficiency virus conversion disease and so on. Presence of thrombocytopenia helps clinicians in assessing the severity of the illness. Conclusion: Finding of thrombocytopenia in patients with acute febrile illness raises the suspicion of Dengue and malaria infection. [55]
3. Very severe illness in patients not at risk for malaria is managed with parenteral antibacterials and glucose. Artesunate, artemether, or quinine is suggested for treatment of severe malaria. However, when illness persists for at least seven days, it is recommended that the apparent cause be treated, that tuberculosis and other HIV related conditions be considered, and that patients with no apparent cause be referred for assessment at the district hospital. Simple fevers in patients with no malaria risk are managed by treating the apparent cause and evaluating after one week.[42]

Current research status on acute febrile illness:
Khety Z et al (2016). has published an article on Studies on Antimicrobial Consumption in a Tertiary Care Private Hospital. The main aim of this observational study was to study the pattern of usage of antibiotics in a tertiary care hospital and the resistance. the rampant use has resulted in by calculating DDI's (defined daily dosages) for each antibiotic used. Defined daily doses (DDDs) of antimicrobials prescribed per 100 bed days are a good measure of antimicrobial consumption. The DDD methodology converts and standardizes readily available product quantity data into crude estimates of clinical exposure to medicines. The DDD is the assumed average maintenance dose for the medication's main indication. There has been a consistent very high increase in the consumption of Meropenem and Ceftriaxone while there is no significant change in the consumption of Metronidazole, Tobramycin, and Vancomycin. The increase in expenditure due to antibiotic usage from 2011 to 2012 was 23% while the increase from 2012 to 2013 was (39)%. It has also identified drugs like Meropenem and Piperacillin/Tazobactam which requires further investigation to assess their appropriateness in different clinical settings. This need to be correlated with the hospital's isolated infective organisms' sensitivity reports.

They gave a conclusion that identified drugs like Meropenem and Piperacillin/Tazobactam which requires further investigation to assess their appropriateness in different clinical settings. This need to be correlated with the hospital's isolated infective organisms' sensitivity reports.[16]

Rani RA et al (2016) has published an article on A Study on Common Etiologies of Acute Febrile Illness Detectable by Microbiological Tests in a Tertiary Care Hospital. The aim of the study was to identify the common etiologies of acute febrile illness which are detectable by employing microbiological tests with correlation of laboratory parameters. This is a retrospective study involving 200 cases of acute febrile illness in a tertiary care hospital. Blood samples were tested for Dengue, Malaria, Typhoid, Leptospirosis, Rickettsial infections and complete blood count analysis. Males and persons with age group of 20-40 were commonly affected. The commonest cause of acute febrile illness was Dengue in 54 cases (27%) with Primary Dengue infection in 45 cases (83%) and Secondary dengue infection in 9 cases ((39)%). Most cases of Dengue were reported in monsoon and post monsoon period. Other causes of acute febrile illness detected were Typhoid in 6cases (4%), Malaria in 4cases(2%) and Rickettsial infections in 2cases (1%). Thrombocytopenia and leucopenia were marked in Dengue cases. Most Typhoid cases had leucopenia and Malaria cases had thrombocytopenia. They gave a conclusion that, although Dengue being the commonest cause of acute febrile illness, other different causes prevailing in tropical countries should be suspected and correct Confirmatory diagnostic tests with clinical findings, relevant laboratory parameters and epidemiology of disease is essential to prevent complications and to reduce morbidity and mortality in patients with acute febrile illness.[56]

Chitra B et al (2016) has published an article on Study on utilization pattern of antibiotics at a private corporate hospital. a retrospective study was carried out in patients who received at least one antibiotic in General medicine department and analyzed for rationality. The results revealed that the purpose of antibiotics prescribed was for prophylaxis and empirical use. Among the study population, smokers were found to have an increased risk of infections, where antibiotics were widely used. Antibiotics were mainly prescribed for AGE, COPD, Pneumonia, LRTI, UTI, PUD, URTI, and Viral fever, ALD, Tuberculosis, Acute Bacillary Dysentery, GERD, Rheumatoid Arthritis and Surgery. Majority of the patients were prescribed with cephalosporin category of antibiotics, followed by fluoroquinolones, penicillin and aminoglycosides. In the study for drug interactions, majority of interactions were seen with levofloxacin and minor interactions with other antibiotics. The pharmacist should play an important role by assessing patient health status and adherence to standard of care by educating the patients on administering medication to prevent resistance from noncompliance. Thus pharmacist should play an important role in health care team by providing information on the rational use of antibiotics for a better patient care.[57]

Kundavaram Paul Prabhakar Abhilash et al (2016), published an article on Acute Undifferentiated Febrile Illness in Patients Presenting to a Tertiary Care Hospital in South India: Clinical Spectrum and Outcome. This prospective observational study was conducted in a tertiary hospital in South India. All adult patients presenting with AUFI of 3–14 days duration were evaluated for etiology, and the differences in presentation and outcome were analyzed. The study cohort included 1258 patients. A microbiological cause was identified in 82.5% of our patients. Scrub typhus was the most common cause of AUFI (35.9%) followed by dengue (30.6%), malaria (10.4%), enteric fever (3.7%), and leptospirosis (0.6%). Both scrub typhus and dengue fever peaked during the monsoon season and the cooler months, whereas no seasonality was observed with enteric fever and malaria. The mean time to presentation was longer in enteric fever (9.9 [4.7] days) and scrub typhus (8.2 [3.2] days). Bleeding manifestations

were seen in 7.7% of patients, mostly associated with dengue (14%), scrub typhus (4.2%), and malaria (4.6%). The requirement of supplemental oxygen, invasive ventilation, and inotropes was higher in scrub typhus, leptospirosis, and malaria. The overall mortality rate was 3.3% and was highest with scrub typhus (4.6%) followed by dengue fever (2.3%). Significant clinical predictors of scrub typhus were breathlessness (odds ratio [OR]: 4.96; 95% confidence interval [CI]: 3.38–7.3), total whole blood cell count >10,000 cells/mm3 (OR: 2.31; 95% CI: 1.64–3.24), serum albumin <3.5 g % (OR: 2.32; 95% CI: 1.68–3.2). Overt bleeding manifestations (OR: 2.98; 95% CI: 1.84–4.84), and a platelet count of <150,000 cells/mm3 (OR: 2.09; 95% CI: 1.47–2.98) were independent predictors of dengue fever. Common comorbidities included diabetes mellitus (10.7%), essential hypertension (6.5%), ischemic heart disease (1.1%), and chronic liver disease (0.8%).They gave a conclusion that The similarity in clinical presentation, diversity of etiological agents, an inability to identify an etiology in a significant number of patients, demonstrate the complexity of diagnosis, and treatment of AUFI in South India. The etiological profile will be of use in the development of rational guidelines for infectious disease control and treatment.[58]

Das D et al (2015) has published an article on Common Infectious etiologies of Acute Febrile Illness in a Remote Geographical Location. This study was conducted to determine various infectious etiologies of acute febrile illness with their clinical presentations, complications and mortality with special emphasis to scrub typhus. This is a cross-sectional study and 205 patients including pediatric patients admitted with acute febrile illness were evaluated. A detailed history was taken and complete physical examination was done in all patients. Basic laboratory tests were done in all cases along with confirmatory tests. the most common cause in this study of acute febrile illness was found to be scrub typhus and gave a conclusion that Scrub typhus was observed to be the common cause of acute febrile illness during the study period and witnessed the emergence of dengue as an outbreak in this region. Prompt recognition of acute febrile illness is important for specific treatment and better outcome in patients. Therefore, this study emphasizes on the fact that an appropriate and early diagnosis of the infectious etiologist of acute febrile illnesses is always important.[59]

Saleh N et al (2015). published an article on Evaluation of antibiotic prescription in the Lebanese community. This study aimed at assessing the appropriateness of antibiotic prescription by non-infectious disease physicians in a community setting in Lebanon.A pilot cross-sectional study was undertaken on community pharmacy patients presenting with antibiotic prescription. It was performed over a period of 4 months in different regions of Lebanon. Participants answered a questionnaire inquiring about socio-demographic characteristics, medical conditions, symptoms that required medical attention, the doctor's diagnosis, the prescribed antibiotic, and whether laboratory tests were ordered to identify the causative organism or not. Data were analyzed using SPSS (39).We studied 270 patients (49.3% males and 50.7% females). This study showed that the most-prescribed antibiotics were the cephalosporins (82%) and that almost half of the illnesses for which antibiotics were prescribed were respiratory tract infections (41%). The study also showed that the choice of the prescribed antibiotic was appropriate in 61.5% of the studied cases, while the prescribed dose and the duration of the treatment were inaccurate in 52 and 64% of the cases, respectively. In addition, fever seemed to be a factor that influenced the physician's prescriptions, since the choice of drug conformity to guidelines increased from 53.7% (1 day of fever) to 88.9% (1 week of fever), and the dose prescription compliance to guidelines was higher (55.9%) for patients suffering from fever compared to those with no fever (38.1%). They gave a conclusion that, a high prevalence of inappropriate antibiotic prescriptions in Lebanon. There-fore, actions should be taken to optimize antibiotic prescription.[60]

Meher BR et al (2014). has published an article on A study on antibiotic utilization pattern in a general medicine ward of a tertiary care teaching hospital. This is a cross sectional observational study done to evaluate the current antibiotic utilization pattern amongst the in patients of medicine department in a Teaching Hospital in eastern India. 840 prescriptions obtained from inpatients of Medicine Department during the period of 1st June 2015 to 31st August 2015 were included in the study. Data was collected in pre-designed case record form. Baseline parameters, use of antibiotics (single/combination), their dose, duration and route of administration and the different regimes of antibiotics prescribed were noted. Out of 840 Indoor prescriptions reviewed, 400 (47.6%) were with antibiotics. The mean age of the patients was (47.76 ± 18.49) years of which 454 (54.05%) were male. The average number of drugs per prescription was 3.8 (3192 / 840) of which 63.5% (2026/3192) were written in generic name. Average number of antibiotics per prescription with antibiotic was 1.5. Oral antibiotics used were 142 (23.35%) compared to 466(76.64%) injectable antibiotics i.e. in 1:3 ratio. Azithromycin (22.5%) was the most common oral antibiotic followed by rifaximin (18.3%). Ceftriaxone (40.6%) was the most common injectable antibiotic used followed by Piperacillin- tazobactam combination (14.6%). A total of 15 types of parenteral and 11 types of oral antibiotics were prescribed Single antibiotic was prescribed in 264 (64%) cases; whereas combination of 2 and 3 antibiotics were

used in 126 (29.5%) and 10 (6.5%) cases respectively. They gave a conclusion that most common disease for which antibiotics prescribed was respiratory tract infection. Most common antibiotic used was ceftriaxone, more than one antibiotic was prescribed and only 11% antibiotics were prescribed in generic name. A strict protocol for prescribers is required to promote rational use of antibiotics which would not only prevent antibiotic resistance but also reduce the treatment expenditure .[61]

Ahmad A et al (2014) has published an article on A Study the Prescription Pattern of Antibiotics in the Medicine Department in a Teaching Hospital. The purpose of the present study was to evaluate the pattern of antibiotic usage in the general medicine department of a tertiary hospital in South India. The objective of the study was to determine the average number of antibiotics prescribed per prescription, to identify the indication for which the antibiotics were commonly used and to determine the most commonly prescribed antibiotics in a tertiary care hospital. This was a prospective observational study. About 200 patients who were prescribed antibiotics were included in the study. The data on antibiotic containing prescriptions from each patient was collected from the inpatient and outpatient department. The study was carried out from January to June, 2013. The data was collected on antibiotics was subjected for descriptive statistical analysis. A total of 200 prescriptions were studied, out of which 139 (69.5%) prescriptions were mono therapy and 61 (30.5%) prescriptions had multiple antibiotics. It was observed that out of 200 patients who were prescribed antibiotics, 110 were male (55%) and 90 were female (45%). Cephalosporins were most commonly prescribed antibiotics and ceftriaxone was prescribed mostly. The most commonly prescribed antibiotics were Cephalosporins and most of the prescriptions contained mono therapy. The antibiotics treatment regimens given in most of the patients were without done culture sensitivity test before prescribing, which lead to irrational prescribing. Rational prescribing of antibiotics avoids polypharmacy and prevents antibiotic resistances. They concluded that out of 200 prescriptions, Cephalosporin class of antibiotics were most frequently prescribed and among them mostly ceftriaxone was the drug of choice. This study reveals that there are many standard treatment guidelines available from various state government agencies. Antimicrobial policies given by central government for rational use of antibiotics in the country are not adhered by physicians.[62]

Chandy SJ et al (2013). published an article on Patterns of antibiotic use in the community and challenges of antibiotic surveillance in a lower-middle-income country setting. This study describes antibiotic patterns and challenges faced while developing such surveillance systems in an LMIC.Surveillance of antibiotic encounters (prescriptions and dispensations) was carried out using a repeated cross-sectional design for 2 years in Vellore, south India. Every month, patients attending 30 health facilities (small hospitals, general practitioner clinics and pharmacy shops) were observed until 30 antibiotic encounters were attained in each. Antibiotic use was expressed as the percentage of encounters containing specific antibiotics and defined daily doses (DDDs)/100 patients. Bulk antibiotic sales data were also collected. Over 2 years, a total of 52,788 patients were observed and 21,600 antibiotic encounters (40.9%) were accrued. Fluoroquinolones and penicillins were widely used. Rural hospitals used co-trimoxazole more often and urban private hospitals used cephalosporins more often; 41.1% of antibiotic prescriptions were for respiratory infections. The main challenges in surveillance included issues regarding sampling, data collection, denominator calculation and sustainability. They gave a conclusion that, Patterns of antibiotic use varied across health facilities, suggesting that interventions should involve all types of health facilities. Although challenges were encountered, our study shows that it is possible to develop surveillance systems in LMICs and the data generated may be used to plan feasible interventions, assess impact and thereby contain resistance.[63]

Tina M. Parker et al (2007). published an article on Concurrent Infections in Acute Febrile Illness Patients in Egypt. They report the occurrence of concurrent infections with multiple acute febrile illness (AFI) pathogens during an ongoing prospective laboratory-based surveillance in four infectious disease hospitals in urban and rural areas of Egypt from June 2005 to August 2006. Patients were screened for Leptospira, Rickettsia typhi, Brucella, or Salmonella enteric serogroup Typhi by various methods including serology, culture, and PCR. One hundred eighty-seven of 1,510 patients (12.4%) evaluated had supporting evidence for the presence of co infections; 20 (1%) of these patients had 2 or more pathogens based upon confirmatory 4-fold rise in antibody titer, culture, and/or PCR. Most co infected patients lived or worked in rural agricultural areas. The high co infection rates suggest that defining the etiologies of AFI is imperative in guiding proper disease treatment, prevention, and control strategies in Egypt. They gave a conclusion, In this study, we determined the proportion of AFI due to concurrent infections using gold-standard laboratory tests. Detection of these co infections at the time of presentation is often difficult, especially with limited laboratory support. Although identifying AFI co infection is challenging ,fortunately, therapy with doxycycline, an inexpensive but useful antibiotic, has been shown to be effective against leptospirosis, brucellosis, typhoid fever, and rickettsiosis.(39) Therefore, clinicians should consider the use of doxycycline for AFI patients in

Egypt who do not respond to other therapies. Analysis of cases from this project will continue so that a better picture of the prevalence of patients with concurrent or serial zoonotic disease exposure can be obtained. In addition, the collected data will be used to assist AFI prevention and control strategies currently used in Egypt. [64]

Riyaz Ahmed Siddiqui et al (2003). published an article on Antibiotic trends in acute febrile illness. It is a record based observational study that was carried out at NKP salve institute of medical sciences and RC, Nagpur. 200 case record files of patients admitted with a diagnosis of acute febrile illness in the dept. of Medicine due to various etiologies were analyzed. Antibiotics prescribed for various causes of acute febrile illness like respiratory tract infections, urinary tract infection, gastrointestinal infection, malarial infections, septicemia, meningitis, pyrexia of unknown origin etc. were noted and data was analyzed for prescription pattern of antimicrobials. Out of 200 patients of febrile illness the common clinical conditions for which antibiotics were prescribed were respiratory tract infections (upper respiratory tract infection 25.5% and lower respiratory tract infection 14%), acute gastroenteritis (20%), and urinary tract infection (13.5%) followed by, pyrexia of unknown origin (8.5%), viral fever (8%), malaria (7%), hepatitis A (1.5%), meningitis (1%) and rickettsial infection (1%). The commonly prescribed antibiotics were ceftriaxone in (19.37%) and cefixime (15.93%) followed by coamoxiclav (12.5%), azithromycin (11.87%), doxycycline (10.31%), ofloxacin and ornidazole (8.43%), levofloxacin (6.25%), ofloxacin (4.68%), ciprofloxacin (1.87%), artesunate (3.75%), artemether and lumefantrine (4.37%) and valacyclovir (0.625%). the study concluded that most common disease for which antibiotics prescribed were respiratory tract infection and gasterointestinal infections. Most common antibiotic used were third generation cephalosporins especially ceftriaxone and cefixime.[1]

Aims And Objectives:-
The present study aims to document the antibiotics used in Acute febrile illness
1. To identify the different trends of antibiotic used in acute febrile illness.
2. To review the different antibiotic combinations prescribed for patients suffering from AFI.
3. To review and analyze common clinical conditions for which antibiotics were prescribed in AFI.
4. To evaluate the major co-morbid conditions.
5. To analyze Patient compliance after counseling.

Methodology:-
Plan of work
A study was carried out to evaluate the clinical use of antibiotics used in acute febrile illness. All the antibiotics containing prescription were monitored to know the percentage of antibiotic used and also the conditions in which it was prescribed. Literatures which support the study were collected and were reviewed for study on clinical use of antibiotics in acute febrile illness.. A standard data entry format for collecting patient's details was designed and during the ward rounds the entire patient data with special reference to the antibiotics prescribed and were recorded in the format.

Materials & methods:-
Source of data:
Case report forms of patients with acute febrile illness.

Method and collection of data:
Study site:
Study conducted at Medicine ward of **Gleneagles Global Hospital** LB.NAGAR.

Study duration:
the study is conducted during a six month period.

Study design:
it is a hospital based prospective observational study conducted on 200 inpatients using antibiotics for acute febrile illness. The data was collected which contains patient demographics (age, sex), date of admission, date of discharge, history of present illness, past medical history, diagnosis, name of the drugs, dosage regimen (form, dose, route, frequency and duration). The knowledge assessment questionnaire form contains about 10 questions to assess the knowledge of patient towards the medications used.

Sample size :
A total of 200 patients from the in-patient department of general medicine in Aware global Hospital, who were prescribed with antibiotics and those who fulfilled the exclusion and inclusion criteria were selected for the study.

Study criteria :
The following study is carried out using the following factors,

Inclusion criteria:
1. Patients with fever and other flu symptoms.
2. Patients with other co morbid conditions diabetes mellitus, hypertension.

Exclusion criteria:
1. Pregnant women and nursing mothers.
2. Outpatients
3. Patients on herbal medicines

Sources of data:
Patient Profile Form:
1. Patient demographic details (age, sex, alcoholic status, smoking status)
2. Chief complaints
3. History of present illness
4. Past medical and medication history
5. Family history
6. Final diagnosis
7. Name of the drugs
8. Dosage regimen (form, dose, route, frequency and duration)
9. Date on which pharmacotherapy was initiated
10. Laboratory data

Knowledge assessment questionnaire contains the following questions:
1. Do you have fever ?
2. How long have you been suffering from fever ?
3. Do you have any other symptoms along with fever (like vomiting, diarrhea, cough, cold, body pains)?
4. Are you using any self medication for these symptoms ?
5. What is your opinion about the medication you are using ?
6. Have you been diagnosed with any infections recently?
7. Is your surroundings hygienic?
8. How often do you experience flies in or around food stalls / restaurants you prefer to eat ?
9. What is your main source of drinking water when you are not at home ?
10. How often do use soap when you wash your hands ?
11. To which allergen you are allergic ?
12. Are you suffering from any co morbid conditions ?
13. Do you think that your disease is well controlled ?
14. Do you have any contact with other patient suffering from fever or infection?
15. Have you been travelling outside the area for the last few months ?

Determination of prescribing patterns:
A suitable data collection form was designed and used data was collected with respect to:
1. Demographic details: name, age, sex
2. Condition and reasons for hospital admission were recorded
3. Drug data: Brand and generic name of the drugs prescribed, dose, route of administration, frequency and their follow up for few days was recorded.

Statistical software:
SPSS Software 17.0

Results:-

Population description:

A study was performed with a total of 200 patients having complaints of AFI admitted in the hospital. The Mean Age was 41years and the standard deviation was 18 years. Of this population, 57% were males and 43% were females, The main demographic characteristics , co-morbidities, diagnosis and treatment have been discussed.

Table 1:-Distribution of subjects based on age in AFI (%)

Age group (in years)	Percentages (%)
15-30	34%
31-45	27%
46-60	23%
61-75	11%
76-90	5%
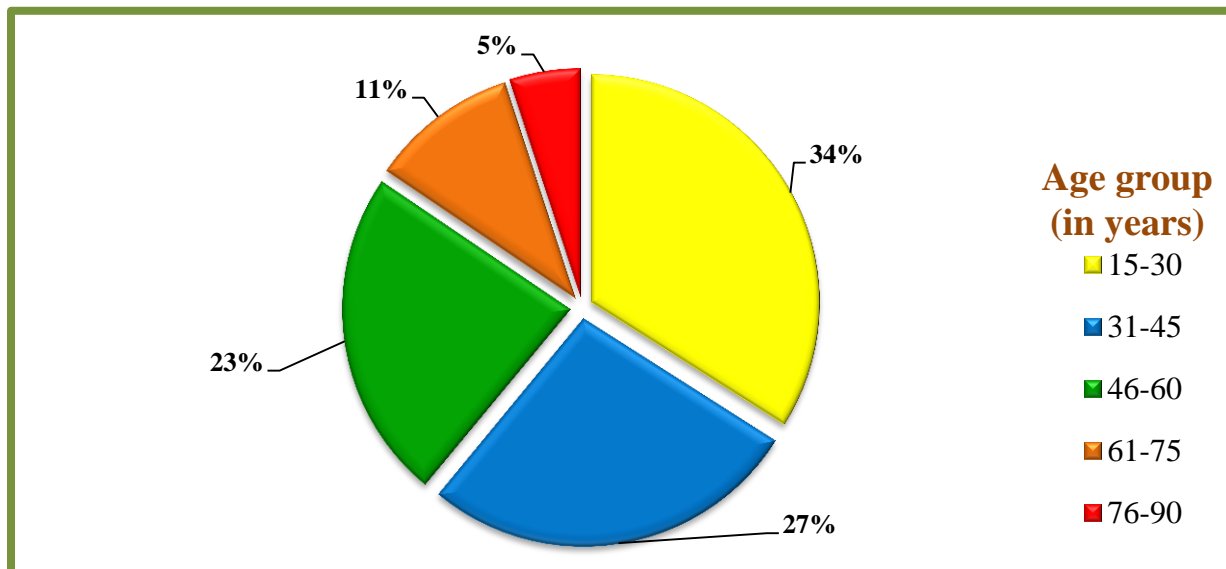
Figure 2:-Pie Chart presentation of distribution of subjects based upon age in AFI (%)

Table 2:-Statistical Presentation of the age group data by Column Statistics in AFI

N	200
Mean	41.47
Std. error of mean	1.284
Std. deviation	18.155

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Figure 3:-Statistical Presentation of the age group data by Column Statistics
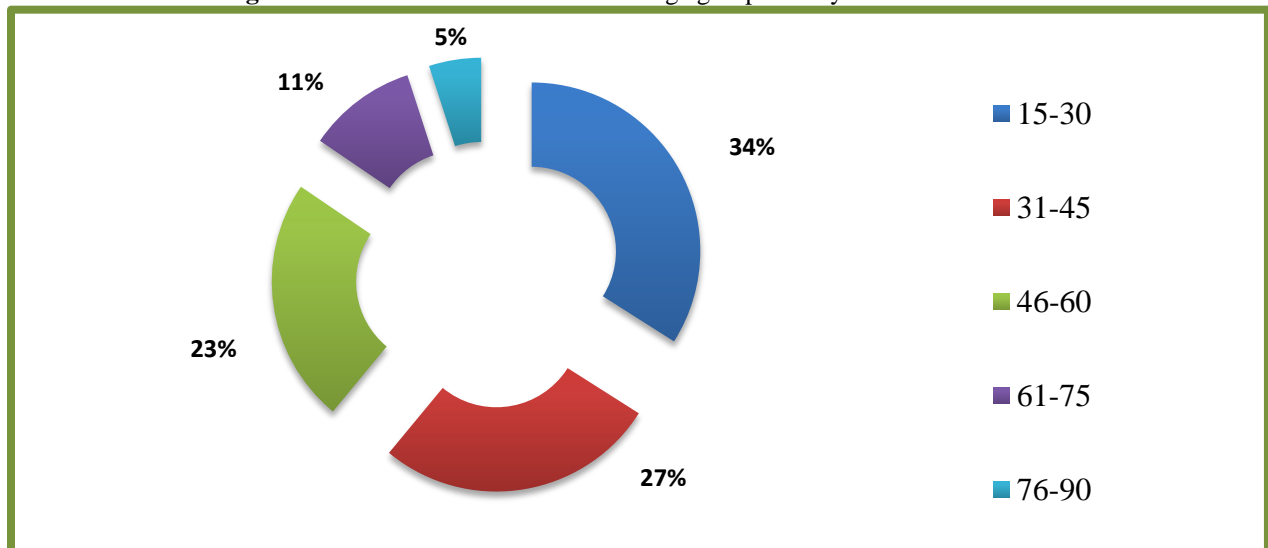
Among the study population, 68 (34%) individuals belonged to the age group of 15-30 years, 54(27%) individuals belonged to the age group of 31-45 years, 47(23%) individuals belonged to the age group of 46-60 years, 21(11%) individuals belonged to the age group of 61-75 years and 10 (5%) individuals belonged to the age group of 76-90 years.

Table 3:-Distribution of subjects based upon gender in AFI (%)

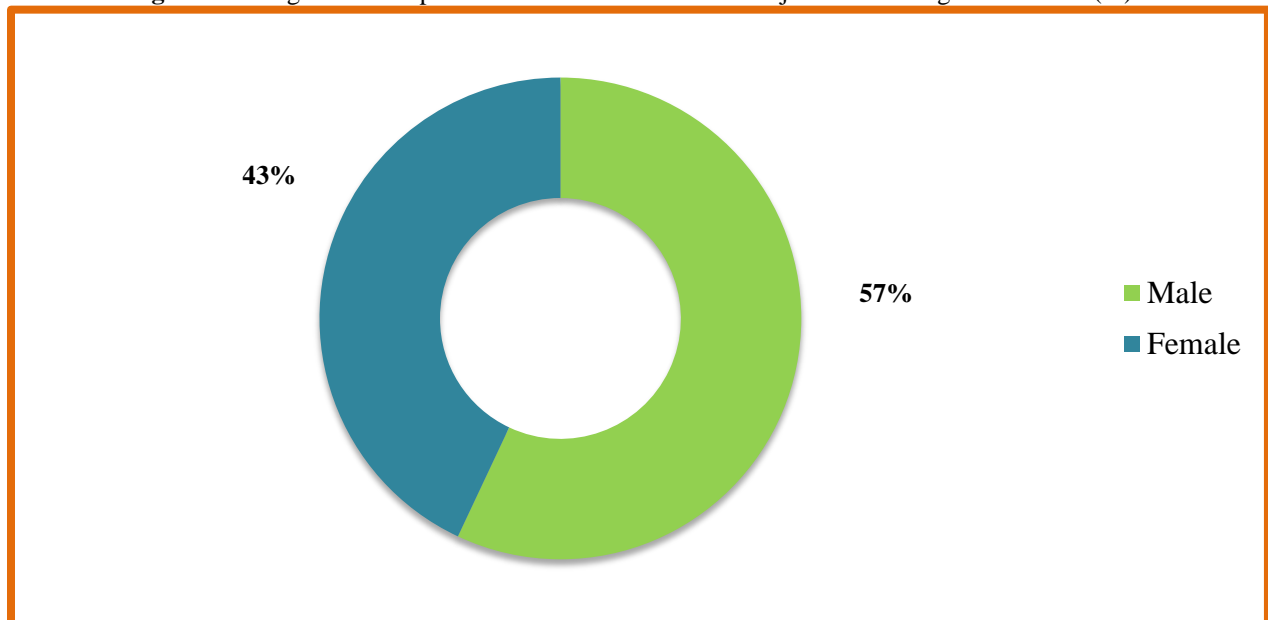| Gender	Percentages (%)
Male	57%
Female	43%

Figure 4:-Doughnut Chart presentation of distribution of subjects based on gender in AFI (%)

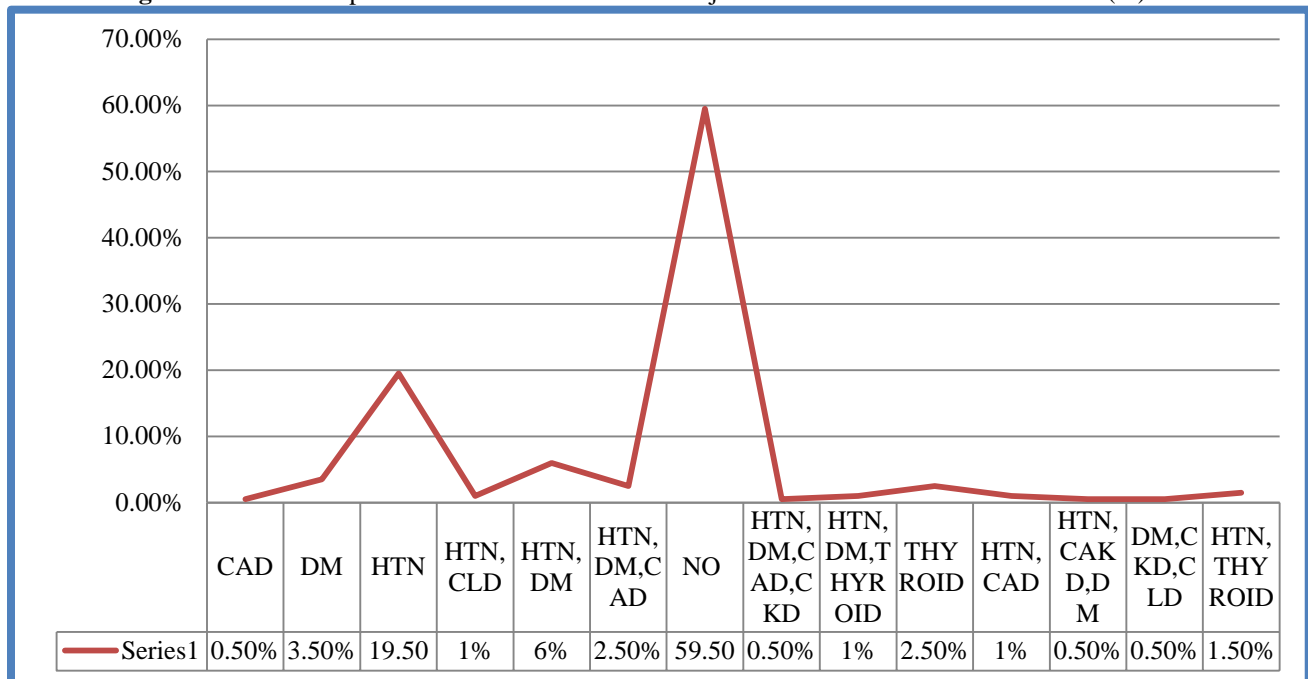**Table 4:-**Statistical Presentation of the data of study population based on gender by Column Statistics

Gender	Frequency	Percentages (%)
Female	86	43%
Male	114	57%
Total	200	100%

Figure 5:-Pie Chart presentation of distribution of subjects based on gender in AFI (%) by Column Statistics
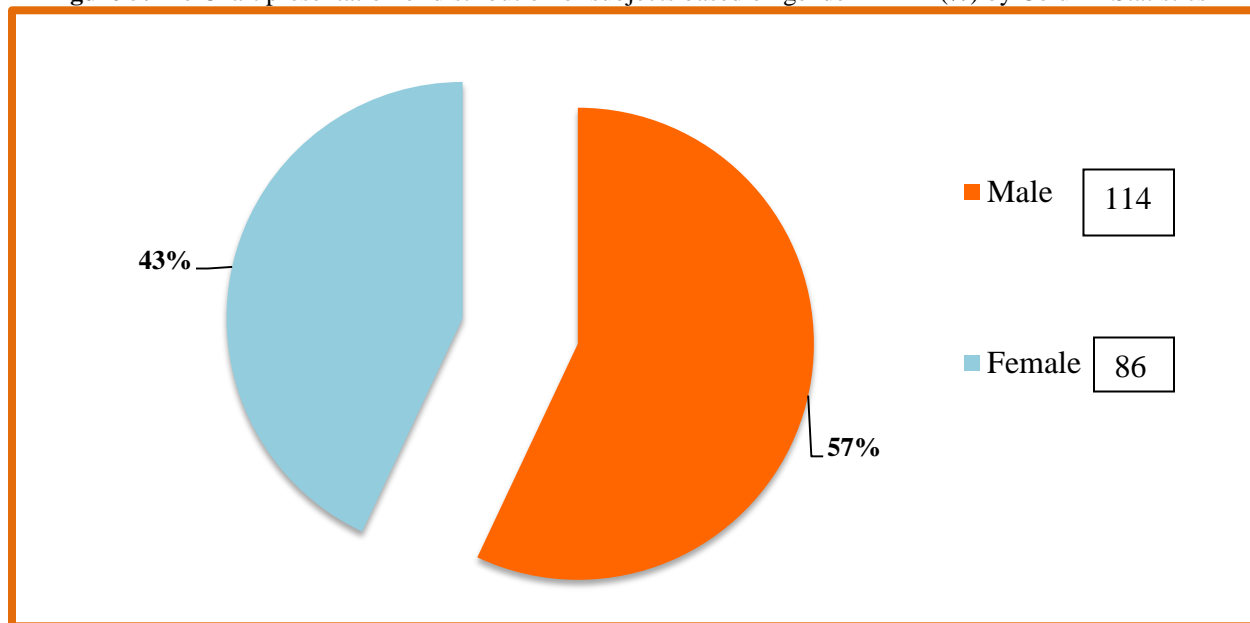
 Among the study population, 114 (57%) individuals were found to be males and 86 (43%) individuals were females.

Table 5:-Distribution of subjects based upon Co-morbidities in AFI (%)

CO-MORBIDITY	PERCENTAGES(%)
CAD	0.5%
DM	3.5%
HTN	19.5%
THYROID	2.5%
HTN,CLD	1%
HTN,DM	6%
HTN,CAD	1%
HTN,DM,CAD	2.5%
HTN,CKD,DM	0.5%
HTN,THYROID	1.5%
HTN,DM,CAD,CKD	0.5%
NO COMORBIDITIES	59.50%
HTN,DM,THYROID	1%
DM,CKD,CLD	0.5%

Figure 6:-Line Chart presentation of distribution of subjects based on co-morbidities in AFI (%)

	CAD	DM	HTN	HTN, CLD	HTN, DM	HTN, DM,CAD	NO	HTN, DM,CAD,CKD	HTN, DM,THYROID	THYROID	HTN, CAD	HTN, CAKD,DM	DM,CKD,CLD	HTN, THYROID
Series1	0.50%	3.50%	19.50	1%	6%	2.50%	59.50	0.50%	1%	2.50%	1%	0.50%	0.50%	1.50%

Table 6:-Statistical Presentation of the data of study population based on co-morbidities by Column Statistics

| CO-MORBIDITIES	FREQUENCY	PERCENTAGES(%)
HTN	39	19.5%
DM	7	3.5%
HTN,DM	12	6%
Combinations	23	11.5%
No Co-morbidities	119	59.5%
Total	200	100%

Table 7:-Statistical Presentation of the data of study population based on gender and co-morbidities in a cross tabular form

Cross tabulations of Gender and Co-morbidities			CO-MORBIDITIES					
			HTN	DM	HTN, DM	NO	Combinations	Total
GENDER	FEMALE	COUNT	23	0	8	45	9	85
		%	27.1%	0.0%	9.4%	52.9%	10.6%	100%
	MALE	COUNT	16	7	4	74	14	115
		%	13.9%	6.1%	3.5%	64.3%	12.2%	100%
TOTAL		COUNT	39	7	12	119	23	200
		%	19.5%	3.5%	6%	59.5%	11.5%	100%

Table 8:-Chi-square tests of the data of study population based on co-morbidities by Column Statistics

CHI-SQUARE TESTS	VALUES	df	Asym p. sig. (2-sided)
Persons chi-square	13.549	4	0.009

Figure 7:-Pie Chart presentation of distribution of subjects based on co-morbidities in AFI (%) by Column Statistics
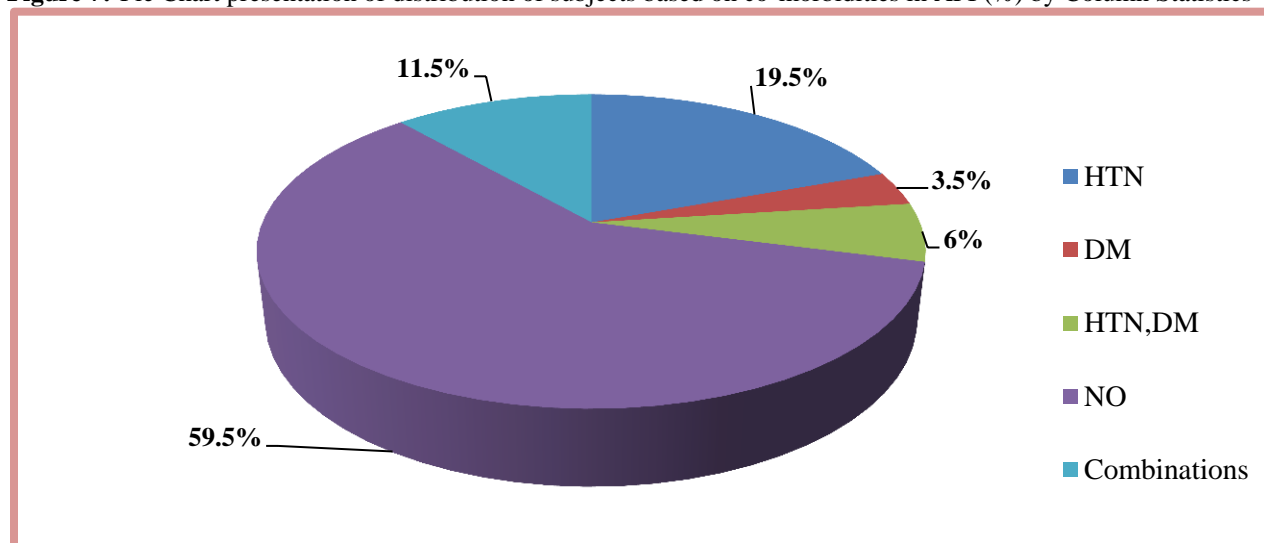
Figure 8:-Column Chart presentation of distribution in Cross Tabular form of subjects based on co-morbidities and gender in AFI (%) by Column Statistics
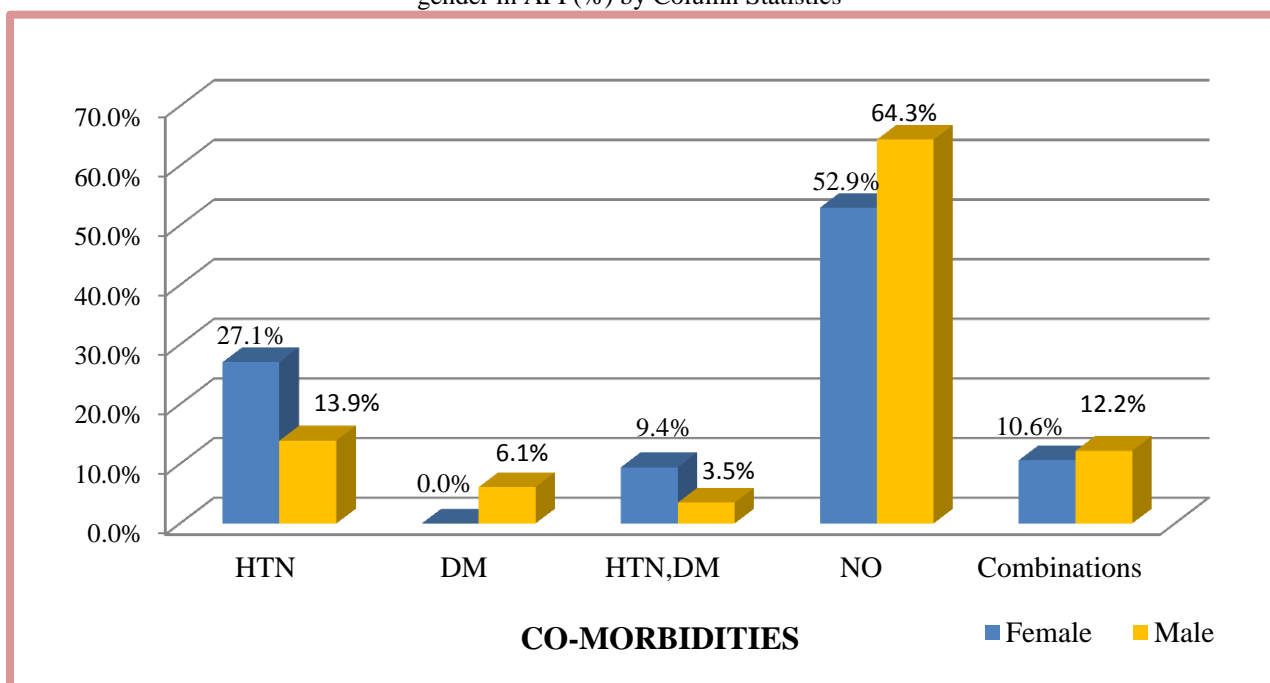
Among the study population, 81 individuals were suffering from AFI with co-morbidities resulted in a percentage of 40.5% and 119 individuals suffering from AFI without Co-morbidities resulted in a percentage of 59.5%.Among the individuals suffering from AFI with co-morbidities, 39(19.5%) individuals had Hypertension,7(3.5%) individuals had Diabetes mellitus type II,12(6%) individuals had both Hypertension and Diabetes mellitus type II and 23(11.5%) individuals had combinations of co-morbidities like Thyroid ,CAD, CLD, etc.

Table 9:-Distribution of subjects based upon Diagnosis in AFI (%)

DIAGNOSIS	PERCENTAGES (%)
Chikungunya	7%
Dengue	24%
Gastroenteritis	6%

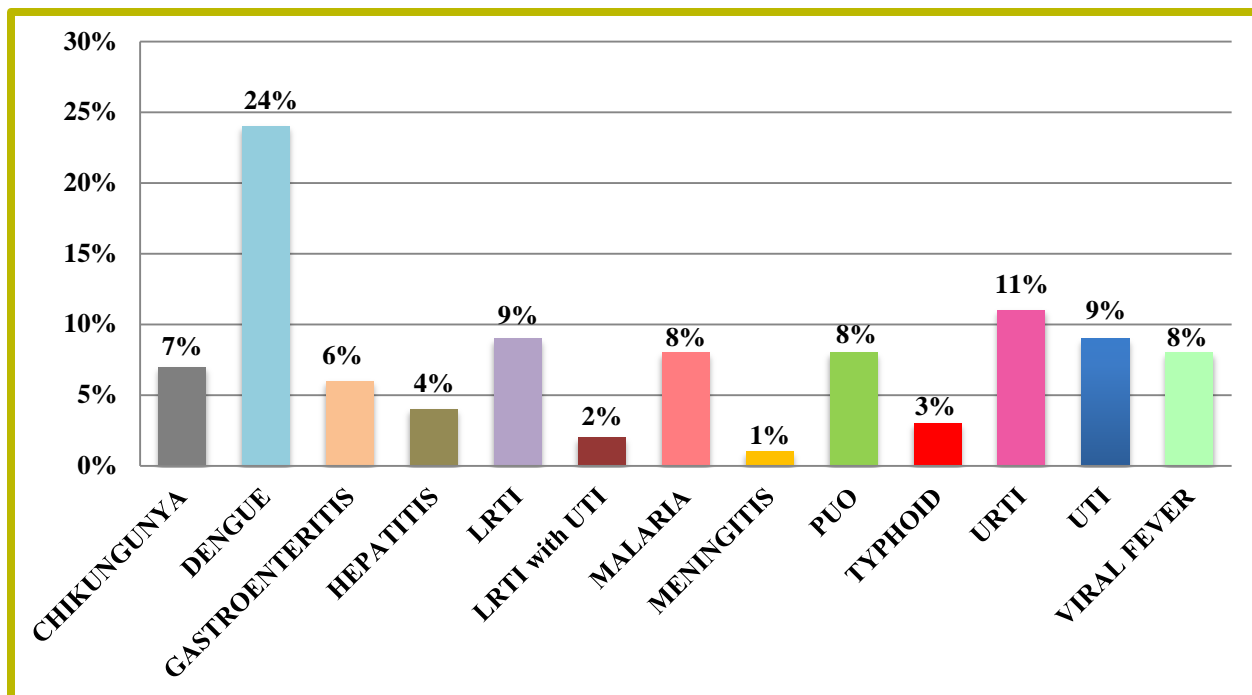|	
Hepatitis	4%
LRTI	9%
LRTI with UTI	2%
Malaria	8%
Meningitis	1%
PUO	8%
Typhoid	3%
URTI	11%
UTI	9%
Viral fever	8%

Figure 9:-Column chart presentation of distribution of subjects based upon Diagnosis in AFI (%)

Among the study population of 200 individuals, the common clinical conditions for which antibiotics were prescribed are Respiratory tract infections (Upper respiratory tract infections 11%, Lower respiratory tract infections 9%), Dengue (24%), Malaria (8%), chikungunya (7%), viral fever (8%), gastroenteritis (6%), hepatitis (4%), Urinary tract infections (9%), pyrexia of unknown origin (8%), meningitis (1%)

Table 10:-Percentage of Antibiotics prescribed in AFI (%)

ANTIBIOTICS	PERCENTAGES(%)
Magnex forte (cefoperazone + sulbactum)	28%
Azee (azithromycin)	15%
Doxy (doxycycline)	6%
Tazact (piperacillin+tazobactum)	6%
Monocef (ceftriaxone sodium)	34%
Fluvir (oseltamavir)	5%
Tazact (piperacillin+tazobactum)	8%
Taxim (cefixme)	3%
Metrogyl (metronidazole)	3%

Fig 10:-Line chart presentation of percentage of antibiotics prescribed in AFI
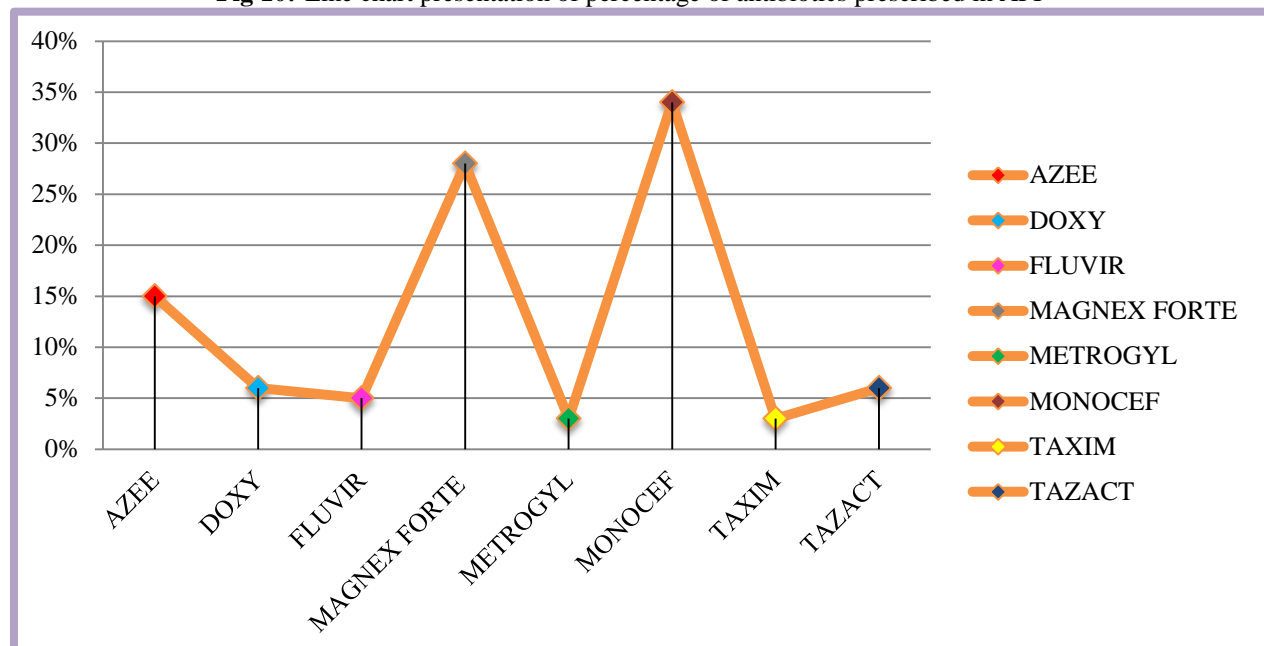
Table 11:-Percentage of antibiotics prescribed in AFI based on no. of antibiotics per prescription

ANTIBIOTIC TREATMENT	PERCENTAGES (%)
Mono therapy	62.5%
Multi therapy	37.5%

Fig 11:-Cone chart presentation of percentage of antibiotics prescribed in AFI
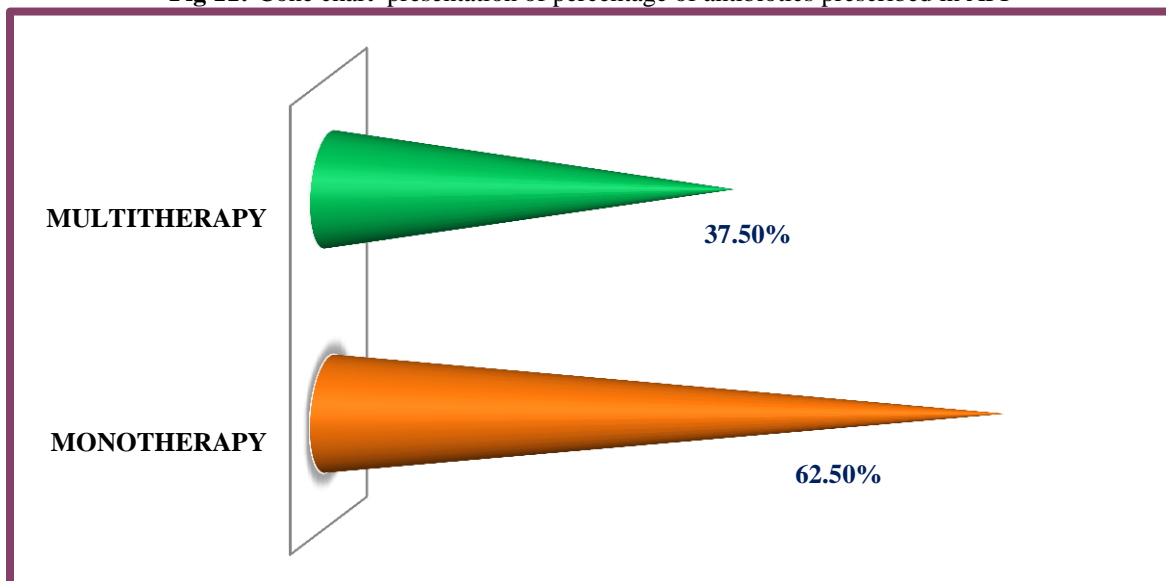
In the study population the most commonly prescribed antibiotics were Magnex forte (cefoperazone + sulbactum) -
28% , Azee (azithromycin)-15%%, Doxy(doxycycline)-6%, Tazact (piperacillin+tazobactum) -6% , Monocef
(ceftriaxone sodium)-34% , Fluvir (oseltamavir)-5% , Taxim(cefixime)-3%, Metrogyl -3% .Among the study
population of 200 individuals 125 (62.5%) of them were treated with antibiotic mono-therapy and 75(37.5%) of
them were given antibiotic multi- therapy.

Table 12:-percentage of antibiotic combinations prescribed in AFI

ANTIBIOTIC COMBINATIONS	PERCENTAGES(%)
MONOCEF+DOXY	3%
MAGNEX FORTE+DOXY	1.5%
MAGNEX FORTE+AZEE+FLUVIR	2.5%
MAGNEX FORTE+AZEE	6%
MONOCEF+AZEE	12%

Fig 12:-Bar presentation of percentage of antibiotic combinations prescribed in AFI
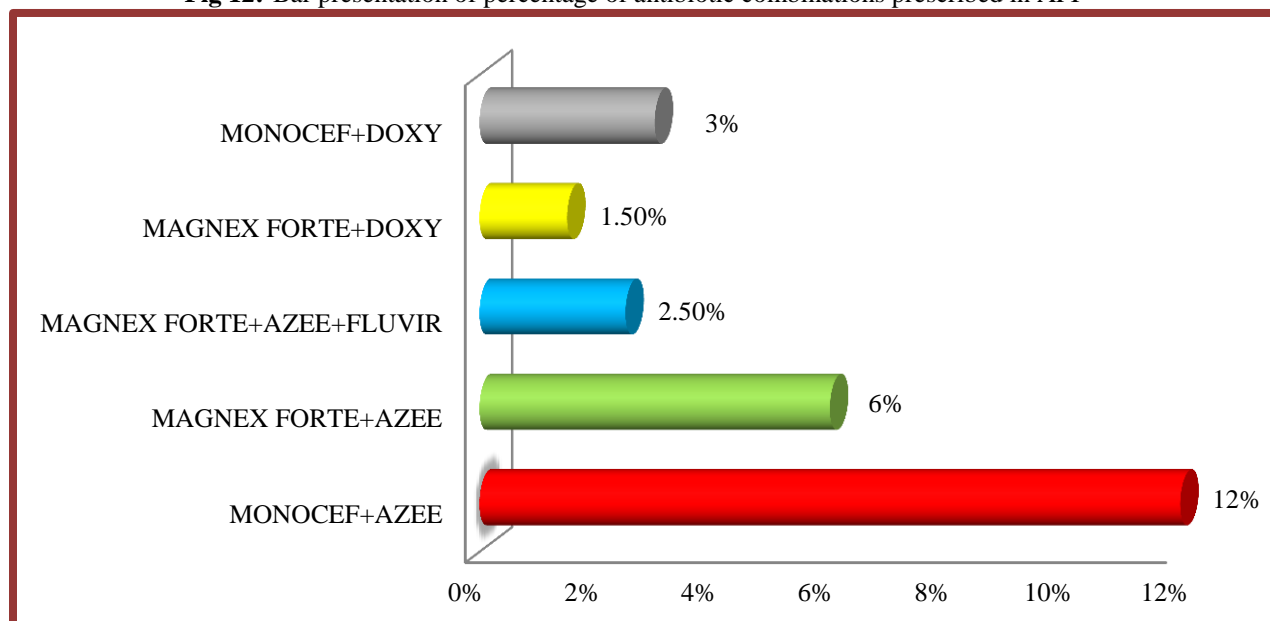
Among the study population of 200 subjects suffering from AFI, most commonly used antibiotic combinations were Monocef and Azee (12%), Magnex Forte and Doxy (1.5%), Monocef and Doxy (3%), Magnex Forte and Azee and Fluvir (2.5%), Magnex Forte and Azee (6%)

Discussion:-
During the study period the patients with age groups between 15-90 years were admitted in the hospital .The age groups between 30-40 years were found to be 34% ,between 31-60 years were found to be 51% and between 61-90 years were found to be 16% .The majority patients in the present study, were between age group 31-60 years whereas in the study conducted previously by Rani R.A.et al, Males and female persons with age group of 20-40 were commonly affected.[56]

Gender wise distribution resulted that majority of patients in the present study, that were admitted in the hospital with the symptoms of acute febrile illness who were prescribed with antibiotics were of male gender that accounted for 57% and females accounted for 43% whereas in the previous study conducted by Ahmed A et al, It was observed that out of 200 patients who were prescribed antibiotics, 110 were male (55%) and 90 were female (45%).[62]The male to female ratio observed in our study is 4:3. According the present and previous studies performed the males accounted for majority of disease burden.

In a therapy wise distribution based on mono and multi antibiotic therapy, In the present study out of 200 prescriptions collected 125(62.5%) prescriptions were of mono antibiotic therapy and 75(37.5%)prescriptions were of multiple antibiotics. In the previous study, A total of 200 prescriptions were studied, out of which 139 (69.5%) prescriptions were mono therapy and 61 (30.5%) prescriptions had multiple antibiotics.[62]

In a discussion based on common cause of acute febrile illness, it was found that Dengue (24%) was the most common cause in the present study. Whereas, in the previous study conducted by Das D. et al, the most common cause of acute febrile illness was found to be scrub typhus and gave a conclusion that Scrub typhus was observed to be the common cause of acute febrile illness during the study period and witnessed the emergence of dengue as an outbreak in this region.[59]

The mean age of patients in the present study was found to be (41.47± 18.155) years out of which 86 (43%) were females and 114 (57%) were males and the average no. of antibiotics per prescription is 1.5 (1-2 drugs) which is similar to the previous study conducted by Meher B.R. et al. But, the study differs in the mean age of the patients which was (47.76 ± 18.49) years of which 454 (54.05%) were male in the previous study.[61]

A study was conducted by Saleh N. et al, which showed that the most-prescribed antibiotics were the cephalosporins (82%) and that almost half of the illnesses for which antibiotics were prescribed were respiratory tract infections (41%).[60] Similarly, the present study showed that the most prescribed antibiotics in acute febrile illness were cephalosporins (49%) but most of them were prescribed for dengue.

According to a previous study conducted by Chandy S.J. et. al, Fluoroquinolones and penicillins were widely used.[63] Whereas, in the present study Cephalosporins were widely used.

In the previous study, Out of 200 patients of febrile illness the common clinical conditions for which antibiotics were prescribed were Respiratory tract infections (Upper Respiratory tract infection 25.5% and Lower Respiratory tract infection 14%), Acute Gastroenteritis (20%), and Urinary tract infection (13.5%) followed by, Pyrexia of Unknown Origin (8.5%), Viral Fever (8%), Malaria (7%), Hepatitis A (1.5%), Meningitis (1%) and Rickettsial infection (1%). The commonly prescribed antibiotics were ceftriaxone (19.37%) and Cefixime (15.93%) followed by Coamoxiclav (12.5%), Azithromycin (11.87%), Doxycycline (10.31%), Ofloxacin and Ornidazole (8.43%), Levofloxacin (6.25%), Ofloxacin (4.68%), Ciprofloxacin (1.87%), Artesunate (3.75%), Artemether and Lumefantrine (4.37%) and Valacyclovir (0.625%).[1] Whereas, in the present study among the study population of 200 individuals, the common clinical conditions for which antibiotics were prescribed are Respiratory tract infections (Upper respiratory tract infections 11%, Lower respiratory tract infections 9%), Dengue (24%) , Malaria (8%) , Chikungunya (7%), Viral fever (8%), Gastroenteritis (6%) , Hepatitis (4%) , Urinary tract infections (9%), Pyrexia of Unknown Origin (8%), Meningitis (1%). In the study population the most commonly prescribed antibiotics were Magnex forte (cefoperazone + sulbactum) - 28% , Azee (azithromycin)-15%%, Doxy(doxycycline)-6%, Tazact(piperacillin+tazobactum) -6% , Monocef(ceftriaxone sodium)-34% , Fluvir (oseltamavir)-5% , Taxim(cefixime)-3%, Metrogyl -3% .

In the previous study Common Co-morbidities included Diabetes Mellitus (10.7 %), essential Hypertension (6.5 %), Ischemic heart disease (1.1 %), and Chronic liver disease.[58] Whereas, in the present study common co-morbidities included Diabetes mellitus (3.5%) and Hypertension (19.5 %).

Conclusion:-
In our present study, we have performed a randomized, prospective and observational study on patient cohorts in Aware Global Hospital to review and analyze different trends of antibiotics used in AFI(acute febrile illness).
1. This study was conducted in 200 patients to review and analyze different trends of antibiotics used in individuals suffering from AFI(acute febrile illness). During the study, the common causes of illness were studied and registered to analyze trends of antibiotics and their combinations that are most commonly used to treat AFI.
2. During our study, it was observed that Dengue and Respiratory tract infections were most commonly the cause of acute febrile illness.
3. Monocef(ceftriaxone) and Magnex forte(cefoperazone and sulbactum) belonging to the class of 3rd generation cephalosporin were most commonly used antibiotics.
4. During the study it was found that majority of the patients were without co-morbidities and were within the age limit of 15-30 years. In the patients who were suffering from AFI with co-morbidities majority of them had Hypertension and Diabetes mellitus type II .
5. During the study it was found that majority of the patients were being treated with antibiotic mono-therapy.
6. Magnex forte and Azee and Monocef and Azee were the most commonly used antibiotic combinations.

7. Further study can be performed by using antibiotic resistance and drug utilization studies as a tool. A study related to adverse effects that will be caused by prolonged and unnecessary use of antibiotics can be done to decrease the risk of toxicity, mortality and improve medication efficacy.

Thus from our study we have concluded that most common diseases for which antibiotics prescribed were dengue and respiratory tract infection. Common antibiotics used were third generation cephalosporins especially ceftriaxone and cefoperazone. Most common antibiotic combinations used were Magnex forte and Azee; Monocef and Azee .

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