"A STUDY OF CLINICO-ETIOLOGICAL PROFILE OF ACUTE FEBRILE ILLNESS IN PAEDIATRIC PATIENTS ADMITTED TO TERTIARY CARE CENTRE IN SOUTH INDIA"

By

Dr. SHRUTI APPAJI

DISSERTATION SUBMITTED TO THE SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

IN

PAEDIATRICS

Under the guidance of

Dr.KRISHNAPPA J

Professor

DEPARTMENT OF PAEDIATRICS,

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR-563101

MAY 2018

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**A STUDY OF CLINICO-ETIOLOGICAL PROFILE OF ACUTE FEBRILE ILLNESS IN PAEDIATRIC PATIENTS ADMITTED TO TERTIARY CARE CENTRE IN SOUTH INDIA "** is a bonafide and genuine research work carried out by me under the guidance of **Dr. KRISHNAPPA J ,** Department of Paediatrics, SDUMC, Kolar.

Date:

Place: Kolar **Dr. SHRUTI APPAJI**

CERTIFICATE BY THE GUIDE

This is to certify that this dissertation entitled **"A STUDY OF CLINICO-ETIOLOGICAL PROFILE OF ACUTE FEBRILE ILLNESS IN PAEDIATRIC PATIENTS ADMITTED TO TERTIARY CARE CENTRE IN SOUTH INDIA"** is a bonafide research work done by **Dr.SHRUTI APPAJI** in partial fulfilment of the requirement for the degree of **M.D IN PAEDIATRICS**, SDUMC, Kolar.

Date:

Place: Kolar

SIGNATURE OF THE GUIDE

Dr.KRISHNAPPA J

Professor

Department Of Paediatrics,

Sri Devaraj Urs Medical College,

Tamaka,Kolar.

CERTIFICATE BY THE CO-GUIDE

This is to certify that this dissertation entitled **"A STUDY OF CLINICO-ETIOLOGICAL PROFILE OF ACUTE FEBRILE ILLNESS IN PAEDIATRIC PATIENTS ADMITTED TO TERTIARY CARE CENTRE IN SOUTH INDIA"** Is a bonafide research work done by **Dr.SHRUTI APPAJI** in partial fulfilment of the requirement for the degree of **M.D IN PAEDIATRICS**, SDUMC, Kolar.

Date:

Place:Kolar

SIGNATURE OF THE CO-GUIDE

Dr. BEENA P M

Professor & HOD ,

Department Of Microbiology,

Sri Devaraj Urs Medical College,

Tamaka, Kolar.

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that this dissertation entitled **"A STUDY OF CLINICO-ETIOLOGICAL PROFILE OF ACUTE FEBRILE ILLNESS IN PAEDIATRIC PATIENTS ADMITTED TO TERTIARY CARE CENTRE IN SOUTH INDIA "** is a bonafide research work done by **Dr.SHRUTI APPAJI** in partial fulfilment of the requirement for the degree of **M.D IN PAEDIATRICS**, SDUMC, Kolar.

Dr. K.N.V. PRASAD M.D
Professor & HOD,
Department of Paediatrics,
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Date:

Place: Kolar

Dr. M.L.HARENDRA KUMAR M.D
Principal,
Sri DevarajUrs Medical College,
Tamaka, Kolar

Date:

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

ETHICS COMMITTEE CERTIFICATE

This is to certify that the Ethics committee of Sri DevarajUrs Medical College & Research Center, Tamaka, Kolar has unanimously approved **Dr.SHRUTI APPAJI** , Post-Graduate student in the subject of DOCTOR OF MEDICINE IN PAEDIATRICS at Sri Devaraj Urs Medical College, Kolar to take up the Dissertation work entitled **"A STUDY OF CLINICO-ETIOLOGICAL PROFILE OF ACUTE FEBRILE ILLNESS IN PAEDIATRIC PATIENTS ADMITTED TO TERTIARY CARE CENTRE IN SOUTH INDIA"** to be submitted to the **SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA,**

Date :

Place :Kolar

Member Secretary

Sri DevarajUrs Medical College,

Kolar–563101

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH

TAMAKA, KOLAR, KARNATAKA

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research, Kolar, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic/research purpose.

Date :

Place :Kolar **Dr. SHRUTI APPAJI**

ACKNOWLEDGEMENT

Academic excellence can be achieved only with the guidance of our teachers. I would take this opportunity to express my sincere thanks to all who have helped in bringing this manuscript into reality.

Words fall short as I express my heartfelt and humble gratitude to my guide to whom I'm ever indebted ***Dr KRISHNAPPA .J,*** *M.D., Professor, Department of Paediatrics, for his guidance and encouragement all along in completing my study. His humble nature, determination, commitment and hunger for knowledge has been my constant source of inspiration. His affection towards students, ever readiness to teach, the painstaking effort to correct errors and his ocean of knowledge has proved the German proverb right " A teacher is better than two books".*

I express my deep sense of gratitude and humble thanks to my teachers of the department of paediatrics, ***Dr.K.N.V.Prasad, Dr.Sudha Reddy.V.R, Dr.BeereGowdaY.C ,Dr.Bhanuchand P, Dr.Murali, Dr Shivaraja*** *for their constant advice, healthy criticism and encouragement throughout the study.*

I am very thankful to ***Dr.Beena P.M*** *my co guide, Professor & HOD department of Microbiology for her constant guidance, help and support throughout the study.*

I am thankful to ***P S Jagnnath*** *sir for helping me in statistical analysis and for his valuable suggestions.*

*I am very much thankful to my colleagues and friends **Dr Rani K.N** and **Dr Kusuma N** and all my fellow postgraduates for being throughout this journey.*

I thank the Almighty and my patients for providing me an opportunity to carry out my study.

*I would like to thank my parents **Dr L Appaji, Dr H.N Sowbhagya**, my brother **Shankara Appaji** , my in laws and all my family members for their constant guidance, love and blessings. Last, but not the least I would like to thank my husband **Dr Vijay C.L** for being the pillar of support and encouragement throughout.*

Dr. SHRUTI APPAJI

ABSTRACT

BACKGROUND: Infections remains a major cause of illness and death among children in the developing countries despite the advances in childhood illness in the recent years. Fever is the most common presenting symptom of paediatric illnesses presenting to health care facilities which account for as much as 20% of paediatric emergency department visits. Morbidity and Mortality can increase to more than 20% in the hospitalised children with febrile illness if not treated appropriately and timely. Acute febrile illness (AFI) is acute onset of fever (≥100.4 degree fahrenheit) lasting for less than 2 weeks and no cause found after clinical history and physical examination. These illness have overlapping signs and symptoms at presentation and lack of specific laboratory diagnosis in the middle and low resource countries, etiological discrimination based on clinical criteria alone is a diagnostic challenge to the treating physician. This, leading to delayed intervention and inappropriate treatment leading to significant morbidity and mortality. There is a need for an improved understanding of etiologies of acute febrile illness based on the clinical, local epidemiological surveillance with supportive diagnostic confirmatory tests which would be critical for developing appropriate management algorithms.

OBJECTIVES:

1) To study the clinical profile of children presenting with AFIs.

2) To identify the various etiologies of AFIs.

MATERIALS AND METHODS: A cross sectional prospective observational hospital based study was conducted over a period January 2016 to May 2017, including children of the age group of 1month to 18years. Children were evaluated with a detailed clinical history (nature and duration of symptoms) and background

characteristics which were noted in a semi-structured Performa was prepared. Based on duration of fever, clinical presentation they were started on empirical treatment and management planned based on the proposed algorithm.

METHOD OF STATISTICAL ANALYSIS: Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Student t test and Chi-square test were used as test of significance for qualitative data. Logistic regression analysis was done on the categorical variables.

RESULTS:

- 750 children with AFI were included in the study group.
- Majority(40.3%) of children with AFI were of school going age group(7 to 13 years) with a median age of presentation was 84months i.e 7 years, with a male preponderance of study population.
- In the study majority (94.9%) of the subjects with AFI presented with fever less than 1 week and the mean duration of fever at admission was 3.8days.
- In our study, 38.3% of the subjects had no confirmed etiological diagnosis of the cases were diagnosed as unclassified fever followed by dengue (28.8%), enteric fever (12.5%), rickettsial fever (10.7%), malaria (8.9%) and leptospirosis (0.8%).
- Vomiting (53.2%) and pain abdomen (47.3%) were the common non specific symptoms among the subjects presenting with AFI and the least common symptom was diarrhoea (2.9%). Hepatomegaly was the common sign accounting to 61.5% of the subjects with AFI.
- Haemogram demonstrated thrombocytopenia in majority of the subjects.
- Malarial cases presented commonly with pain abdomen (76.1%) and chills and rigors(41.8%). 91.1% of the cases had splenomegaly , 50% had associated hepatomegaly with 13% of the cases had clinical pallor on examination. Thrombocytopenia (61.2%)and anaemia (53.7%)were the common findings on the haemogram.

- Subjects with rickettsial fever had pain abdomen(52.5%) and headache(45%) as the presenting complaint. The typical maculopapular rash(91.3%)was the most common sign followed by hepatomegaly(82.5%). On Hemogram leucocytosis (83.3%) and thrombocytopenia(66.6%) were the common findings.
- Enteric fever subjects had vomiting and pain abdomen as the common symptoms and majority of the subjects had Hepatomegaly(93.6%). Leucocytosis (80.9%) was the common association on hemogram.
- Cases with leptospirosis all were associated with pain abdomen and hepatomegaly. 83.3% of the subjects had leucocytosis and thrombocytopenia on the hemogram.
- Cases of dengue, 50% presented with pain abdomen , vomiting and headache. Majority (90.7%) had hepatomegaly and thrombocytopenia(95.8%) and leucopenia (63%) as the common hemogram findings.
- In the study, complications were more commonly associated with dengue.

CONCLUSION: Significant proportion of the children of the cases presenting with AFI have been labelled as unclassified fever in the study, suggests the need for widening the spectrum of laboratory tests, to aid for better management. This in turn would help in bridging the knowledge gap of locally prevalent diseases. Hence, as demonstrated by the study we conclude that, the collective perception of nonspecific symptoms at presentation, clinical signs and laboratory parameters help in syndromic evaluation of the children presenting with AFI which in turn would aid in early initiation of the treatment and management protocol. Thus, would help in decreasing the morbidity and mortality in children due to AFI.

KEY WORDS : Acute Febrile Illness, Children, Syndromic

ABBREVATIONS

AFI	Acute Febrile Illness
^{O}C	degree Celsius
^{O}F	degree Fahrenheit
WHO	World Health Organization
RMSF	Rocky Mountain Spotted Fever
DALY's	Disability- Adjusted Life Years
NVBDCP	National Vector Borne Diseases Control Program
DIC	Disseminated Intravascular Coagulation
RDT	Rapid Diagnostic Test
HRP	Histidine Rich Protein
PLDH	Parasite Lactate Dehydrogenase
SFG	Spotted Fever Group
ESR	Erythrocyte Sedimentation Rate
CRP	C Reactive Protein
ELISA	Enzyme Linked Immuno Sorbent Assay
IFA	Indirect Fluorescent Antibody
ICT	Immuno Chromatographic Test
RICT	Rapid Immunochromatographic Test
IPA	Immuno Peroxidase Assay
DHF	Dengue Hemorrhagic Fever
NS1Ag	Non Structural 1 Antigen

MAT	Microscopic Agglutination Test
CSF	Cerebro Spinal Fluid
AUFI	Acute Undifferentiated Febrile Illness
EDTA	Ethylenediaminetetraacetic acid
Pf	Plasmodium Falciparum
MP	Malarial Parasite
OR	Odds Ratio
CI	Confidence Interval
ARDS	Acute Respiratory Distress Syndrome

TABLE OF CONTENTS

SL.NO	CONTENTS	PAGE
1.	INTRODUCTION	**1**
2.	OBJECTIVES OF THE STUDY	**4**
3.	REVIEW OF LITERATURE	**5**
4.	MATERIALS AND METHODS	**37**
5.	RESULTS	**48**
6.	DISCUSSION	**83**
7.	CONCLUSION	**92**
8	LIMITATIONS OF THE STUDY	**94**
9.	SUMMARY	**95**
10.	BIBLIOGRAPHY	**98**
11.	ANNEXURES	
	• PORFORMA	**105**
	• INFORMATION SHEET	**108**
	• CONSENT FORM	**109**

LIST OF TABLES

TABLE NO	TABLES	PAGE
1	Normal and febrile body temperature ranges	7
2	Socio economic BG Prasad s Scale	43
3	Analysis by Chi –Square Test	46
4	Etiology of Acute Febrile Illness	48
5a	Age wise distribution of study population	49
5b	Comparison of age wise distribution of cases among different subgroups of acute febrile illness	50
6a	Gender wise distribution of study population	51
6b	Comparison of distribution of gender among the different subgroups of acute febrile illness	52
7	Distribution of study population according to religion	53
8	Distribution of study population on the basis of family type	54
9	Distribution of study population according to BG Prasad socio economic classification.	55
10a	Distribution according to duration of fever at presentation	56
10b	Comparison of duration of fever among different subgroups of acute febrile illness	57
11	Comparison of clinical symptoms of various AFI	58
12	Correlation of clinical signs with various AFI cases	61

13	Laboratory characteristics in various AFI cases	**64**
14	Etiological and laboratory correlation of AFI	**66**
15	Analysis of significant parameters in Malarial illness	**68**
16	Analysis of significant parameters in Rickettsial fever	**71**
17	Analysis of significant parameters in Enteric fever	**74**
18	Analysis of significant parameters in Dengue fever	**77**
19	Analysis of significant parameters in Unclassified AFI	**80**

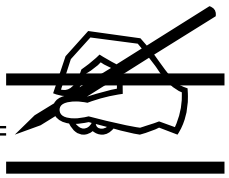
LIST OF FIGURES

FIGURE NO	FIGURE	PAGE NO
1	Pathophysiology of fever	**6**
2	Patterns of fever	**8**
3	Flowchart of children with AFI	**42**
4	Algorithm depicting the methodology of the study	**45**
5	Pie diagram showing etiological distribution of AFI cases	**48**
6a	Pie diagram showing distribution of AFI cases according to age	**49**
6b	Bar diagram showing association of mean age of presentation and AFI	**50**
7a	Pie diagram showing distribution of AFI cases according to gender	**51**
7b	Bar diagram showing distribution of gender and AFI cases	**52**
8	Pie diagram showing distribution of AFI cases according to religion	**53**
9	Pie diagram showing distribution of AFI cases according to family type	**54**
10	Pie diagram showing distribution of AFI cases according to socio economic status	**55**
11a	Pie diagram showing distribution of AFI cases according to duration of fever	**56**

11b	Bar diagram showing distribution of AFI cases according to duration of fever and etiology	**57**
12a	Bar diagram showing association of symptoms with AFI cases	**59**
12b	Bar diagram showing association of symptoms with AFI cases	**60**
13a	Bar diagram showing association of signs with AFI cases	**62**
13b	Bar diagram showing association of signs with AFI cases	**63**
13c	Bar diagram showing association of signs with AFI cases	**63**
14	Bar diagram showing association of laboratory parameters with AFI cases	**65**
15	Bar diagram showing laboratory confirmation of various AFI cases	**67**
16a	Bar diagram showing comparison of signs and symptoms of malaria and other AFI cases	**69**
16b	Bar diagram showing comparison of signs and symptoms of malaria and other AFI cases	**70**
16c	Bar diagram showing comparison of laboratory parameters of malaria with other AFI cases	**70**
17a	Bar diagram showing comparison of signs and symptoms of rickettsial fever with other AFI cases	**72**
17b	Bar diagram showing comparison of signs and symptoms of rickettsial fever with other AFI cases	**73**

17c	Bar diagram showing comparison of laboratory parameters of rickettsial fever with other AFI cases	**73**
18a	Bar diagram showing comparison of signs and symptoms of enteric fever with other AFI cases	**75**
18b	Bar diagram showing comparison of signs and symptoms of enteric fever with other AFI cases	**76**
18c	Bar diagram showing comparison of laboratory parameters of enteric fever with other AFI cases	**76**
19a	Bar diagram showing comparison of signs and symptoms of dengue fever with other AFI cases	**78**
19b	Bar diagram showing comparison of signs and symptoms of dengue fever with other AFI cases	**79**
19c	Bar diagram showing comparison of laboratory parameters of dengue fever with other AFI cases	**79**
20a	Bar diagram showing comparison of signs and symptoms of unclassified fever with other AFI cases	**81**
20b	Bar diagram showing comparison of signs and symptoms of unclassified fever with other AFI cases	**82**
20c	Bar diagram showing comparison of laboratory parameters of unclassified fever with other AFI cases	**82**

INTRODUCTION



INTRODUCTION

Infections remain a major cause of illness and death among children in the developing countries despite the advances in the prevention of childhood infections, particularly through immunization[1]. Fever is the most common presenting symptom of paediatric illnesses presenting to health care facilities in the developing world and is the leading reason in the tropics for people to seek the health care facilities[2] . Children with fever account for as much as 20% of paediatric emergency department visits. Morbidity and Mortality can increase to more than 20% in the hospitalised children with febrile illnesses if not treated appropriately and timely[3].

Acute febrile illness (AFI) is acute onset of fever (≥100.4 degree fahrenheit) lasting for less than 2 weeks and no cause found after clinical history and physical examination[4,5].

Acute febrile illness in children signifies systemic inflammation, typically can be in response to a viral, bacterial, parasitic infections or less commonly, to a non infectious etiology. These cases can range from mild conditions to life threatening bacterial and viral illness. Infectious causes of AFI which are of major concern in South Asia include Malaria, Dengue, Typhoid/Paratyphoid, Chikungunya, Leptospirosis and Scrub Typhus[6]. It has been analysed that among the overall burden of deaths related to infectious diseases in South Asia, around 63% are in children aged less than 5 years[7]. It has been noted that these infectious diseases present with nonspecific symptoms such as fever, headache, malaise, vomiting, pain abdomen etc and systemic signs which are characteristic of the individual diseases are usually seen later in the course of the illness, by then significant morbidity would have set in. In the western world AFI is mainly due to viral illness, but in developing countries including India , it can be due to potentially treatable life threatening illnesses such as

malaria, leptospirosis, Hanta virus infection and Japanese encephalitis[8]. Due to overlapping of the signs and symptoms of acute febrile illnesses at presentation and lack of specific laboratory diagnosis in the middle and low resource countries, etiological discrimination based on clinical criteria alone is a diagnostic challenge to the treating physician[6,9]. This leads to unnecessary investigations in turn leading to wastage of resources. As the treatment and management of acute febrile illness needs differential diagnosis of the etiological agent, this difficulty contributes to missed diagnosis, delayed intervention and inappropriate treatment leading to significant morbidity and mortality[10].

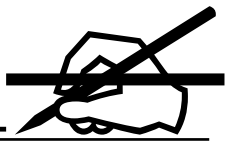
The global burden of disease due to diarrhoea and pneumonia in children has been estimated at the syndromic level by a comprehensive, standardized and high quality multi-centre etiological research. There is lack of such an approach for fever without localizing features in children, even though there is evidence of significant burden of infectious diseases. Illness and case fatality due to some febrile diseases (e.g., dengue, malaria) are estimated, while others have been neglected (e.g., leptospirosis, Q fever)[3]. Research on the etiological agent of acute febrile illness faces a number of challenges, especially in children in relation to atypical clinical presentations, unpredictable progression of the course of illnesses, collection of blood samples for evaluation and various others. The conventional diagnostic methods has wide range of complexities that is, they remain available in the province of reference laboratories. Reference diagnostic methods for several key infections during the acute phase for some causes of fever have shortcomings of practicality, sensitivity, specificity or combinations of these. The diagnostic tests available have great limitations in relation to cost in middle and low income countries. Due to the gap in the knowledge of locally prevalent common etiologies of AFI adding onto the

nonspecific signs and symptoms of the infectious diseases and lack of accurate diagnostic tests there is surge in irrational use of antimalarial and antibacterial agents contributing to the increase in the development of antimalarial and antimicrobial resistance [6,7].

Historically, malaria has been reported as a leading cause of childhood AFI, but over the past decade it has been observed that there has been decline in the incidence and mortality due to malaria dramatically. This decline is due to the intense control programs thus, increasing the public awareness. At the same time, there has been increase in other emerging infections replacing malaria as a causes of AFI is noted[11]. There is a need for active surveillance of the various causes of AFI, as the etiological spectrum of the infectious diseases causing acute febrile illness varies with geographical area, patients age, seasonal patterns adding onto the diagnostic and therapeutic challenge to the treating clinicians in resource limited settings thus, delaying appropriate treatment[9].

There is a need for an improved understanding of aetiologies of acute febrile illness based on the clinical, local epidemiological surveillance with supportive diagnostic confirmatory tests which would be critical for developing appropriate management algorithms. In our study, we aim to correlate clinic etiological profile of acute febrile illness in children presenting to our hospital and to delineate common infectious etiological agents prevalent in our region.

OBJECTIVES



OBJECTIVES

1) To study the clinical profile of children presenting with AFIs.

2) To identify the various etiologies of AFIs.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Fever

Fever is one of the most common symptom in children presenting to health care facility in developing world. **Fever** is defined as a rectal temperature ≥38°C (100.4°F)[12].

Pathogenesis of Fever

Body temperature is regulated by thermosensitive neurons located in the preoptic or anterior hypothalamus that respond to changes in blood temperature as well as by cold and warm receptors located in skin and muscles. Thermoregulatory responses include redirecting blood to or from cutaneous vascular beds, increased or decreased sweating, regulation of extracellular fluid volume via arginine vasopressin, and behavioural responses.

Three different mechanisms produce fever:

- Pyrogens
- Heat production exceeding the loss and
- Defective heat loss.

Pyrogens can be exogenous which include mainly infectious pathogens and drugs. Endogenous pyrogens that are produced from macrophages stimulated by microbes, microbial toxins, or other products of microbes or by hypothalamus stimulated by the endotoxin that directly affect thermoregulation[12].

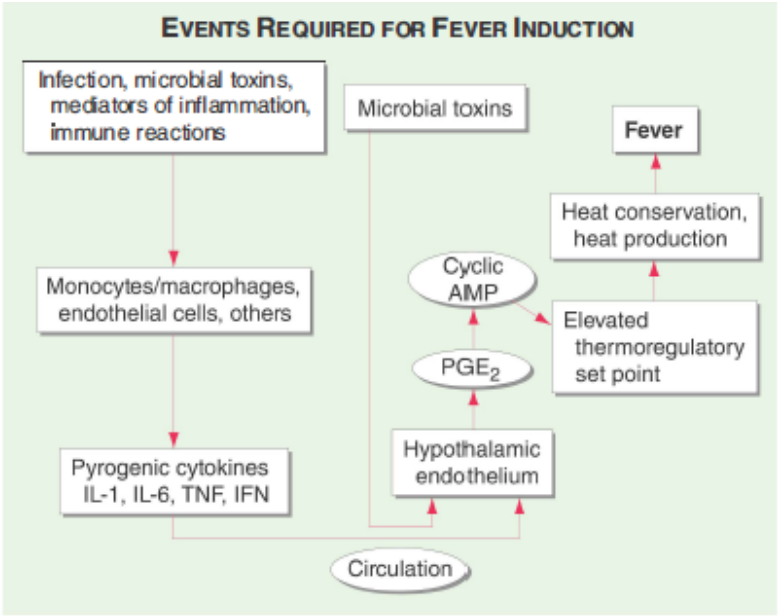


Figure 1: Pathophysiology Of Fever[13]

Etiology

The causes of fever can be organized into 4 main categories[12]:

- Infectious
- Inflammatory
- Neoplastic
- Miscellaneous.

Self-limited viral infections and uncomplicated bacterial infections are the most common causes of acute fever in children.

Clinical significance:

The clinical usefulness of fever patterns is dubious, although there are some notable exceptions. The **onset, duration, character and pattern** of the fever can provide clues to the underlying etiology. Fever has been classified based on:

1. Height of body temperature[14], classified into

- low grade
- moderate grade
- high grade
- hyperpyrexia

Body temperature	°C (degree Celsius)	°F(Fahrenheit)
Normal	37–38	98.6–100.4
Mild/low grade fever	38.1–39	100.5–102.2
Moderate grade fever	39.1–40	102.2–104.0
High grade fever	40.1–41.1	104.1–106.0
Hyperpyrexia	>41.1	>106.0

Table 1. Normal and febrile body temperature ranges (rectal temperatures).

The height of body temperature may have some diagnostic and prognostic implications. Studies have attributed high grade fevers in infants/ children to serious bacterial infections and at equally high risk for viral illness[15]

2. Based on the pattern of fever[16] : there are five types

i. Intermittent: Body temperature is elevated but fall to normal each day.

Types of intermittent fever are Quotidian: periodicity every 24hrs (eg. Pl falciparum malaria) Tertian: periodicity every 48hrs (eg. Pl vivax and ovale malaria) Quartan: periodicity every 72hrs (eg. Pl malariae malaria)

ii. Remittent: Body temperature remains above the baseline and fluctuation is more than 2^0C in a day. Is seen in infective endocarditis.

iii. Continuous or sustained: Body temperature never touches the baseline

and daily fluctuations are less than 1^{o} C. It is characteristic of typhoid fever or typhus, although commonly seen in bacterial endocarditis, tuberculosis, fungal disease, urinary tract infections and bacterial pneumonia .

iv. Hectic: Body temperature remains above the baseline and fluctuation is more than 1.5^{0} C in a day. Is seen in serious bacterial infections.

v. Relapsing : A variant of the intermittent pattern, fever spikes are separated by days or weeks of intervening normal temperature .

Although the classical fever patterns are not diagnostic, at times fever curves can be suggestive and aid clinicians in diagnosis. Fever curves have limited diagnostic usefulness in hospital-acquired infections. In community-acquired infections, characteristic fever curves are more important, but are a function of geographic location.

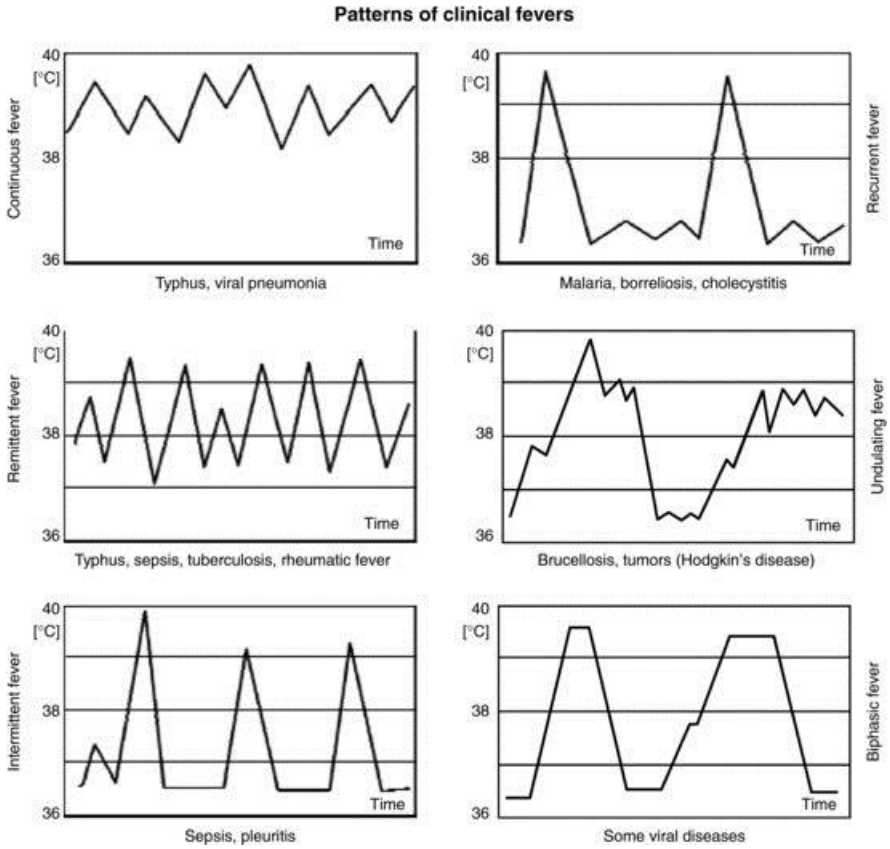


Figure 2 : Patterns Of Fever

3. Duration of fever [16]

For diagnostic purposes, fevers may be viewed as acute, subacute, or chronic, and with or without localizing signs. Febrile patients with localizing signs present few difficulties in diagnosis. Diagnosing patients without localizing signs, however, is a diagnostic challenge.

4. Defervescence of fever [12,16]

Viral infections typically are associated with a slow decline of fever over a week, whereas bacterial infections are often associated with a prompt resolution of fever after effective antimicrobial treatment is employed.

Acute febrile illness

Acute febrile illness is characterised by[17]

1. Rectal temperature more than 101^0 F
2. Fever of less than two weeks duration
3. Absence of abnormalities on physical examination
4. Normal urine analysis

Other terms used to describe AFI are undifferentiated febrile illness, fever without localizing signs, minor illness, febrile illness of short duration and three day fever[4].

Usually fever are approached in a diagnostic perspective as presenting with or without localizing signs. The common Infectious diseases presenting as acute febrile illnesses without localizing signs, include typhoid fever, malaria, ehrlichiosis, roseola infantum, typhoidal tularemia, typhoidal, Epstein-Barr virus (EBV), mononucleosis, and miliary tuberculosis, are the most difficult diagnostic problem. The pre eruptive stages of Rocky Mountain spotted fever (RMSF), viral hepatitis, dengue and the

childhood exanthems are further examples. If no localizing signs are present, analysis of temperature and characteristic fever patterns, clinical course are of clinical importance, and may provide the only clue to guide further testing or suggest the diagnosis[16]

AFIs without localising sign are a significant cause of morbidity, mortality and economic burden to developing tropical nations due to the delay in their diagnosis contributed by the lack of availability of the diagnostic tests at the point of care thus, delaying the initiation of the treatment. Even though guidelines are available for the management of acute febrile illness by WHO, but there is a need for knowledge of locally prevalent diseases to rationalize the management in that field due to the variations in the epidemiological pattern and presentation of the AFI's [2,10].

There are limited studies on causative agents of AFIs in children in literature. Due to the lack of epidemiological data and the prevalence of infectious diseases specific to the region, it is a diagnostic dilemma for the treating physician due to the overlapping signs and symptoms of the diseases. WHO and other guidelines available for the management of the infectious diseases such as dengue, malaria, rickettsial, leptospirosis, typhoid and various others. The epidemiology of the common infectious diseases presenting as AFI's in children to our hospital are discussed.

Burden of disease

In the era of epidemiological transition with advent of vaccinations infectious diseases still remain a major burden of disease in low and middle income countries. India being one of the developing countries suffers disproportionately from the burden of

infectious diseases. India the second most populous country in the world is in the midst of a triple burden of diseases; the unfinished agenda of communicable diseases, non-communicable diseases linked with lifestyle changes, and emergence of new pathogens and overstretched health infrastructure[18,19].

The emerging infectious diseases account for 26 per cent of annual deaths worldwide. Nearly 30 per cent of 1.49 billion disability-adjusted life years (DALYs) are lost every year to diseases of infectious origin. The burden of morbidity and mortality associated with infectious diseases falls most heavily on people in low and middle income countries especially on infants and children (about three million children die each year from malaria and diarrhoeal diseases alone)[18,20].

It has been noted on literature survey 1,407 species of human pathogens, with 177 (13%) species regarded as emerging or re-emerging. Distribution of pathogens by groups shows that 37 per cent of emerging and re-emerging pathogens are viruses and prions followed by protozoa (25%). Viruses are the major pathogens among the emerging and re-emerging infectious diseases. Examples: dengue, yellow fever, ebola haemorrhagic viruses. Antimicrobial resistance to the infectious pathogens has been of raising concern. Example: vancomycin resistance staphylococcus aureus. This add on to failure of response to the standard treatment, thus leading to prolonged illness and increased risk of death[19].

Communicable diseases account for nearly half of India's disease burden. Many infections are associated with poor sanitation, contaminated food, inadequate personal hygiene, or access to safe water and lack of basic health services- conditions common to large parts of India. Favourable environmental, demographic and socio-economic factors further put India at a risk of epidemics of emerging infections[20].

MALARIA

Malaria is one of the major public health problems of the country. Around 1.5 million confirmed cases are reported annually by the National Vector Borne Disease Control Programme (NVBDCP), of which 40–50% are due to Plasmodium falciparum. Malaria is curable if effective treatment is started early. Delay in treatment may lead to serious consequences including death. The transmission of malaria, emergence & spread of drug resistance represents a considerable challenge for its control[21, 22].

Epidemiology

Malaria is the principal areas of transmission are Africa, Asia, and South America. P falciparum and P malariae are found in most areas. P vivax is predominant in India, Bangladesh, Sri Lanka, Pakistan and Central America. The magnitude of the problem is enhanced by drug resistance to standard antimalarial drugs particularly to chloroquine[22].

Etiology

Malaria is caused by intracellular *Plasmodium* protozoa transmitted to humans by female *Anopheles* mosquitoes. Prior to 2004, only 4 species of *Plasmodium* were known to cause malaria in humans: *P. falciparum,P. malariae, P. ovale*, and *P. vivax*. In 2004 *P. knowlesi* (a primate malaria species) was also shown to cause human malaria. Malaria also can be transmitted through blood transfusion, use of contaminated needles, and transplacentally from a mother to the fetus[23, 24].

Pathogenesis

Plasmodium species exist in a variety of forms and have a complex life cycle that enables them to survive in different cellular environments in the human host (asexual phase) and the mosquito (sexual phase)[22, 24].

In humans there are 2 phases:

- Exoerythrocytic phase : in hepatic cells
- Erythrocytic phase: in red blood cells.

The **exoerythrocytic phase** begins with inoculation of sporozoites into the bloodstream by a female *Anopheles* mosquito. The sporozoites enter the hepatocytes of the liver, where they develop and multiply asexually as a schizont. After 1-2 weeks, the hepatocytes rupture and release thousands of merozoites into the circulation. The schizots of *P. ovale*, and *P. vivax* remain dormant in the liver cell for weeks, months, or as long as 5 years before releasing merozoites and causing relapse of infection.

The **erythrocytic phase** of *Plasmodium* asexual development begins when the merozoites from the liver penetrate erythrocytes. Once inside the erythrocyte, the parasite transforms into the ring form**,** which then enlarges to become a trophozoite. The trophozoite multiplies to produce a number of small erythrocytic merozoites that are released into the bloodstream when the erythrocyte membrane ruptures, which is associated with fever. Over time, some of the merozoites develop into male and female gametocytes that complete the *Plasmodium* life cycle when they are ingested during a blood meal by the female anophelus mosquito.

The male and female gametocytes fuse to form a **zygote** in the stomach cavity of the mosquito. After a series of further transformations, sporozoites enter the salivary gland of the mosquito and are inoculated into a new host with the next blood meal.

Four important pathologic processes have been identified in patients with malaria: fever, anaemia, immune-pathologic events and tissue anoxia[23].

Clinical features:

The usual incubation periods are 9-14 days for *P. falciparum*, 12-17 days for *P. vivax*, 16-18 days for *P. ovale,* and 18-40 days for *P. malariae* [24].

The classic presentation of malaria is **paroxysms** of fever alternating with periods of fatigue but otherwise relative wellness. Febrile paroxysms are characterized by high fever, sweats, and headache, as well as myalgia, back pain, abdominal pain, nausea, vomiting, diarrhoea, pallor and jaundice.

Physical signs may include splenomegaly (common), hepatomegaly, and pallor as a consequence of anaemia.

Complications / severe malaria: Cerebral malaria, severe anaemia, hypoglycaemia, algid malaria, black water fever, pulmonary edema, jaundice, hemoglobinuria, spontaneous bleeding/ DIC[22, 23].

Diagnosis

Laboratory findings:

- Anaemia
- Thrombocytopenia,
- Normal or low leukocyte count.
- Erythrocyte sedimentation rate is often elevated.

Microscopy of stained thick and thin blood smears remains the **gold standard** for confirmation of diagnosis of malaria. It is highly sensitive, helps to detect malarial parasites at low densities and to quantify the parasite load. It is also possible to distinguish the various species of malaria parasite and their different stages.

Rapid diagnostic tests (RDT's) are immuno chromatographic tests to detect plasmodium specific antigens in the blood samples. Tests utilise monoclonal antibodies that are targeted towards the specific antigens of the parasite. Targeted antigens which are presently used in the RDT's are :

- Histidine rich protein II (HRP II) : these are secreted by the asexual forms and the gametocytes of the P. falciparum. These are more specific RDT's
- Parasite lactate dehydrogenase(p LDH): a metabolic enzyme produced by all species of plasmodium in both sexual and asexual forms.
- Plasmodium aldolase : a new antigen detected . An enzyme of the glycolytic pathway secreted by all the species of the plasmodium.

It is noted that RDT's are fairly sensitive in areas of high parasite density and in low parasite densities areas the sensitivity is low often yielding false negative results. False positive results also develop when gametocytes when gametocytes are present and the asexual forms are eradicated by the therapy[23].

RICKETTSIAL DISEASES

Rickettsia are obligate intracellular proteobacteria spread by eukaryotic vectors like ticks, mites, fleas and lice[25].

Epidemiology:

Epidemiology of these infections is based on geographic and temporal distribution of their vectors. SFG is reported from Maharashtra, Karnataka and Tamil Nadu while

scrub typhus is reported from almost all states and union territories of India. Rickettsial diseases can occur throughout the year, but more commonly seen from May to February. Rickettsial diseases occur at all ages including neonates [26,27].

Etiology :

Rickettsia are divided into four biogroups namely

- Spotted fever group (SFG): Rocky Mountain spotted fever, Rickettsial pox, Indian Tick Typhus or Mediterranean spotted fever or Boutonneuse fever
- Typhus group: Epidemic louse borne typhus, Brill–Zinsser disease and Endemic/Murine flea Borne typhus;
- Scrub typhus group
- Miscellaneous group: Ehrlichiosis, Anaplasmosis, TIBOLA and DEBONEL

Rickettsia conorii causing Indian tick typhus and *Orientia tsutsugamushi* causing Scrub typhus are common etiological agents in India[25,27].

Pathogenesis : the direct bite from the tick/ contact with infested feaces cause the rickettsial organisms to attach the endothelium. Diffuse endothelial infection (infective vasculitis) leading to microvascular leakage and vascular lumen obstruction[26].

Clinical features :

Fever associated with myalgia, headache and arthralgia are the common presenting symptoms.

Rash: Though considered as a hallmark of the disease is seen in only 30-40% of the cases. Mainly seen with SFG which appears on day 2 to 5 of illness . Typically

maculopapular non blanching involving palms and soles. In severe cases they can be purpura fulminans.

Eschar: Pathognomic of the disease, is a crusty necrotic lesion with or without surrounding erythematous halo, which suggest the location of the vector bite. It is painless, nonpruritic and about 1 cm in diameter. More commonly seen with the scrub typhus group.

*Hepatosplenomegaly, lymphadenopathy, Edema, Conjunctival injection***.**

Systemic presentations: Aseptic meningitis or meningo-encephalitis. pneumonia, gastroenteritis, hepatic manifestations and acute renal failure are another presentations of rickettsial diseases.

Complications: Disseminated intravascular coagulation, Acute Respiratory Distress syndrome, Hemophagocytic Lymphohistiocytosis, purpura fulminans, gangrene and myocarditis[25,26,27].

Diagnosis[27, 28] :

Laboratory features that support the diagnosis

• Normal to low total leukocyte count with a shift to left in early stages and leukocytosis

• Thrombocytopenia

• Raised ESR and CRP

• Hyponatremia

• Hypoalbuminemia and

• Elevated hepatic transaminases

Serology: These tests are usually positive after first week of illness. These are bio group-specific and not species specific. Four-fold rise in titres in two serum samples, 2-4 weeks apart, favours diagnosis.

- Weil Felix test is used if other tests are not available. It has lower sensitivity but better specificity. A single titre above 1:80 may indicate possibility of infection, but at a high cut-off titre (1:320) has a better positive predictive value and specificity.
- IgM ELISA has high sensitivity and specificity and hence preferred.
- IFA is gold standard test but has disadvantages of being expensive, not easily available and needing a lot of expertise and sophisticated instruments.
- *RICT*: Rapid immunochromatographic test is not recommended at present for diagnosis.
- PCR: Specificity of PCR is almost 100%, while sensitivity is 22.5%- 36.1% (for nested PCR) and 45%-82% (for Realtime PCR)
- *Isolation* of organisms by cell culture and laboratory animals and immunostaining of skin rash or eschar biopsy are not useful for clinical purpose.

In countries like India, where PCR and IFA are not commonly available, properly performed paired serological tests like ELISA have high positive predictive value[28].

Scoring system

The scoring system proposed by Rathi, *et al*. for diagnosis of SFG rickettsioses using clinical, laboratory, and epidemiological features with a diagnostic cut off score of 14 has high sensitivity (96.1%) and specificity (98.8%)[27].

Rickettsial diseases pose multiple problems to clinicians. Treatment of these infections is inexpensive and highly effective in early course of the disease but it is extremely difficult to make a diagnosis at this stage due to low index of suspicion, non-specificity of signs and symptoms and absence of low cost, rapid and widely available diagnostic test hence there are proposed case definitions for early initiation of treatment[29].

Case Definitions[27]

Suspected case: A patient having compatible clinical scenario, suggestive epidemiological features and absence of definite alternative diagnosis.

Probable case: Suspected case having either eschar, or having rapid (<48 hours) defervescence with anti-rickettsial therapy, or having suggestive laboratory features, or having Weil-Felix test positive with titre of 1:80 or more in OX2, OX19 or OXK or positive IgM ELISA for rickettsia (optical density >0.5).

Confirmed case: Suspected case having rickettsial DNA detected in whole blood or tissue samples, or fourfold rise in antibody titres on acute and convalescent sera detected by immunofluorescence assay (IFA) or immunoperoxidase assay (IPA).

ENTERIC FEVER

Typhoid fever is a global health problem. Its real impact is difficult to estimate because the clinical picture is confused with those of many other febrile infections. Additionally, the disease is underestimated because there are no bacteriology laboratories in most areas of developing countries. The term enteric fever includes both typhoid and paratyphoid fever. Nearly 90% of the cases are due to typhoid while 10% are due to paratyphoid infections[30, 31].

Epidemiology :

There are more than 27 million cases worldwide each year, culminating in an estimated 217,000 deaths to typhoid fever.In areas of endemicity and in large outbreaks, most cases occur in persons aged between 3 and 19 years (WHO). The burden of enteric fever has been increased due to the development of antimicrobial resistance[30].

Humans are the only natural host and reservoir. The infection is transmitted by ingestion of food or water contaminated with faeces [32].

Etiology :

Typhoid fever is caused by Salmonella species, a Gram-negative bacterium belonging to the family Enterobacteriaceae. Among the various serovars salmonella typhi and paratyphi are the common organisms causing infection[31.32].

Pathogenesis :

Bacteria following ingestion infects the reticulo endothelial system and then enter the blood stream to infect the various organs of the body (liver, spleen, bone, heart, CNS) leading to localised infection and suppuration. Salmonella pathogenicity islands are an important virulence factor[33].

Clinical features [32]:

Incubation Period : 1 to 2 weeks (3-60 days).

It varies from mild illness associated with fever with chills, (classically described as step ladder fever) and non specific signs such as malaise, headache, abdominal discomfort, coated tongue and slight dry cough.

Acute Enteritis: The most common clinical presentation of salmonellosis. There is an abrupt onset of nausea, vomiting, and crampy abdominal pain in the peri-umbilical area and right lower quadrant, followed by mild to severe watery diarrhoea containing blood and mucus.

Rose spots are the faint salmon coloured macules on trunk and abdomen seen during 2nd week of illness seen in only 25% of the cases.

In the 3rd week of illness **hepatospleenomegaly**, intestinal bleeding and perforation seen in 3% of the cases.

Complications : Seen in 10-15% of the patients seen commonly in the 2nd and 3rd week of the illness. Includes intestinal perforation, hepatic dysfunction, encephalopathy, renal damage.

Diagnosis[31,32,33]:

Haematological tests: Leucocytosis with shift to left is a common feature noted in children. Thrombocytopenia indicates severe infection

Cultures :

Blood culture: Is the definitive diagnosis of typhoid fever. S. typhi is isolated from blood, bone marrow or a specific anatomical lesion. Positive cultures are seen in 40-50% of the patients.

Bone marrow asrpiration culture: has a very high yield with sensitivity and specificity of 80 and 95% respectively.

Stool culture : 30% of the cases are positive in second and third week of the illness.

Skin snip cultures from rose spots: has a high yield and positivity in 63% of the cases.

Serological tests: Widal test has limited utility in endemic areas due to high false positive and false negative errors.

Typhidot/ enzyme immunoassay test: is based on the detection of both IgM and IgG against the 50KD outer membrane protein antigen of *S typhi.*

Other newer diagnostic tests include detection of monoclonal antibodies, S.typhi specific antigen and PCR

DENGUE

Dengue has been identified as one of the 17 neglected tropical diseases by WHO as mentioned in their first report on neglected tropical diseases (2010). Although the full global burden of the disease is still uncertain, the patterns are alarming for both human health and the economy. Dengue is the most rapidly spreading mosquito-borne viral disease of mankind, with a 30- fold increase in global incidence over the last five decades. It is a major public health concern throughout the tropical and subtropical regions of the world[34] .

Epidemiology

India alone accounts for almost 34% of the global burden. There is an upsurge in the cases during the period July–November, of dengue/DHF has been observed. The disease has a seasonal pattern; the cases peak after the monsoons and are not uniformly distributed throughout the year[34,35].

Etiology :

Dengue viruses, are categorized under the genus Flavivirus. These viruses contain single stranded RNA and are small in size (50 nm). There are four dengue virus serotypes which are designated as DENV-1, DENV-2, DENV-3 and DENV- 4. Aedes aegypti is the vector for transmission[34,35].

Clinical features:

Incubation period ranges from 7 to 14 days.

The clinical presentations depend on various factors such as age, immune status of the host, the virus strain and primary or secondary infection. Infection with one dengue serotype gives lifelong immunity to that particular serotype.

The clinical course of illness passes through the following three phases:

- Febrile phase: characterised by high grade fever which peaks for 48-72 hrs following which it starts declining. Associated with non-specific constitutional symptoms such as generalised myalgia, headache, nausea, pain abdomen and vomiting.
- Critical phase: 3 -6 days of illness characterised by increased capillary permeability. Associated with Warning signs (abdominal pain/ tenderness, vomiting, hepatomegaly, clinical fluid accumulation, raised hematocrit, thrombocytopenia) and bleeding manifestations requiring close monitoring.
- Convalescent phase: characterised by improvement in the general wellbeing and appetite associated with restoration of the intravascular compartment[36].

The WHO classification has 3 severity categories[35]:

i. Dengue fever

ii. Dengue fever with warning signs

iii. Severe dengue

Complications: Major GI / intra-cerebral bleed. Hepatic/ renal failure, encephalopathy and in rare cases Guillian Barre syndrome.

Diagnosis[36] :

Haemtological tests:

- Raise in Hct level > 20% suggestive of hemoconcentration is a warning sign.
- Trombocytopenia.
- WBC count may be normal or leucopenia usually lymphopenia seen at the end of febrile phase.

Biochemical tests: Hyponatremia, metabolic acidosis, elevated serum glutamic transaminase, low albumin levels.

Serological tests:

- Detection of viral non-structural protein 1 (NS1) during initial illness.
- Detection of IgM antibodies
- Fourfold raise in dengue Ig G in paired samples[34].
- Detection of Viral RNA/ genome by PCR is confirmatory.

LEPTOSPIROSIS

Leptospirosis is a common and widespread zoonosis caused by aerobic, motile spirochetes of the genus *Leptospira.* Leptospirosis is grossly under reported because of lack of awareness of the disease and non-availability of diagnostic tests[37].

Epidemiology

The incidence of Leptospirosis in developing countries is 10 - 100/1,00,000 cases per year. By this estimate, India reports 0.1 - 1.0 million cases per year, More than 100 deaths/year of leptospirosis are reported from Gujarat, Kerala and Maharashtra[37,38]

Leptospirosis infect many species of animals, including rats, mice, moles, livestock (such as cattle, goats, sheep, horses, and pigs), wild mammals like raccoons and

domestic dogs. Groups at high risk for leptospirosis include persons exposed occupationally or recreationally to contaminated soil, water or infected animals. Transmission via animal bites and directly from person to person has been rarely reported[37,39].

Etiology

Pathogenic leptospires belong to 9 species, which include more than 300 antigenicaly distinct serovars. A single serovar can produce a variety of distinct syndromes, and a single clinical manifestation may be caused by multiple serotypes[39].

Pathogenesis :

Leptospires enter humans through abrasions in skin and mucous membrane. They enter the blood stream and cause endothelial damage of blood vessels and also cause ischemic damage of end organs[39,40].

Clinical features:

The incubation period is 7—14 days, but ranges from 2—21 days.

Leptospirosis can manifest in many ways. The various syndromes of presentation are as follows.

1. Acute febrile illness: The anicteric form usually mild characterised with non specific symptoms such as fever, headache, chills, conjunctival suffusion and severe myalgia.

2. Weil‘s syndrome: Icteric form mimics acute viral hepatitis associated with polyserositis, cholecystitis, acute renal failure, haemorrhagic manifestations and myocarditis with cardiac arrhythmias. Seen very rarely in children.

3. Pulmonary Haemorrhage with respiratory failure

4. Meningitis / Meningo-encephalitis[37]

Diagnosis:

Laboratory investigations:

- Elevated TLC with Relative neutrophilia (> 80%) and lymphopenia
- Platelets are reduced
- Elevated serum bilirubin, liver enzymes moderately raised (Serum alkaline phosphatase, S amylase, CPK).
- Positive CRP

Serological tests:

- Detection of Ig M antibodies in 2nd week of illness (most sensitive)
- A single high or four fold raise in IgG titres in paired samples is suggestive of infection
- Microscopic agglutination test (MAT) is the gold standard
- DNA hybridization techniques / nucleic acid amplification procedures / PCR

Demonstration of organism in culture

- Not in practice.
- Isolation of leptospira can be done before 2nd week of the illness.
- Leptospira can be isolated form blood / CSF in first 10 days of illness and from urine after 14days.

Diagnosis of leptospirosis requires high index of suspicion. Modified Faine's criteria has been useful for the diagnosis which includes Part A (clinical data), part B (epidemiological factors) and part C (bacteriological and laboratory finding)[39,40].

In a prospective study done by ***P Malavika*** and others between September 2007 and August 2008 in Sub Saharan Africa, among 870 cases of febrile illness 467 were infants and children. Among the paediatric group 268 (57.4%) were tested for acute Q fever of which 7 (2.6%) were positive. Acute SFGR was tested in 243 (52.0%) paediatric patients, results were positive in18 (7.4%). 243 (52.0%) pediatric patients were tested for acute TGR, none were positive. Clinical features associated with Acute Q fever were hepato- or splenomegaly (P = .028), anemia (P = .009), leukopenia (P= .013), jaundice (P= .007), and onset during the dry season (P= .021). Acute SFGR was associated with leukopenia (P= .003) and with evidence of other zoonoses. Thus they concluded Q fever and SFGR, but not TGR, are common causes of febrile illness in northern Tanzania and are likely to be endemic. Need for greater awareness among clinicians and a reliable single-sample diagnostic test to improve patient management, which would result in better patient outcomes, and helps in estimating the disease burden for these infections[41].

In a prospective cohort study by ***John A*** et al in 870 subjects in Northern Tanzania including children between 2months to 13 years of age, it was identified that actual cause of fever being malaria in only 1.6%, in contrast to clinical diagnosis of malaria being made in 60.7%. Other bacterial, mycobacterial, and fungal bloodstream infections accounted for 9.8%, 1.6%, and 2.9% respectively. Acute bacterial zoonoses was identified among 26.2% of the admissions; 13.6% had brucellosis, 33.9% leptospirosis, 20.3% had Q fever, 30.5% had spotted fever group rickettsioses, and 1.8% had typhus group rickettsioses. Adding to the etiology 7.9% of participants had a confirmed acute arbovirus infection, all due to chikungunya. It was noted that bacterial zoonoses or arboviral infection was not considered as a differential to any

patient admitted with the febrile illness. They concluded that malaria which was uncommon was over diagnosed, while others (invasive infections, bacterial zoonoses and arboviral infections) though highly prevalent were overlooked. They pointed out the important mismatches between clinical diagnosis with actual diagnoses that would have major implications for patient care, disease control and prevention, and limiting the use of antimalarial medications. They stressed on the need for an integrated approach to the syndrome of fever is needed to rationalize treatment and control strategies in resource-limited areas[42].

Mario Rosario et al conducted the first prospective, multicentre, active surveillance, cohort study in dengue endemic Asian countries including Indonesia, Malaysia, Philippines, Thailand and Vietnam to determine the incidence density of acute febrile episodes in children aged 2–14 years. They found that the overall incidence density of acute febrile illness was 33.6 per 100 person years, with 19.3% of 1500 healthy children experiencing one febrile episode. Testing of acute and convalescent sera from febrile participants was done for dengue, chikungunya, hepatitis A, influenza A, leptospirosis, rickettsia, and Salmonella Typhi. Overall, 289 participants had acute fever, 57% were IgM-positive for at least one of the diseases tested. 35% of the febrile participants had IgM ELISA positive for chikungunya making it most common aetiology. It was followed by S. Typhi positive in 29.4%. The overall incidence density of dengue per 100 person-years was 3.4 confirmed by non-structural protein 1 (NS1) antigen positivity and 7.3 by serology. Dengue was diagnosed in 11.4% and 23.9% of febrile children by NS1 positivity and serology, respectively. Of the febrile episodes not clinically diagnosed as dengue, 5.3% were dengue-positive by NS1 antigen testing and 16.0% were dengue-positive by serology. They concluded that ,

the most common identified causes of paediatric acute febrile illness among the diseases tested were chikungunya, S. Typhi and dengue. There is a need for laboratory confirmation of all dengue cases which are clinically diagnosed to refine disease burden estimates[6].

Kheng chheng et al conducted a prospective study to comprehensively analyse the demographic, clinical, laboratory and outcome of febrile children. The study was conducted over a period of one year between October 2009 to October 2010 in hospitalized children less than 16yrs of age in South East Asia. All children were assessed by locally modified IMCI guidelines. It was noted that there were 1225 episodes of febrile illness in 1180 children. Median age was 2years with 850 febrile episodes in children less than 5 years. It was identified that cause of fever in almost 50% of cases included dengue (16.2%), scrub typhus (7.8%) , Japanese encephalitis (5.8%) and in 6.3% with blood stream infections (salmonella typhi accounted for 1.8%, Streptococcus pneumonia of 1.1%, Escherichia coli, Haemophilus influenzae , Staphylococcus aureus, Burkholderia pseudomallei culture positive cases noted in 0.7%,0.6%,0.5% and 0.5% respectively. There were 69 deaths (5.6%), including those due to clinically diagnosed pneumonia (19), dengue virus (5), and melioidosis (4). It was noted that comorbid under-nutrition was prevalent in 44% of episodes and a major risk factor for acute mortality were HIV infection and cardiac disease. They concluded that the study can be used to develop rational guidelines for treatment and control of infectious diseases in South East Asia[43].

A clinical based acute fever surveillance was done by ***Kasper*** et al over a period of 3 years from December 2006 to 2009 in South central Cambodia. The study had 9,997

patients (including children aged between 2yrs and 18 years). They were able to identify aetiology in 38.0% of patients. Influenza was the most frequent pathogen accounting for 19.9% , followed by dengue (8.9%), malaria (7.2%), and bacterial pathogens(6.3%) in their study. In addition, 3.5% of enrolled patients were infected with more than one pathogen. The common presenting symptoms of the febrile participants included headache (69.5%), cough (57.5%), sore throat (46.6%), chills (48.1%)and malaise (46.8%). Among the participants 65.7% presented with clinical features which were characteristic of influenza like illness. They concluded that febrile illness can differ by region and country thus requiring syndromic based surveillance studies based on methodical evaluation of area specific aetiologies which can aid in diagnosis, treatment and control programs that help guide public health responses in developing nations[44].

Tara C Muller and others conducted a 3-year cross-sectional prospective observational study which was designed to investigate the causes of acute malaria-negative febrile illness in Cambodia. The study was done from January 2008 to December 2010, including children between 7 to 18 years. 1193 febrile patients and 282 non-febrile individuals as controls were recruited according to the eligibility criteria. Malaria RDTs and routine clinical examination were performed on site by health centre staff. Venous samples and nasopharyngeal throat swabs were collected and subjected to molecular diagnostic tests for malaria parasites, Leptospira, Rickettsia, O. tsutsugamushi, Dengue- and Influenza virus. Blood cultures and smears were also taken from all febrile individuals. 73.3% (874/1193) of febrile patient samples had at least one etiological agent identified by molecular diagnostic testing. Most frequent pathogens detected were P. vivax (33.4%), P. falciparum (26.5%),

pathogenic Leptospira (9.4%), Influenza viruses (8.9%), Dengue viruses (6.3%), O. tsutsugamushi (3.9%), Rickettsia (0.2%), and P. knowlesi (0.1%). In the control group, it was noted that a potential pathogen was identified in 40.4%, among which most common being malaria parasites and Leptospira. Clinic-based diagnosis of malaria RDT negative cases was poorly predictive for pathogen and appropriate treatment. Thus concluding, that further studies are required to understand their impact on clinical disease and epidemiology, which help to fill the knowledge gaps across each level of health care. Need for involvement of physicians, nurses and other health care professionals from various levels of health care as well as health policy makers to develop effective clinical guidelines, required to from appropriate intervention which are in line with the current clinical management[45].

Ragini singh and others conducted a retrospective study to identify the etiological pattern in an epidemic of acute febrile illness including children in Uttarakhand during monsoon period. The study identified common aetiology of febrile illness in 1141 patients being dengue (71.2%) followed by malaria (12.8%), typhoid (8.1%), scrub typhus (6%) and mixed infections (1.9%). It was noticed that it was primarily a dengue epidemic with significant various combination of infections suffered by febrile patients. Thus requiring greater awareness among treating clinicians for the possibility of co infections in a patients presenting with acute febrile illness[10].

A hospital based cross-sectional study was conducted by ***Choline Mahendel*** et al in north-eastern Tanzania. The study included patients aged 2 to 59 months presenting with febrile episodes to the outpatient department. Blood samples and urine samples were examined for malaria parasites, human immunodeficiency virus (HIV) and

bacterial infections. Diagnosis was based on both clinical and laboratory investigations. It was noted that a total of 867 patients with a median age of 15.1 months were enrolled from January to October 2013. Respiratory tract infections was the leading clinical diagnosis accounting to 46.8%. Gastroenteritis was diagnosed in 21.2% of patients. Malaria infection was confirmed in 8.3% of patients. Bacterial infection in blood and urine accounted for 3.2% and 17.7% respectively. HIV infection was confirmed in 1.2% of patients. Respiratory tract infections and gastroenteritis was frequent in patients under 36 months of age (87.3% and 91.3% respectively). Co-infections was identified in 25.5% of patients. The cause of fever was unidentified in 7.5% of the febrile children. They concluded that different proportions of infectious aetiology found among febrile children reflects the causes of fever in the study area. They highlighted the need to optimise patient management by developing malaria and non-malaria febrile illnesses management protocols[46].

Kemebradikumo P et al conducted a study in Nigeria delta region to ascertain the proportion of febrile illnesses attributable to malaria and non-malaria causes among children admitted to a tertiary health institution, where presumptive treatment of all fevers as malaria was being practised due to the difficulty in differentiating the causes of febrile illness in malaria-endemic regions. Their study included 190 children with febrile illness. Standard techniques were used to identify micro-organisms. The proportion of fevers attributable to malaria only was 48.42%, whereas the proportion of fevers attributable to bacterial infection only was 12.63%. The cause of fever was not identified in 32.63% of patients. In conclusion it was stated that other causes of fever to be kept in mind other than malaria in malaria endemic regions, as just over

half of the fevers could be linked to malaria. And the need for diagnostic facilities to be strengthened, and physicians to be educated on other causes of fever[9].

In 2009, a 3 month study conducted by ***Olga D*** and others in Puerto Rico including children. 284 enrolled patients with fever of unknown origin for 2–7 days duration were tested for Leptospira, entero-viruses, influenza,and dengue virus. It was found that with enhanced active febrile illness surveillance 31 dengue, 136 influenza, and 3 enterovirus cases were confirmed. In 112 patients no cause could be identified. Nearly half (48%) of the confirmed dengue cases met clinical criteria for influenza. Clinical manifestations of haemorrhage was more likely with patients with Dengue than influenza patients i.e 81% versus 26%. Similarly rash, 39% versus 9%, and a positive tourniquet test 52% versus 18%. Laboratory findings such as Mean platelet and white blood cell count were lower among dengue patients. It was noted that clinical diagnosis could be particularly difficult when outbreaks of other AFI occur during dengue season due to nonspecific and similar manifestations in early phase of the disease. Concluding that surveillance and improved knowledge among clinicians of patients‘ final diagnoses can be useful in improving physicians‘ clinical diagnostic skills and broadening their differential diagnosis, and assisting public health authorities in prioritizing limited resources[47].

Stephen R. Manock and others conducted a longitudinal observational study of 533 patients including children above 5 years presenting to two hospitals in the Ecuadorean Amazon basin with acute undifferentiated febrile illness (AUFI) from 2001 through 2004. They identified pathogens responsible for fever in 122 (40.1%) of 304 patients who provided both acute and convalescent blood samples. Leptospirosis was found in 40 (13.2%), malaria in 38 (12.5%), rickettsioses in 18 (5.9%), dengue

fever in 16 (5.3%), Q fever in 15 (4.9%), brucellosis in 4 (1.3%), Ilhéus infection in 3 (1.0%), and Venezuelan equine encephalitis (VEE), Oropouche, and St. Louis encephalitis virus infections in less than 1% of these patients. They stated until simple, affordable tests are available to accurately determine the aetiology of AUFI early in its course, a combination of epidemiologic surveillance, focused public health efforts, and broad spectrum empiric therapy will have to suffice[48].

In an observational study by ***Gowri Veligandla*** and others in a tertiary care centre in South India, 116 patients including 39 children with febrile illness were enrolled to identify the aetiology and prevalence of AUFI. The patient`s blood and serum sample were collected and various diagnostic tests for Malaria, Dengue, Typhoid, Scrub typhus, Leptospirosis, Chikungunya were done. In the study, Typhoid was the leading cause of AUFI 28(24.14%), followed by Dengue 12(10.35%), Malaria 6(5.17%) and Scrub typhus 2(1.72%). However 5(4.31%) cases had mixed infections. Sixty three (54.31%) undiagnosed infections were reported. They concluded that there is need for active surveillance of AUFI. Since majority of cases remain undiagnosed, there is a need for further research to create a diagnostic algorithm that will aid in timely management of the patients with AUFI. As the second largest group affected with AUFI in the study population are in the school going age group, highlighting the need for further research in the incidence, prevalence and aetiology of paediatric AUFI cases[49].

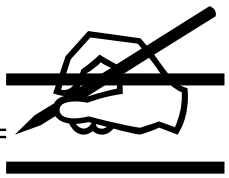
M A Andrews and others conducted a study in 2007 and 2012 to describe the pattern of AUFI in central Kerala during monsoon season. They retrospectively studied the pattern of AUFI in the months of June and July in 2007 and prospectively in

2012.Preset diagnostic criteria were used to classify the cases into common aetiologies involved. The demographic, clinical and laboratory parameters were analysed. It was noted there were 273 cases of AUFI in the months of June and July 2007. Out of the 273 patients, 113 (41.4%) were diagnosed to have leptospirosis, 41 (15%) to have dengue fever and 34 (12.5%) Chikungunya. Eighty five (31%) cases could not be classified. In June and July 2012 a total of 96 patients with AUFI were enrolled. Major aetiologies identified were leptospirosis 23 (23.96%), dengue 12 (12.50%) and miscellaneous (unclassified) 61 (63.54 %). Thus, Leptospirosis constituted a significant proportion of cases in both series. In a large number of patients with AUFI, the exact cause could not be identified. In 2007 and 2012 mortality in cases of leptospirosis was 24 (21.2%) and 6 (26.09%) respectively. No patients with either dengue fever or Chikungunya died in both epidemics. Case fatality was less in 2012 but the percent of patients died due to leptospirosis among patients admitted to the hospital remained almost the same[8].

A prospective epidemiologic study aiming to discover the aetiologies of acute undifferentiated febrile illness in a tropical region like Thailand by ***Leelarasamee A*** and others was conducted in 2004. Patients aged over two years old who presented with fever at ten community-based hospitals were included. Of the 1,240 patients enrolled only 1,137 case records and results of the serological tests were available for analysis. Etiologies could be found in 471 cases (38.7%). Primary bacteraemia was detected in 36 cases (3.2%). E. coli, streptococci, salmonella, Enterobacter spp. and S. aureus were the five most common blood isolates. Serological studies revealed positive results for scrub typhus (7.5%), influenza (6.0%), dengue fever (5.7%), murine typhus (5.3%), enteric fever (1.9%), chikunkunya infection (1.1%),

leptospirosis (1.1%) and melioidosis (0.9%). Thirteen cases succumbed to their illness (1.1%) in this study. Concluding that the etiologies in the majority (61.3%) of AUFI remained unknown. Rickettsial infection, influenza and dengue fever are the most common identifiable diseases in a tropical country like Thailand especially during the rainy season. A management guideline for diagnosis and treatment of the AUFI with emphasis on primary bacteremia and antimicrobial-treatable AUFI was proposed[50].

METHODOLOGY



MATERIAL AND METHODS

Study hospital:

R L Jalappa hospital Kolar, a tertiary level hospital catering to the health care needs of the people of Kolar district.

Study population:

Children between 1 month to 18 years of age admitted to paediatric ward at RLJH with fever less than 2 weeks of duration over a period of January 2016 to May 2017 were registered for the study.

Study design :

Hospital Based Prospective Observational Cross Sectional Study.

Inclusion criteria :

Children aged between 1 month to 18 yrs admitted at RLJH with fever ($\geq 100.4^0$ F) of less than 2 weeks.

Exclusion Criteria :

1) Patients with Immunocompromised state, hematological malignancies, connective tissue disorders or auto-immune diseases.

2) Patients with definitive diagnosis.

Sample size :

Sample size is estimated based on the reference study no.10 with 95% confidence intervals and absolute error of 5%. Estimated minimum sample size was 689.

Sample size calculation:

Calculated with the equation

$$n = \frac{Z_{\alpha}^{2} p q}{d^{2}}$$

where, n= sample size

Z_{α}^{2}= standard deviation 1.96(which is at 95% confidence interval)

p = prevalence (p1- 71.2, p2-12.8,p3-8.1, p4-6)

q =(1-p)

d= absolute error of 5%

n = 315+172+115+87= 689.

Expecting a non compliance of 10% total subjects included is 750

Study tools:

Performa (Annexure 1)

Children were evaluated with a detailed clinical history (nature and duration of symptoms) and background characteristics including nutritional status, immunization status, and socio-demographic variables. A semi-structured Performa was prepared. Based on duration of fever, clinical presentation they were started on empirical treatment and management planned.

Blood sampling:

For all cases satisfying the inclusion criteria and who had consented were included in the study. With aseptic precautions venous blood sample of 1ml each was collected in BD Vacutainer® SST™ II Advance(REF367954) for serological investigations (dengue, rickettsial, leptospira, RDT for malaria) and BD Vacutainer®

K2EDTA(REF 367856) for CBC, smear for malarial parasite and urine samples collected in sterile containers. 4ml of venous blood collected in BacT/ ALERT® PF Plus culture bottles. The samples were sent to the laboratory for further analysis.

Method of laboratory analysis

Haemogram :

Done by automated haematology analyser based on the principle of electrical impedance[52].

Blood culture:

Automated aerobic Bact Alert system was used for blood culture, it is based on the principle of detection of CO_2 produced by the organism by colorimetric sensor. The samples thus collected were sent to microbiological laboratory where they were incubated for a period of 7 days.

Widal test:

A serodiagnostic test used for the diagnosis of typhoid (Stained Salmonella: Antigen set for Widal test by ARKRAY Healthcare Pvt. Ltd) test was carried out as per the manufacturers‘ orders. Is a quantitative tube tests. The test is based on the principle of direct agglutination reaction. The smooth suspension of killed Salmonella bacilli carries “O” and “H“ when the patients serum sample (containing antibodies to S. typhi and S. paratyphi)is incubated with respective antigens, visible agglutinations occur. A rising titre of antibodies are indicative of enteric fever.

NS1Ag determination for dengue :

It is a solid phase enzyme linked immunosorbant assay. J. Mitra & Co. Pvt.Ltd:Dengue NS1Ag MICROLISA kit used and manufacturer‘s instructions were

followed. Helps in qualitative detection of NS1antigens in human serum or plasma. < 9 units is negative, 9 – 11 units is equivocal and > 11 units suggests positive test.

Dengue IgM :

Is an enzyme immunoassay based on IgM CAPTURE ELISA. J. Mitra & Co. Pvt.Ltd:Dengue IgM MICROLISA kit used and manufacturer‘s instructions were followed. Is an invitro qualitative estimation of IgM antibodies. IgM antibodies present in patients serum binds to antihuman IgM antibodies coated in the microtitre wells. These antibodies are detected by enzyme conjugate horse radish peroxidase conjugated with dengue antigens. The proportion of dengue antibodies are detected by addition of chromogenic substrate which are read by an ELISA reader for absorbance at 450nm.

Rapid card test for malaria:

Is an immunoassay based on sandwich principle. J. Mitra & Co. Pvt.Ltd:Advantage MAL CARD used and manufacturer‘s instructions were followed. The conjugate contains colloidal gold conjugated to monoclonal anti-pan specific p LDH (parasite lactate dehydrogenase) antibody. The test uses monoclonal anti-Pf p LDH and monoclonal anti-Pan specific p LDH antibody immobilised on a nitrocellulose strip. The test sample was added to the device. On addition of assay buffer, the red blood cells get lysed. If the sample contains P. falciparum and/or P.vivax/ P.malariae/ P. ovale, the colloidal gold antibody conjugate complexes the Pf. Specific p LDH / Pan specific p LDH in the lysed sample. The complexes migrates through the nitrocellulose strip by capillary action. When the complex meets the line of the corresponding immobilised monoclonal antibody , the complex is trapped forming a purplish band which confirms a reactive test result. Absence of coloured

band indicates a non-reactive test result. A red procedural control line which develop at ―C‖ region indicates the test is performed properly.

Peripheral smear for malarial parasite:

Thick and thin smears are stained with JSB stain and studied under the microscope for identification of the malarial parasite[53].

Weil Felix test :

Plasmatec febrile antigens (stained antigen suspensions are killed bacteria, stained to enhance the reading of the agglutinins) MICROPATH® Antigens/ Febrile Antigen Kit were used for both the rapid slide and tube agglutination tests against human sera for the detection of the agglutinins. All positive tests by rapid slide tests are confirmed by tube agglutination tests.

Leptospirosis

Is an enzyme immune assay based on indirect ELISA. J. Mitra & Co. Pvt.Ltd: Lepto IgM MICROLISA kit used and manufacturer‘s instructions were followed. IgM antibodies present in patients serum binds to the recombinant proteins of leptospira genus representing the immunodominant epitopes coated in the microtitre wells. These antibodies are detected by enzyme conjugate horse radish peroxidase conjugated with anti IgM antibodies. The proportion of leptospira antibodies are detected by addition of chromogenic substrate.

Urine microscopy:

Urine microscopic examination done to rule out urinary tract infections.

Methodology-

After taking ethical clearance and informed written consent from the parents, children between 1 month to 18 yrs admitted to RLJH with fever of less than 2 weeks, over the study period were included in the study. Children with axillary temperature of ≥100.4^0 F recorded at the time of admission/ following admission were registered for the study.

Total of 794 children were enrolled of which 44 children were excluded from the study in view of definitive diagnosis established on physical examination on day 1 or 2 of admission.

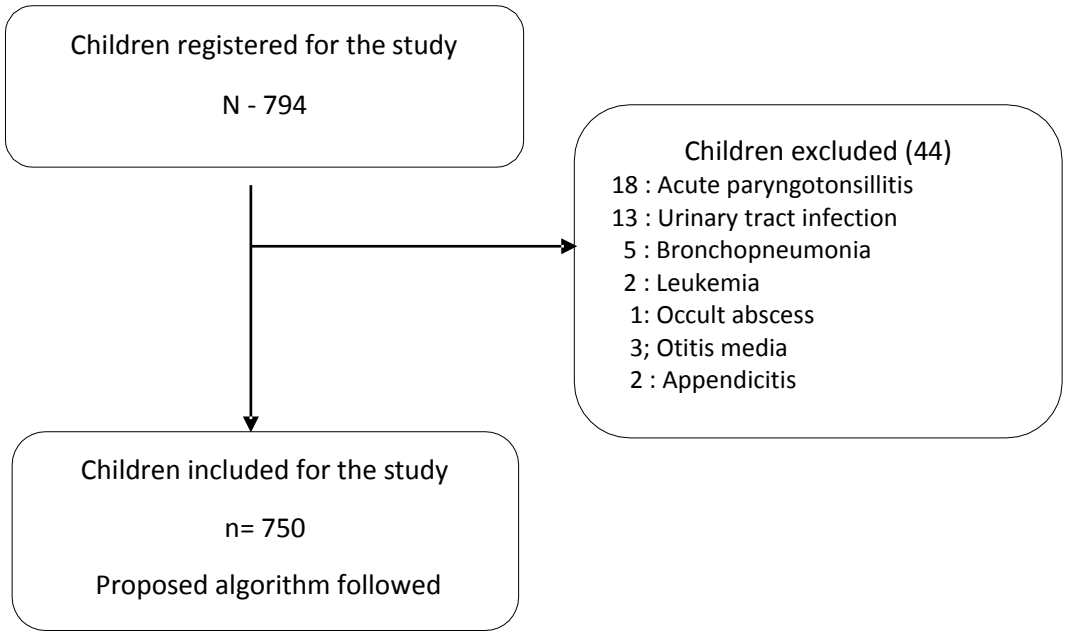


Figure 3 : Flowchart of children with acute febrile illness

Included children were evaluated on the basis of the proposed algorithm (fig .4), which was based on our clinical approach to AFI , to avoid unnecessary tests and overzealous treatment. The tests were done within the limitations of laboratory tests available in our institute.

Step 1: Detailed history of the fever (duration and pattern) and other associated symptoms. Social and demographic details were recorded. Socio economic status was assessed according to BG Prasad's Scale[54].

SOCIOECONOMIC CLASS	Per Capita Monthly Income
CLASS I	≤ 6277
CLASS II	3139- 6276
CLASS III	1883- 3138
CLASS IV	942-1882
CLASS V	< 942

Table 2: Socioeconomic Status (BG Prasad's Scale)

Step 2 : Recording of temperature at admission and during the hospital stay.

Step 3 : A detailed clinical examination was performed. Length of the child was measured on an infantometer to the nearest centimetre till the age of two years and thereafter height on a stadiometer. Weight of the child was recorded on beam type of weighing scale to the nearest 100 g. Children were examined for pallor and was labelled as anaemia if pallor was present in the conjunctiva and/or mucous membrane and/or colour of palmar creases was similar to the rest of the palm[55]. Rashes, flushing, hepatomegaly and splenomegaly were noted[56].

Step 4 : In case of definitive diagnosis patients were excluded from the study.

Step 5: First week of Fever: Routine laboratory investigations (CBC,CRP, urine routine) and blood culture , Peripheral smear and Rapid card for MP (due to the endemicity of malaria in and around Kolar) and Dengue serology – Ns1Ag and IgM ELISA for Dengue .

Step 6: Second week of fever : Relevant investigations as deemed necessary based on clinical suspicion were sent (Weil-felix for Rickettsia, Widal for Enteric fever, and Lepto IgM ELISA for leptospira).

Step 7: All patients were followed uptil discharge.

Step 8: Unclear diagnosis considered when the results of relevant investigations are inconclusive.

Step 9: Convalescent sear was tested after 2 to 4 weeks of illness in patients with negative serological diagnosis and who were willing.

Diagnostic criteria[57] :

Dengue fever : dengue (ELISA)Ns1Ag positive & IgM positive + other serologies negative OR seroconversion on convalescent sera.

Malaria – Malaria parasite (morphological forms – Falciparum, Vivax or mixed) visualized on thick and thin blood smears OR positive Rapid card(ICT) for malarial parasite.

Enteric fever – Blood culture positive for Salmonella typhi or S. paratyphi or other serologies negative OR fourfold rise in titre on the WIDAL (Tube agglutination test).

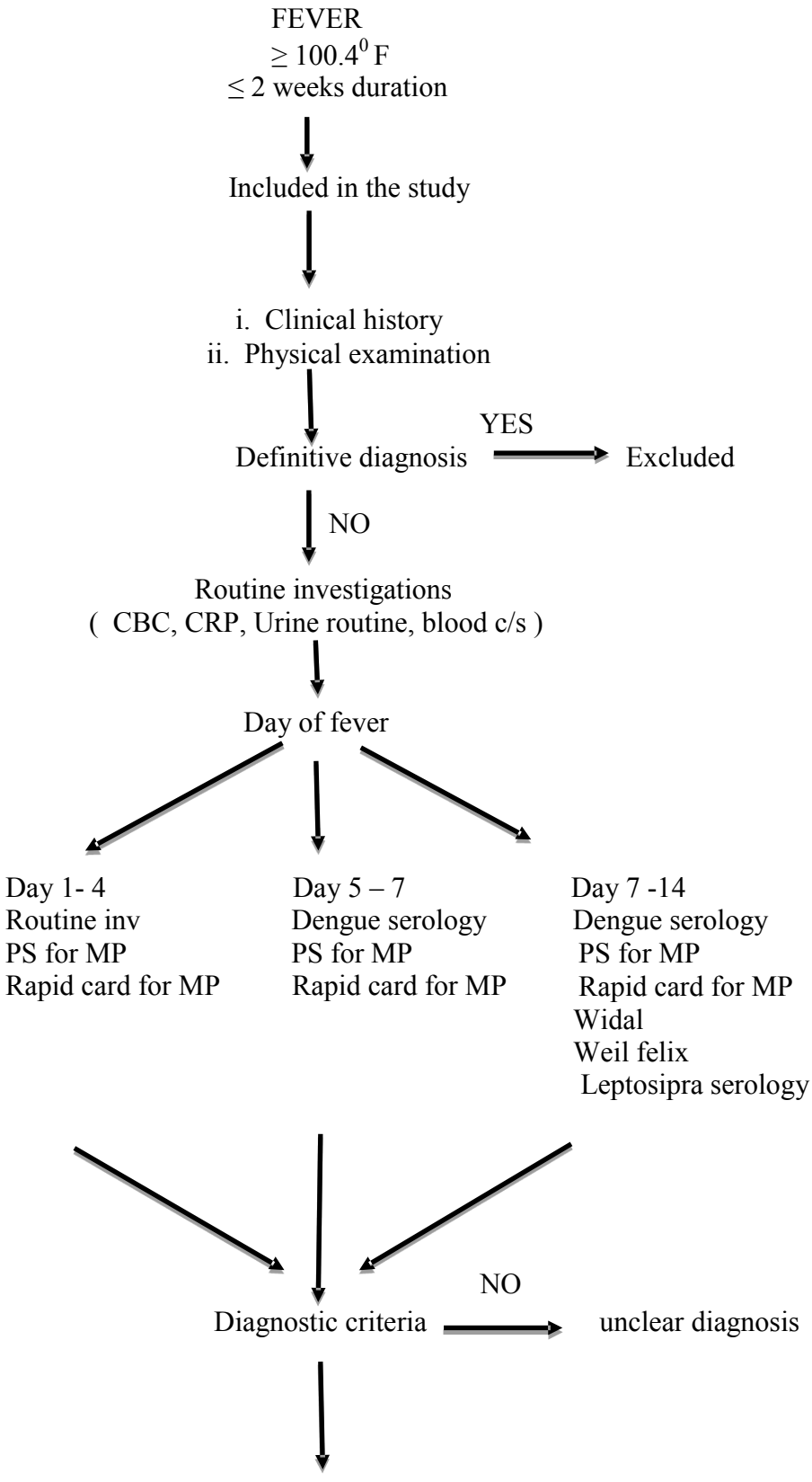
Leptospirosis – Leptospira IgM positive (ELISA) + other serologies negative.

Spotted fever rickettsiosis – other serologies negative OR weil felix positive with rash .

Scrub typhus – Eschar + weil felix positive OR weil felix positive + defervesence within 48 hrs of initiation of Doxycycline OR seroconversion on convalescent sera.

Unclear/ Unclassified diagnosis – After complete evaluation a definitive diagnosis was not made.

Figure 4 : Algorithm depicting the methodology of the study



Statistical analysis :

Method of Statistical Analysis:

The following methods of statistical analysis have been used in this study.

The results for each parameter (numbers and percentages) for discrete data and average (mean ± standard deviation) for each parameter were presented in tables and figures.

1**) Proportions were compared using Chi-square test of significance**

Chi-Square (χ^2) test for (r x c tables)

Rows	Columns			Total
	1	2……..	c	
1	a_1	a_2	a_c	t_1
2	b_1	b_2	b_c	t_2
.	.	……	.	.
.	.	……..	.	.
r	h_1	h_2	h_c	t_r
Total	n_1	n_2	n_c	N

Table 3: Analysis by Chi- square

a,b…..h are the observed numbers.

N is the Grand Total

$$\chi^2 = N\left[\frac{1}{t^1}\sum_1^c \frac{a^i^2}{n^i} + \frac{1}{t^2}\sum_1^c \frac{b^i^2}{n^i} + \ldots\ldots\ldots\ldots + \frac{1}{t^r}\sum_1^c \frac{h^i^2}{n^i} - 1\right]$$

DF=(r-1)*(c-1), where r=rows and c=columns

DF= Degrees of Freedom (Number of observation that are free to vary after certain Restriction have been placed on the data)

2. Student "t' test.

The student_t' test was used to determine whether there was a statistical difference between the groups in the parameters measured.

Student's t test is as follows:

. $t=\frac{\bar{x}_1-\bar{x}_2}{s\sqrt{\frac{1}{n_1}+\frac{1}{n_2}}} \sim\sim\sim t_{n1+n2-2}$ Where $s^2=\frac{(n_1-1)s_1^{\ 2}+(n_2-1)s_2^{\ 2}}{(n_1+n_2-2)}$

3. Logistic Regression

The association between potential Sign, symptoms and laboratory finds related risk factors among disease (for ex: Malaria vs Other AFI) were initially studied through univariate analysis. The categorical variables were assessed using $\chi 2$. Odds Ratio (OR) and 95% Confidence Interval (CI) were calculated. To estimate the independent effect of the factors that were significantly associated with Disease the confounding effect they may have on each other, logistic regression analysis was done. The variables were included if their respective univariate analysis yielded P <0.10. A backward stepwise elimination procedure based on the likelihood statistics, (using removal probability of 0.10 and considering the change in classification accuracy) was also performed to identify the best subset of variables.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram. **p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data. EPI Info (CDC Atlanta), Open Epi, Med calc and Medley's desktop were used to estimate sample size, odds ratio and reference management.

RESULTS

RESULTS

Table 4: ETIOLOGY OF ACUTE FEBRILE ILLNESS

FINAL DIAGNOSIS	FREQUENCY	PERCENT
Malaria	67	8.9
Rickettsial fever	80	10.7
Enteric fever	94	12.5
Leptospirosis	6	0.8
Dengue	216	28.8
Unclassified fever	287	38.3
Total	750	100.0

In the study, majority of the cases were with the diagnosis of unclassified fever 287 (38.3%) , followed by dengue 216(28.8%), enteric fever 94(12.5%), rickettsial fever 80(10.7%), malaria 67(8.9%) and leptospirosis 6(0.8%).

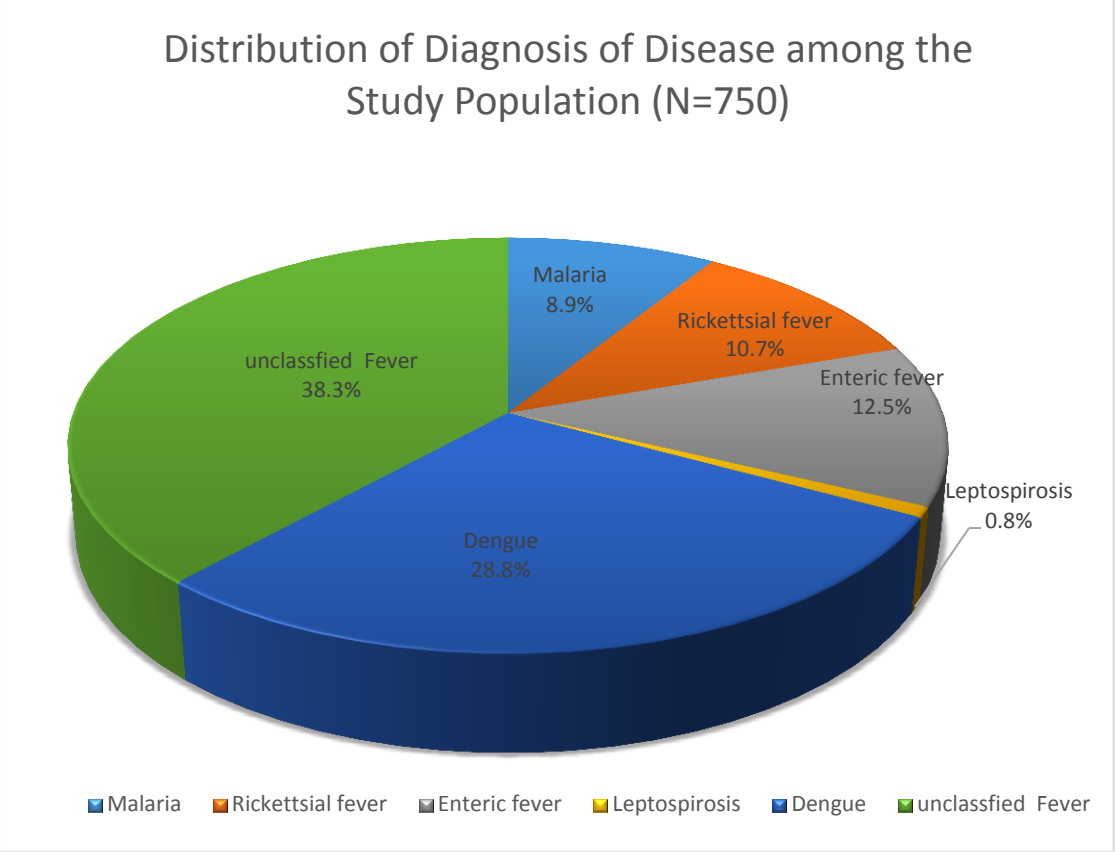


Figure 5: PIE DIAGRAM SHOWING ETIOLOGICAL DISTRIBUTION OF AFI CASES

I Demographic details

Table 5a : AGE WISE DISTRIBUTION OF STUDY POPULATION

AGE	FREQUENCY	PERCENT
<1 yr	38	5.1
1-3 yrs	138	18.4
4-6 yrs	183	24.4
7-13 yrs	302	40.3
14-18 yrs	89	11.9
Total	750	100.0

In the study , it was observed that 38 (5.1%) of the subjects belonged to the age group of 1 month to 12 months, while 138(18.4%) were in the age group of 1 to 3 years, 183 (24.4%) in the age group of 4 to 6 years, 302(40.3%) that was the majority in the age group of 7 to 13years and 89 (11.9%) in the age group of 14 to 18 years.

N	Mean Age (months)	SD	Median	Min.	Max.
750	88.2	54.940	84.0	1	216

In the study the mean age of children presenting with AFI was 88.2 months

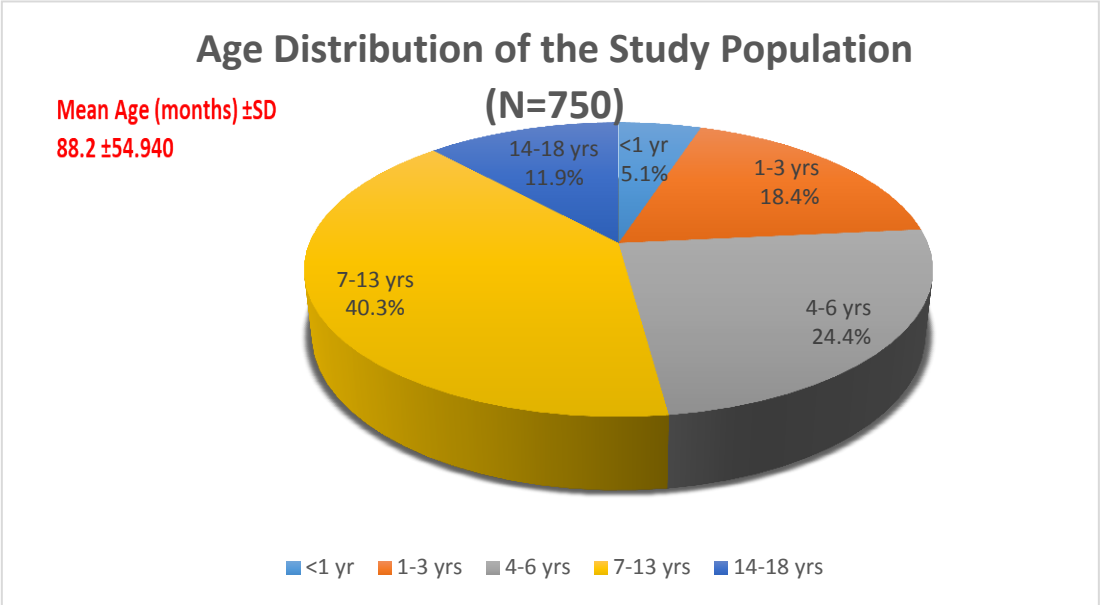


Figure 6a : PIE DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO AGE

TABLE 5b: COMPARISON OF AGE WISE DISTRIBUTION OF CASES AMONG DIFFERENT SUBGROUPS OF ACUTE FEBRILE ILLNESS

	Malaria (N=67)		Rickettsial fever (N=80)		Enteric fever (N=94)		Leptospirosis (N=6)		Dengue (N=216)		Unclassified Fever (N=287)		Total (N=750)	
	n	%	n	%	n	%	n	%	N	%	n	%	n	%
Age(Mean± SD)	80.96±49.712		79.84±48.191		91.81±48.127		108.00±33.082		98.19±57.352		83.18±57.472		88.2±54.940	

It was noted in the study, that mean age of presentation was higher in cases of leptospirosis (108± 33.08) followed by dengue (98.19±57.352) and enteric fever (91.81±48.127). Mean age of presentation was lower in cases of Rickettsial fever (79.84±48.191)

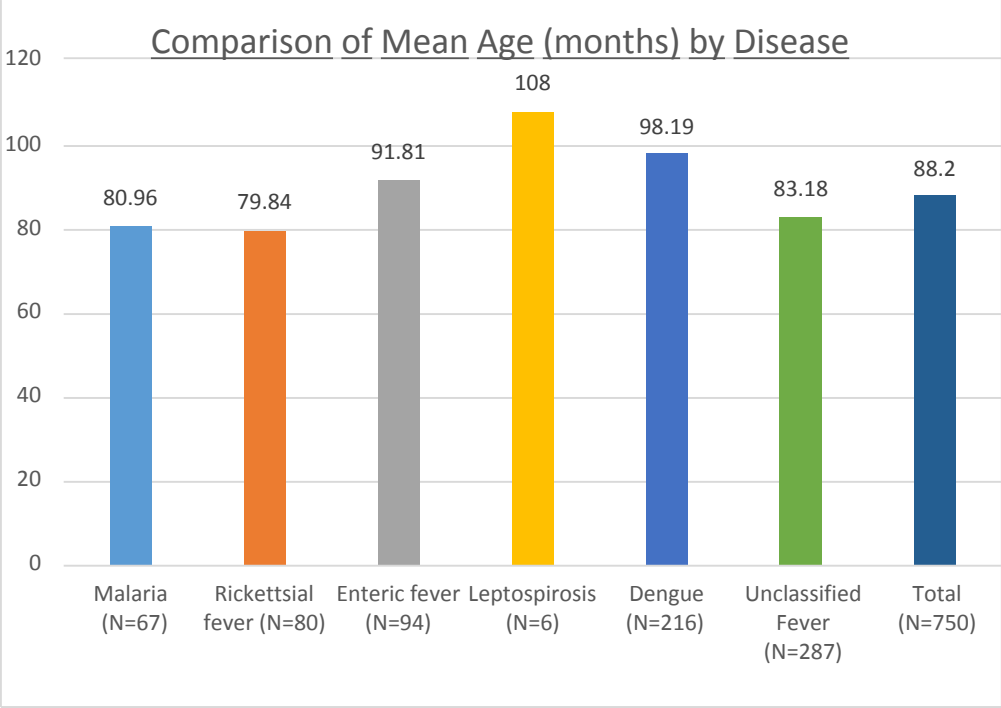


Figure 6b: BAR DIAGRAM SHOWING ASSOCIATION OF MEAN AGE OF PRESENTATION AND AFI

Table 6a: GENDER WISE DISTRIBUTION OF STUDY POPULATION

GENDER	FREQUENCY	PERCENT
Male	398	53.1
Female	352	46.9
Total	750	100.0

It was observed that 398 (53.1%) of subjects were males and 352 (46.9%) were females

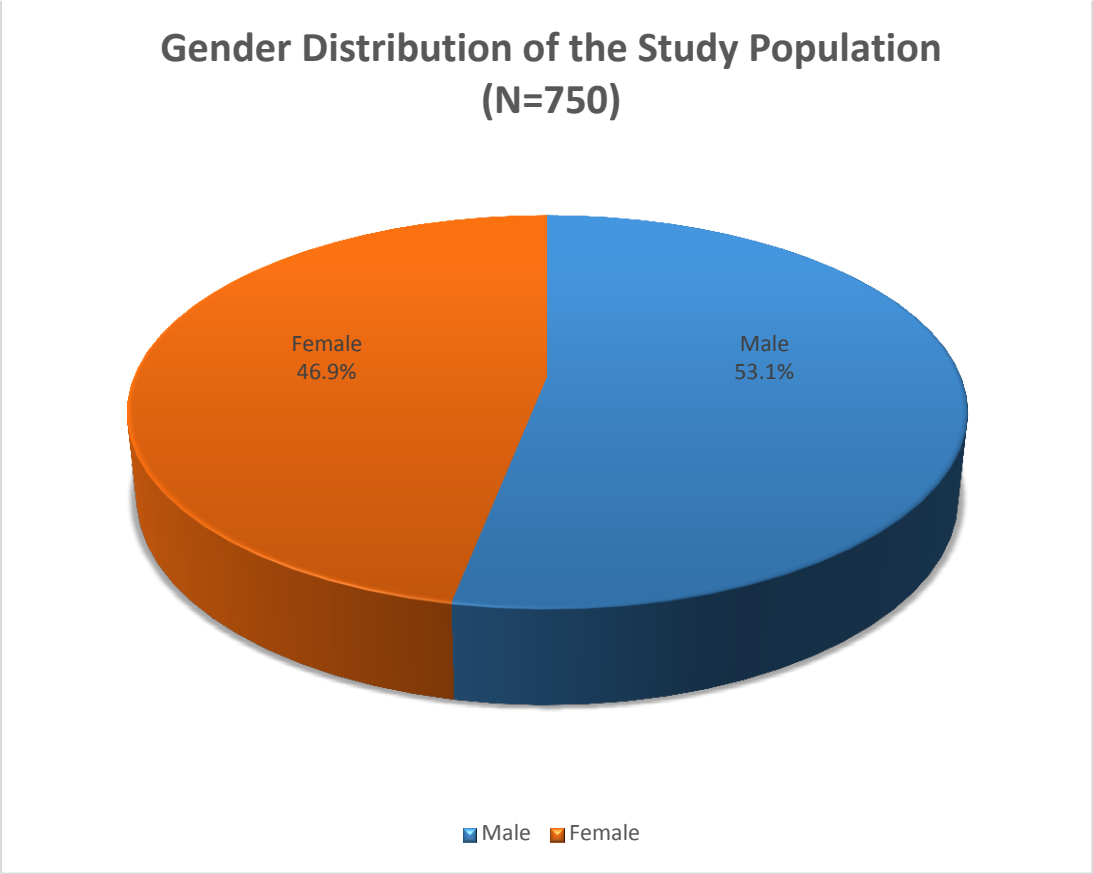


Figure 7a : PIE DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO GENDER

TABLE 6b :COMPARISON OF DISTRIBUTION OF GENDER AMONG THE DIFFERENT SUBGROUPS OF ACUTE FEBRILE ILLNESS

Gender:	Malaria (N=67)		Rickettsial fever (N=80)		Enteric fever (N=94)		Leptospirosis (N=6)		Dengue (N=216)		Unclassified Fever (N=287)		Total (N=750)		P value
	n	%	n	%	n	%	n	%	N	%	n	%	n	%	
Male	37	55.2 %	48	60. 0%	61	64.9 %	2	33.3%	91	42.1 %	15 9	55.4 %	39 8	53.1 %	***0.002***
Female	30	44.8 %	32	40. 0%	33	35.1 %	4	66.7%	12 5	57.9 %	12 8	44.6 %	35 2	46.9 %	

In the study it is noted that cases of malaria, rickettsial, enteric and unclassified fever had male predominance where as, leptospirosis and dengue had female preponderance.

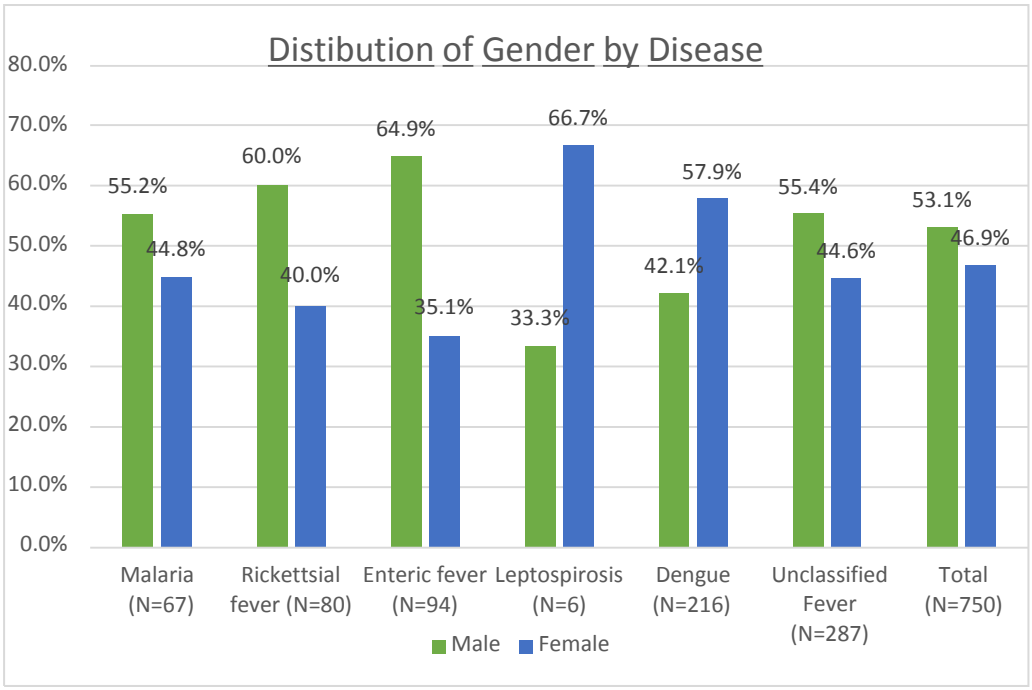


Figure 7b : BAR DIAGRAM SHOWING DISTRIBUTION OF GENDER AND AFI CASES

Table 7: DISTRIBUTION OF STUDY POPULATION ACCORDING TO RELIGION

RELIGION	FREQUENCY	PERCENT
Hindu	644	85.9
Muslim	92	12.3
Christian	14	1.9
Total	750	100.0

In the study it was observed that majority of the subjects 644(85.9%) were Hindus followed by 92(12.3%), 14(1.9%) were Muslim and Christians respectively.

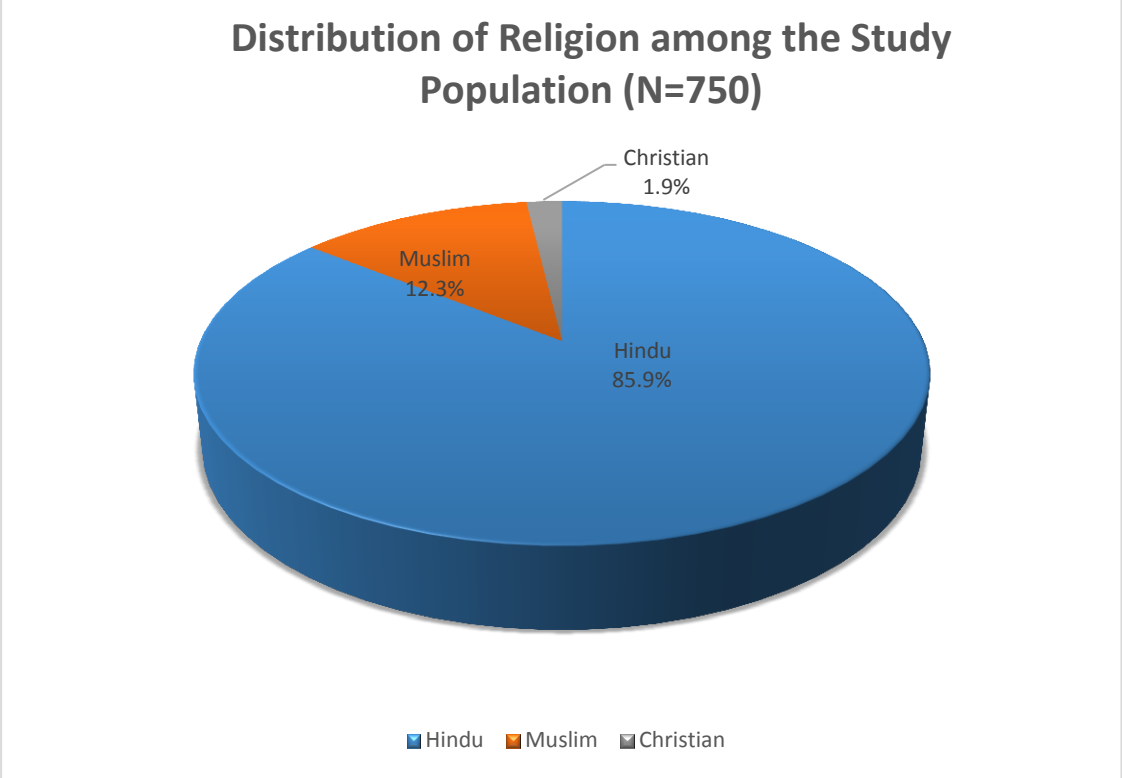


Figure 8: PIE DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO RELIGION

Table 8: DISTRIBUTION OF STUDY POPULATION ON THE BASIS OF FAMILY TYPE

Family Type	Frequency	Percent
Nuclear	627	83.6
Joint	123	16.4
Total	750	100.0

In the study majority of the subjects 627 (83.6%) were from nuclear family and 123(16.4%) were from joint family.

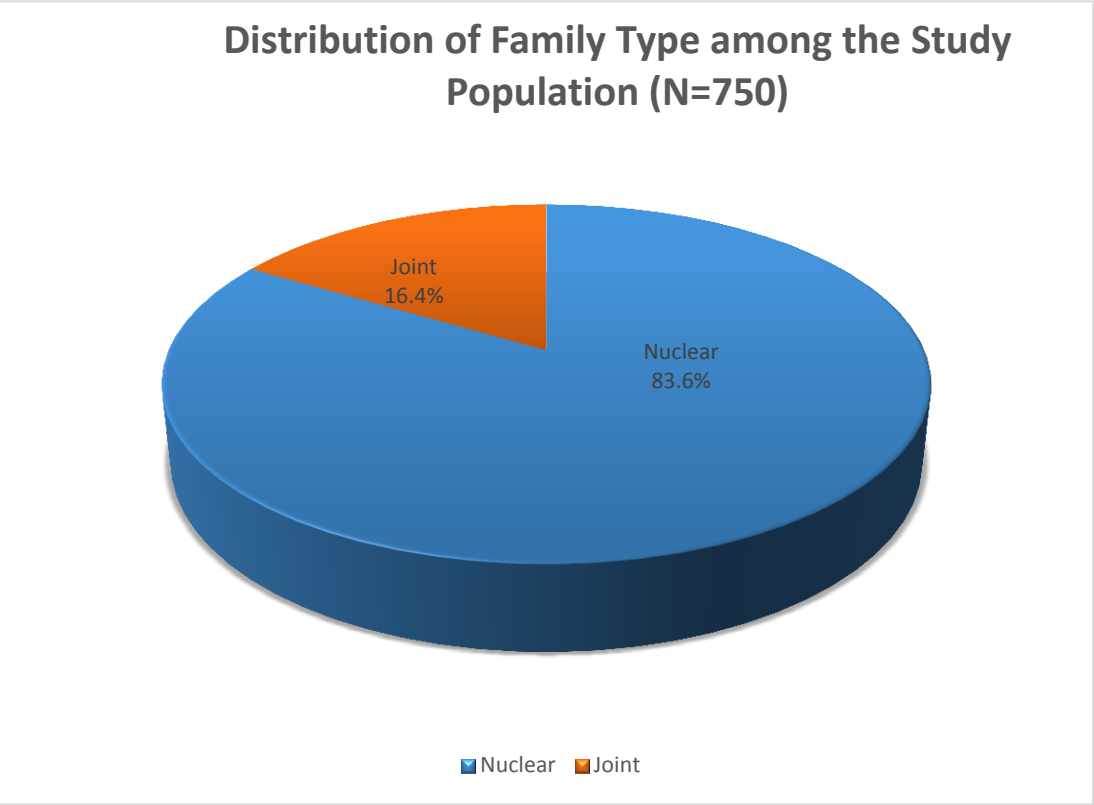


Figure 9: PIE DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO FAMILY TYPE

Table 9 : DISTRIBUTION OF STUDY POPULATION ACCORDING TO B G PRASAD SOCIO ECONOMIC CLASSIFICATION.

SOCIO ECONOMIC STATUS	FREQUENCY	PERCENT
Class I	17	2.3
Class II	363	48.4
Class III	208	27.7
Class IV	156	20.8
Class V	6	0.8
Total	750	100.0

Analysis of socio-economic status among the studied families revealed almost half of the families belonging to class II . Class III and IV combined constituted nearly the remaining half.

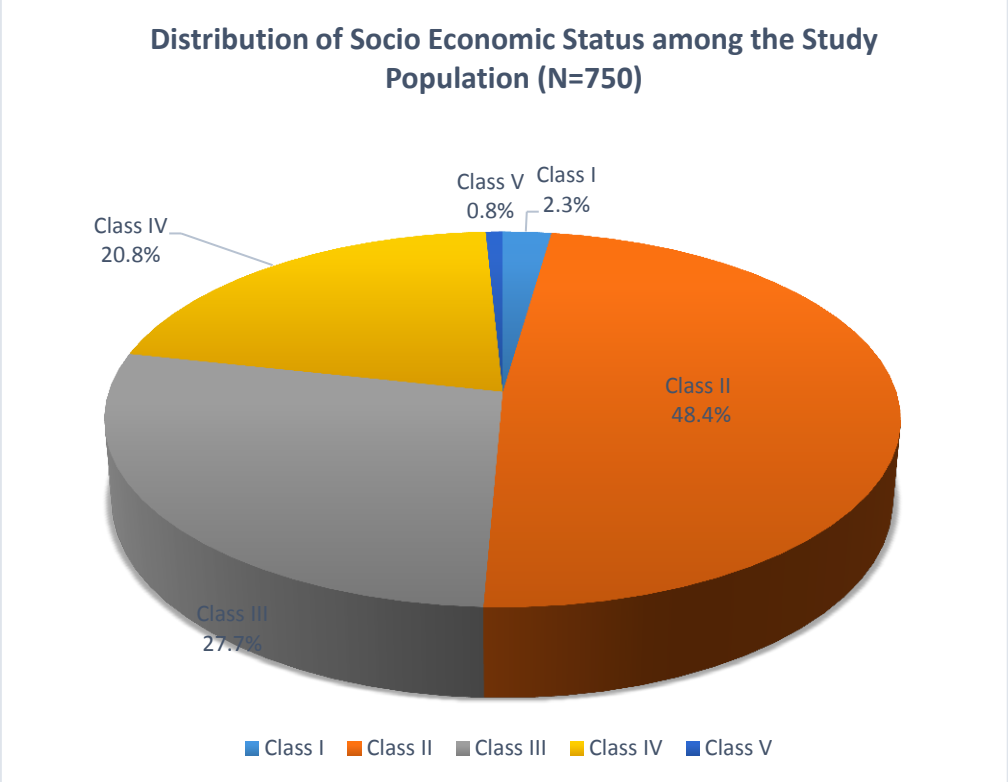


Figure 10: PIE DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO SOCIO ECONOMIC STATUS

Table 10a : DISTRIBUTION ACCORDING TO DURATION OF FEVER AT PRESENTATION

FEVER DURATION	FREQUENCY	PERCENT
<1 Week	712	94.9
>=1 Week	38	5.1
Total	750	100.0

In the study, it was observed that majority 712(94.9%) presented with fever of less than 7days and 38(5.1%) with fever of 7 to 14 days.

Mean Fever duration (days)

N	Mean	SD	Median	Min.	Max.
750	3.8	1.438	4.0	1	10

The study subjects with AFI 3.8 days was the mean duration of fever at presentation to the hospital.

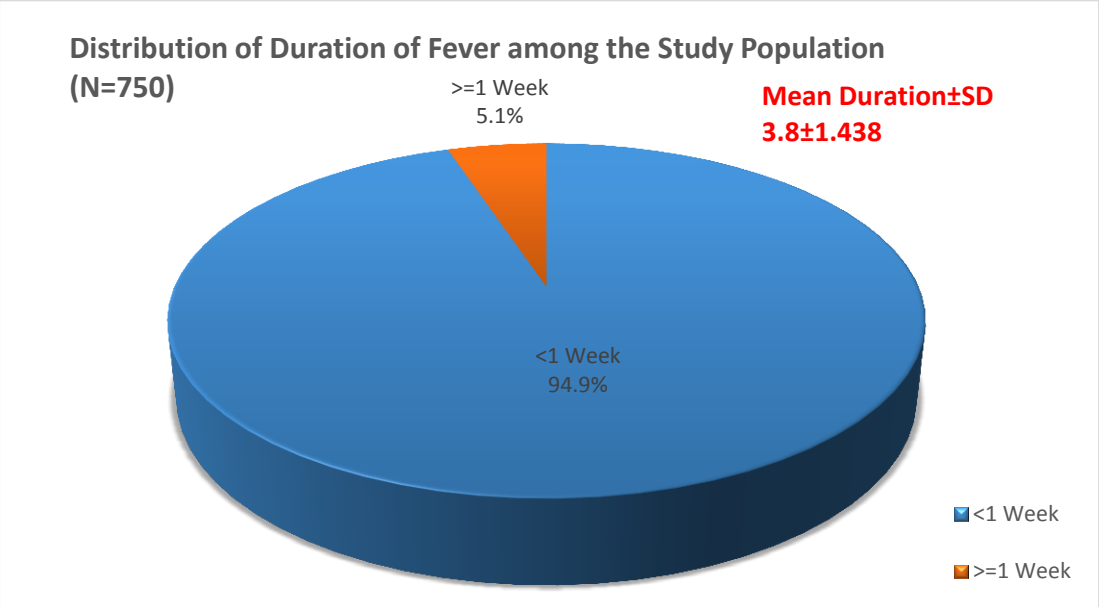


Figure 11a: PIE DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO DURATION OF FEVER

TABLE 10b : COMPARISON OF DURATION OF FEVER AMONG DIFFERENT SUBGROUPS OF ACUTE FEBRILE ILLNESS

Fever Duration:	Malaria (N=67)		Rickettsial fever (N=80)		Enteric fever (N=94)		Leptospirosis (N=6)		Dengue (N=216)		Unclassified Fever (N=287)		Total (N=750)		P value
	n	%	n	%	n	%	n	%	N	%	n	%	n	%	
<1 Week	58	86.6%	63	78.8%	89	94.7%	4	66.7%	211	97.7%	287	100.0%	712	94.9%	<0.001
>=1 Week	9	13.4%	17	21.3%	5	5.3%	2	33.3%	5	2.3%	0	0.0%	38	5.1%	

It was observed in the study, majority of the subjects in each sub group of AFI presented with fever of duration less than 1 week.

Most of the cases of leptospirosis 33.3%, 21.3% of rickettsial fever and only 2.3% of the dengue fever presented with fever of more than 1 week duration.

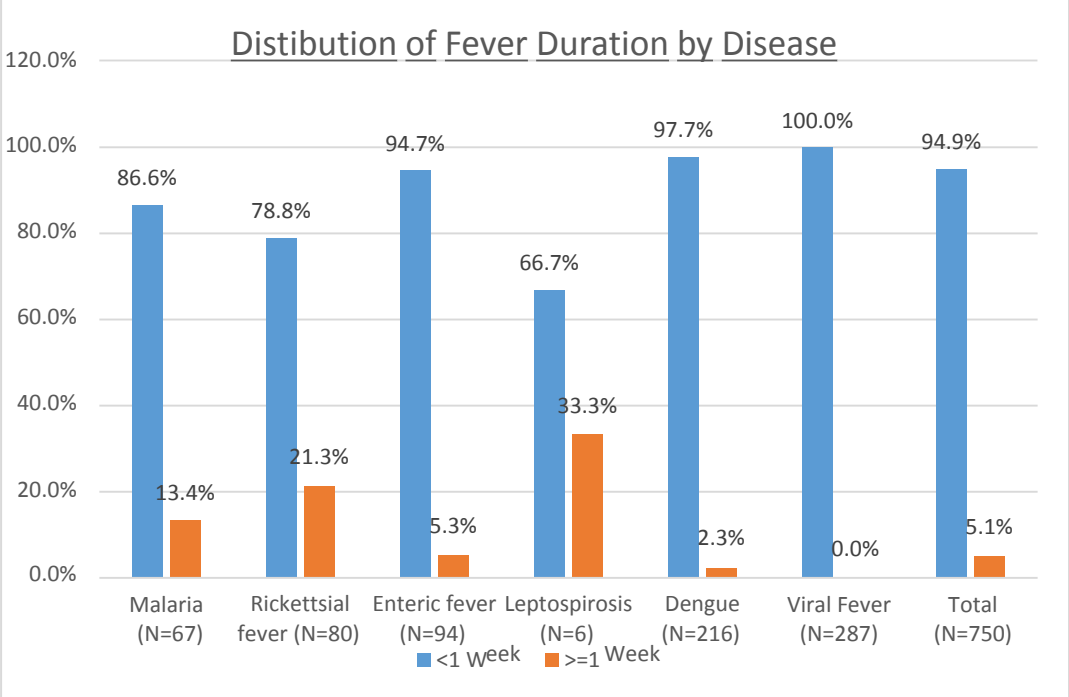


Figure 11b : BAR DIAGRAM SHOWING DISTRIBUTION OF AFI CASES ACCORDING TO DURATION OF FEVER AND ETIOLOGY

Table 11 :COMPARISON OF CLINICAL SYMPTOMS OF VARIOUS AFI

	Malaria (N=67)		Rickettsial fever (N=80)		Enteric fever (N=94)		Leptospirosis (N=6)		Dengue (N=216)		Unclassified Fever (N=287)		Total (N=750)	
	n	%	n	%	N	%	n	%	n	%	n	%	n	%
Rigors	28	41.8 %	0	0.0%	0	0.0%	0	0.0%	0	0.0%	18	6.3%	51	6.8%
Chills	28	41.8 %	0	0.0%	0	0.0%	5	83.3 %	8	3.7%	89	31.0 %	130	17.3 %
Pain Abdomen	51	76.1 %	42	52.5 %	42	44.7 %	6	100.0%	147	68.1 %	67	23.3 %	355	47.3 %
Vomiting	16	23.9 %	29	36.3 %	64	68.1 %	5	83.3 %	129	59.7 %	156	54.4 %	399	53.2 %
Myalgia	1	1.5%	8	10.0 %	16	17.0 %	5	83.3 %	31	14.4 %	120	41.8 %	181	24.1 %
Diarrhoea	2	3.0%	0	0.0%	1	1.1%	1	16.6 %	2	0.9%	12	4.2%	22	2.9%
Headache	3	4.5%	36	45.0 %	12	12.8 %	4	66.6 %	111	51.4 %	61	21.3 %	228	30.4 %

In the study it was observed that most common symptom in children with AFI was vomiting and pain abdomen accounting for 399(53.2%)and 355(47.3%) respectively. Least common symptom diarrhoea was seen in 22 (2.9%)of cases.

In cases of malaria pain abdomen 51(76.1%) was the common symptom and fever was associated with chills and rigors in 28 (41.8%)of cases.

In rickettsial disease pain abdomen 42(52.5%), headache 36(45%) and vomiting 29 (36.3%) were the associated non specific symptoms.

In enteric fever vomiting 64(68.1%), pain abdomen 42(44.7%) and myalgia 16(17%) were the common associated symptoms.

In leptospirosis all the cases were associated with pain abdomen 6(100%) and fever with chills, vomiting and myalgia were the associated non specific symptoms.

In dengue associated common non specific symptoms were pain abdomen 147(68.1%), vomiting 129(59.7%) and headache 111(51.4%).

In unclassified fever vomiting 156(54.4%), myalgia 120(41.8%), fever with chills89(31%), pain abdomen 67(23.3%) and headache 61(21.3%).

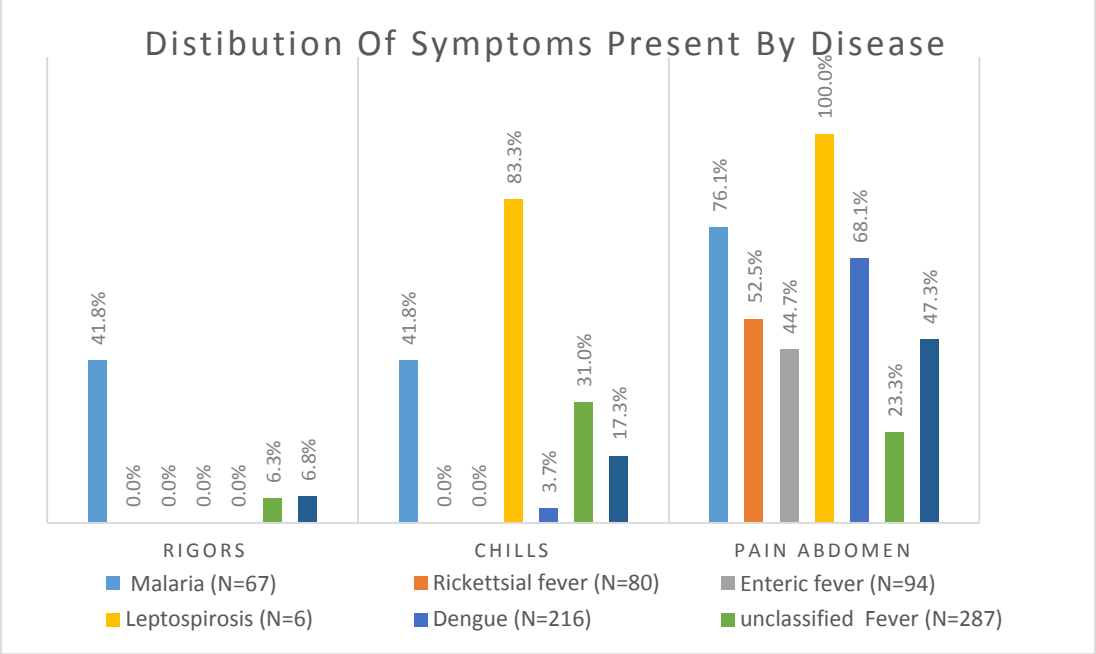


Figure 12a : BAR DIAGRAM SHOWING ASSOCIATION OF SYMPTOMS WITH AFI CASES

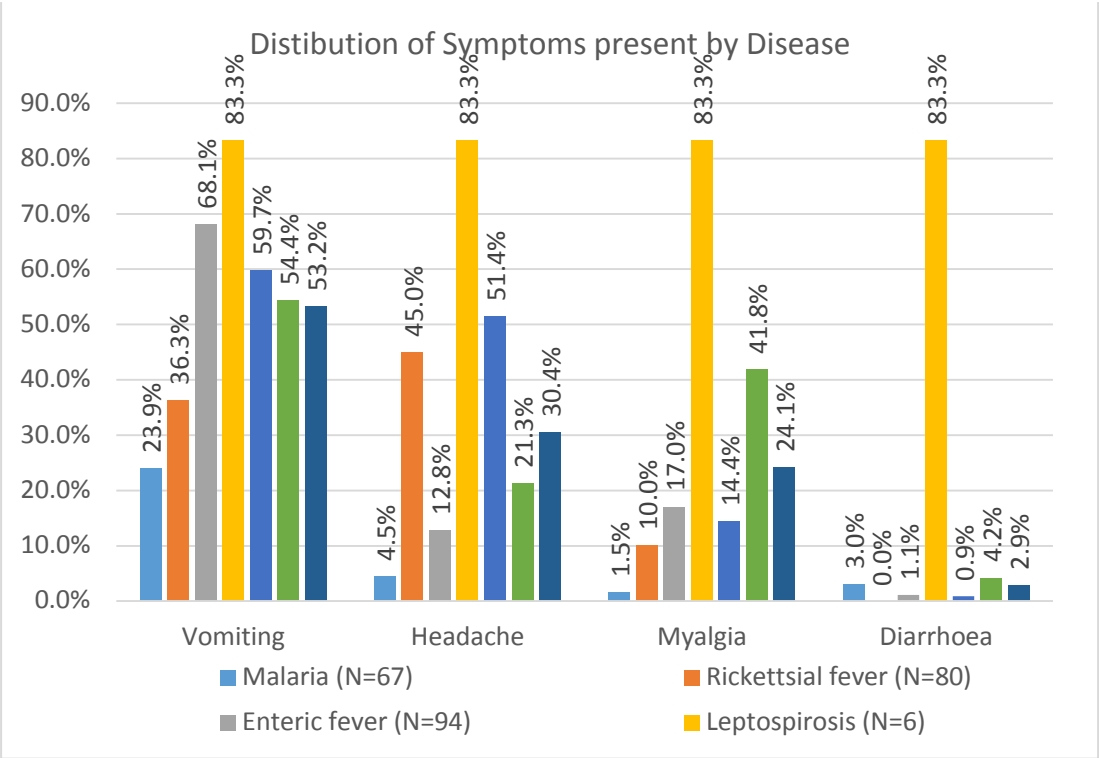


Figure 12b: BAR DIAGRAM SHOWING ASSOCIATION OF SYMPTOMS WITH AFI CASES

Table 12: CORRELATION OF CLINICAL SIGNS WITH VARIOUS AFI CASES

	Malaria (N=67)		Rickettsial fever (N=80)		Enteric fever (N=94)		Leptospirosis (N=6)		Dengue (N=216)		unclassified Fever (N=287)		Total (N=750)	
	N	%	n	%	N	%	n	%	n	%	n	%	n	%
Flushing	1	1.5 %	0	0.0 %	3	3.2 %	2	33.3%	142	65.7 %	92	32.1 %	240	32.0 %
Pallor	13	19.4 %	1	1.3 %	4	4.3 %	5	83.3%	3	1.4 %	9	3.1 %	35	4.7 %
Coated Tongue	0	0.0 %	0	0.0 %	16	17.0 %	4	66.7%	1	0.5 %	1	0.3 %	22	2.9 %
Bleeding Manifestation	1	1.5 %	2	2.5 %	2	2.1 %	1	16.7%	22	10.2 %	2	0.7 %	30	4.0 %
Rash	09	13.4 %	73	91.3 %	18	19.1 %	0	0.0%	73	33.8 %	41	14.3 %	214	28.5 %
Hepatomegaly	34	50.7 %	66	82.5 %	88	93.6 %	6	100.0 %	196	90.7 %	71	24.7 %	461	61.5 %
Splenomegaly	61	91.0 %	30	37.5 %	15	15.9 %	1	16.7%	24	11.1 %	9	3.1 %	140	18.6 %
Ascites	2	3.0 %	4	5.0 %	1	1.1 %	3	50.0%	44	20.4 %	11	3.8 %	65	8.7 %
ARDS	0	0.0 %	1	1.3 %	0	0.0 %	2	33.3%	11	5.1 %	1	0.3 %	15	2.0 %
Pl Effusion	0	0.0 %	1	1.3 %	0	0.0 %	3	50.0%	6	2.8 %	0	0.0 %	10	1.6 %
Shock	0	0.0 %	0	0.0 %	0	0.0 %	0	0.0%	12	5.6 %	0	0.0 %	12	1.3 %
Encephalitis	0	0.0 %	1	1.3 %	0	0.0 %	0	0.0%	6	2.8 %	0	0.0 %	7	0.9 %

In the study it was observed that common signs in children with AFI was hepatomegaly and flushing accounting for 461(61.5%), and 240(32.0%) respectively.

In malaria identified signs were splenomegaly 61(91%), hepatomegaly 34(50.7%) and pallor 13 (19.4%).

In rickettsial disease rash typical of rickettsial infection 73(91.3%), hepatomegaly 66(82.5%), and spleenomagly 30(37.5%) were the observed signs. There was 1 case of rickettsial encephalitis.

In enteric fever hepatomegaly 88(93.6%), rash 18(19.1%), coated tongue 16(17.1%) and spleenomagly 30(37.5%) were the observed signs.

In leptospirosis hepatomegaly was the consistent feature seen in all cases. Ascites and pleural effusion were noted in 3(50%) cases and ARDS noted in 2(33.3%) cases.

In dengue associated signs were hepatomegaly, flushing, rash and splenomegaly accounting for 196 (90.7%), 142(65.7%), 73(33.8%) and 24(11.1%) respectively. Other signs such as Ascites, bleeding manifestations, shock and encephalitis were seen in 44(20.4%), 22(10.2%), 12 (5.6%) and 2.8% of cases respectively.

In unclassified fever flushing, hepatomegaly and rash were the identified signs in 92(32.1%), 71(24.7%) and 41(14.3%) respectively.

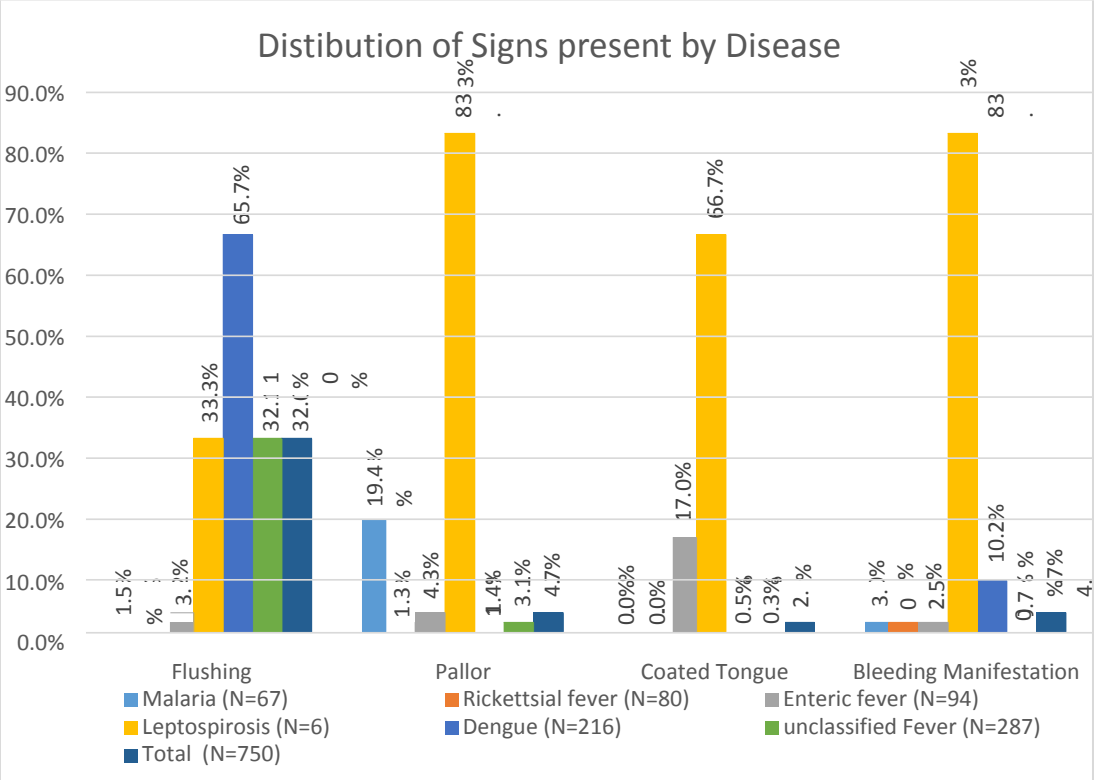


Figure 13a : BAR DIAGRAM SHOWING ASSOCIATION OF SIGNS WITH AFI CASES

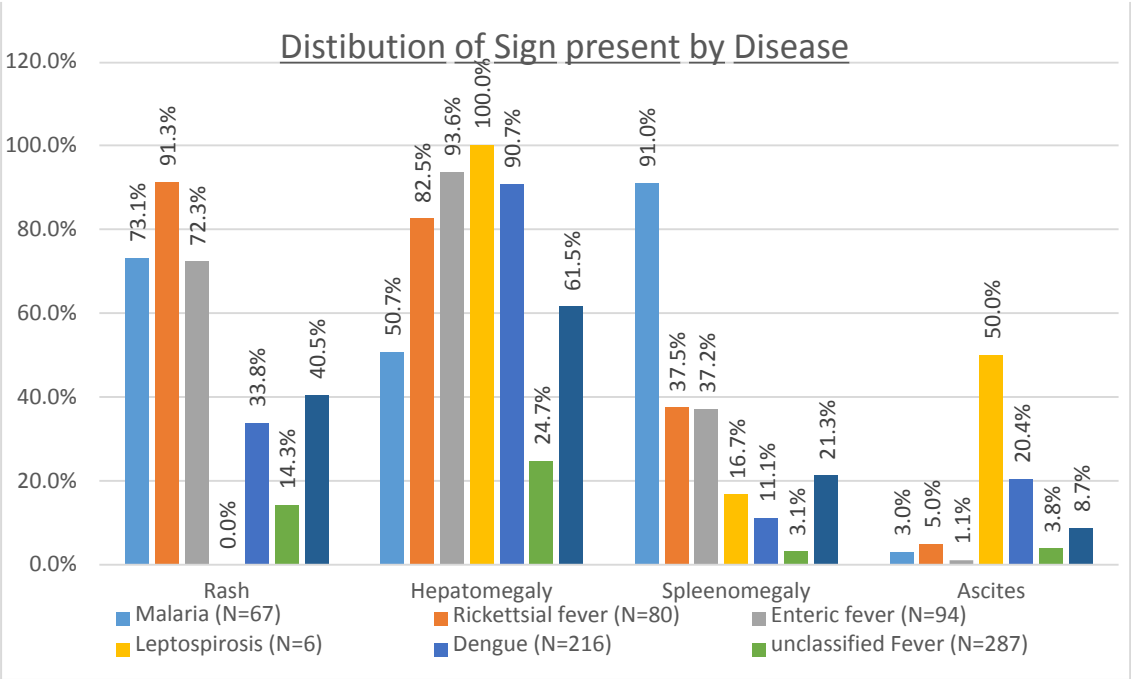


Figure 13b : BAR DIAGRAM SHOWING ASSOCIATION OF SIGNS WITH AFI CASES

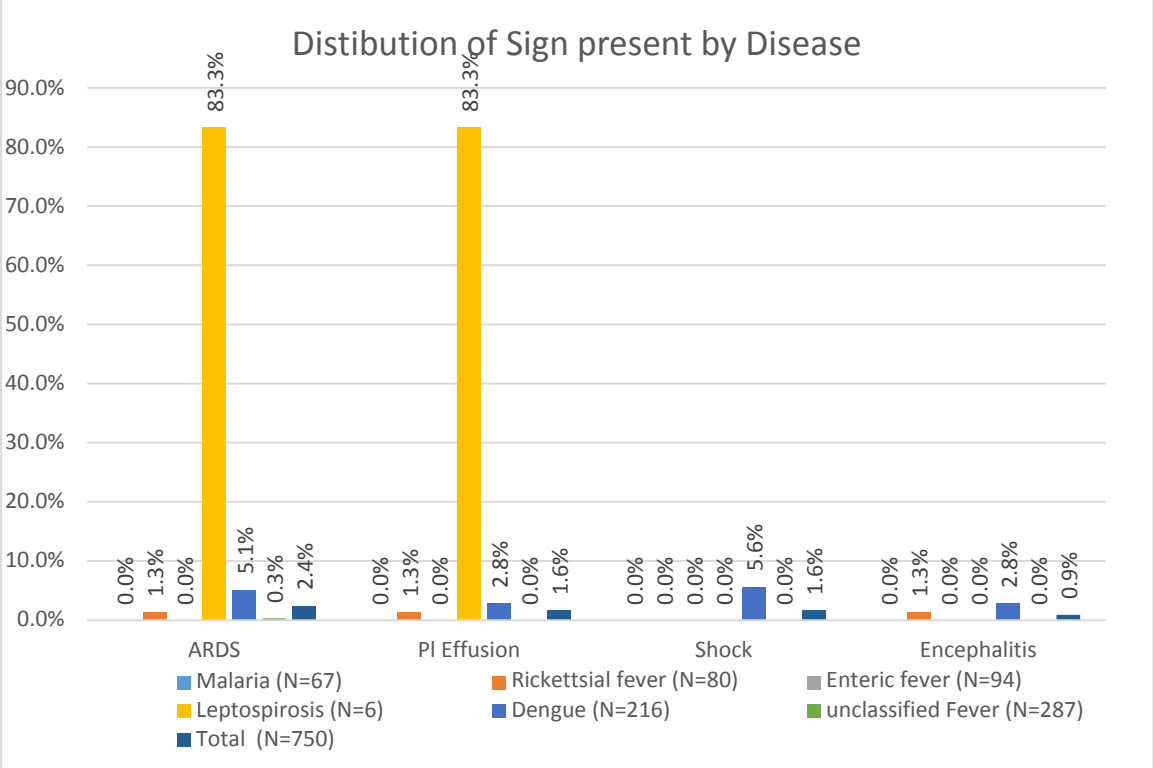


Figure 13c : BAR DIAGRAM SHOWING ASSOCIATION OF SYMPTOMS WITH AFI CASES

Table 13: LABORATORY CHARACTERISTICS IN VARIOUS AFI

	Malaria (N=67)		Rickettsial fever (N=80)		Enteric fever (N=94)		Leptospirosis (N=6)		Dengue (N=216)		Unclassified Fever (N=287)		Total (N=750)	
	n	%	N	%	n	%	n	%	n	%	n	%	n	%
Anaemia	36	53.7%	4	5.0%	19	20.2 %	1	16.7%	11	5.1%	59	20.6 %	130	17.3%
Leucocytosis	18	26.9%	31	38.8%	76	80.9 %	5	83.3%	3	1.4%	12	4.2%	145	19.3%
Leucopenia	7	10.4%	5	6.3%	0	0.0%	2	33.3%	136	63.0 %	55	19.2 %	205	27.3%
Thrombocytopenia	41	61.2%	33	41.3%	26	27.7 %	4	66.7%	207	95.8 %	141	49.1 %	452	60.3%

In the study, hemogram showed majority of the cases with AFI had thrombocytopenia 452(60.3%).

In malaria haemogram showed thrombocytopenia, anaemia and leucocytosis in 41(61.2%), 36(53.7%) and 18(26.9%) cases respectively.

In rickettsial fever haemogram showed thrombocytopenia and leucocytosis in 33(41.3%) and 31(38.8%) cases respectively.

In enteric fever haemogram showed leucocytosis, thrombocytopenia and anaemia in 76(80.9%), 26(27.7%) and 19(20.2%) cases respectively.

In leptospirosis haemogram showed leucocytosis and thrombocytopenia in 5(83.3%) and 4(66.6%) cases respectively.

In dengue haemogram showed thrombocytopenia 207(95.8%) and leucopenia 136(63%).

In unclassified fever haemogram showed thrombocytopenia , anaemia and leucocytosis in 41(61.2%), 36(53.7%) and 18(26.9%) respectively.

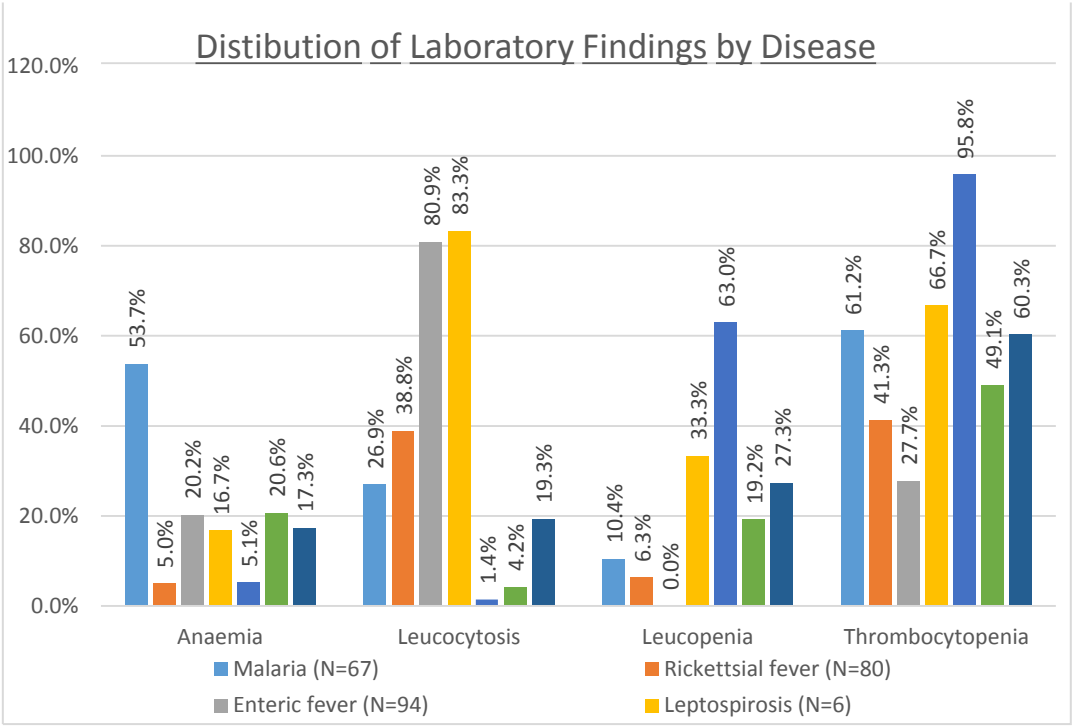


Figure 14 : BAR DIAGRAM SHOWING ASSOCIATION OF LABORATORY PARAMETERS WITH AFI CASES

Table 14 : ETIOLOGICAL AND LABORATORY CORRELATION OF AFI

	LABORATORY CONFIRMATION	CLINICAL DIAGNOSIS
Malaria	16 16 smear positive , 13 rapid card positive	67
Rickettsial fever	53 positive for weil felix	80
Enteric fever	63 63 widal positive, 4 blood c/s positive	94
Dengue fever	216 93 NS1Ag +, 73 IgM +, 50 IgM and NS1Ag +	216
Leptospirosis	4 cases with positive for IgM lepto	6
Unclassified fever		287

In the study on laboratory confirmation of various etiologies of AFI it was observed that

- Of the 67 finally diagnosed AFI cases of malaria, Smear positive cases were 16 (23.88%) and Rapid card positive for malarial parasite were 13 (19.4%). All rapid card test positive cases were positive even on smear examination.
- 216 cases of finally diagnosed dengue all had laboratory confirmation. Laboratory evidence of NS1 Ag positive was noted in93 cases(43.0%) , IgM positive in 73(33.8 %) cases and Both Ns1Ag and IgM positive 50(23.2%) cases.
- Among the 94 diagnosed cases of enteric fever, 63 (67%) cases demonstrated widal positivity and 4 (4.25%) had blood culture positive for salmonella typhi.All blood culture positive cases were positive by widal test also.
- Out of the 80 diagnosed rickettsial cases , 53 (66.25%) cases were positive by Weil felix test.

- IgM positive for leptospira was demonstrated by 4 (66.7%) cases of the 6 finally diagnosed cases of Leptospirosis.

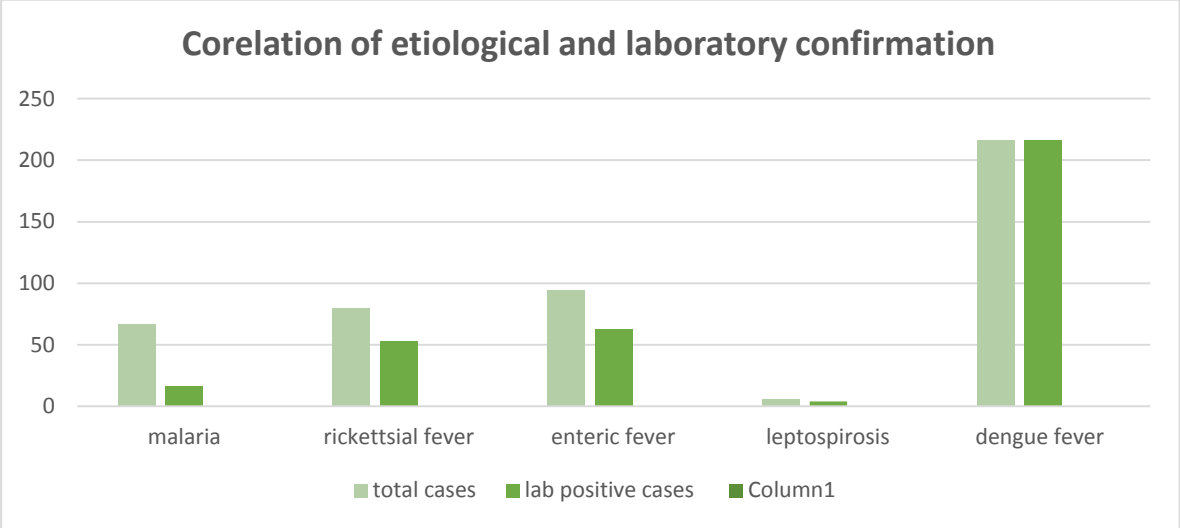


Figure 15: BAR DIAGRAM SHOWING LABORATORY CONFIRMATION OF VARIOUS AFI CASES

Table 15: ANALYSIS OF SIGNIFICANT PARAMETERS IN MALARIAL ILLNESS

	Malaria (N=67)		Other AFI (N=683)		P value	Adjusted Odds Ratio*	95% CI	
	n	%	n	%			Lower	Upper
Rigors	28	41.8%	23	3.4%	<0.001	57.128	12.747	256.036
Chills	28	41.8%	102	14.9%	<0.001	4.049	1.335	12.284
Pain Abdomen	51	76.1%	304	44.5%	<0.001	4.314	1.501	12.397
Vomiting	16	23.9%	383	56.1%	<0.001	0.251	0.089	0.711
Myalgia	1	1.5%	180	26.4%	<0.001	0.096	0.007	1.418
Diarrhoea	2	3.0%	20	2.9%	0.979			
Headache	3	4.5%	225	32.9%	<0.001	0.078	0.010	0.587
Shock	0	0.0%	12	1.8%	0.274			
Flushing	1	1.5%	239	35.0%	<0.001	0.018	0.001	0.286
Pallor	13	19.4%	22	3.2%	<0.001			
Coated Tongue	0	0.0%	22	3.2%	0.136			
Bleeding Manifestation	1	1.5%	29	4.2%	0.494			
Rash	9	13.4%	205	30.0%	<0.001			
Hepatomegaly	34	50.7%	427	62.5%	0.059			
Splenomegaly	61	91.0%	99	14.5%	<0.001	48.737	14.380	165.178
Ascites	2	3.0%	63	9.2%	0.083			
ARDS	0	0.0%	18	2.6%	0.179			
Pl Effusion	0	0.0%	12	1.8%	0.274			
Encephalitis	0	0.0%	7	1.0%	0.405			
Anaemia	36	53.7%	94	13.8%	<0.001	10.160	3.533	29.217
Leucocytosis	18	26.9%	127	18.6%	0.102			
Leucopenia	7	10.4%	198	29.0%	0.001			
Thrombocytopenia	41	61.2%	411	60.2%	0.871			

*Logistic Regression

A logistic regression was performed to ascertain the effects of rigors, chills, pain abdomen, vomiting, myalgia, headache, flushing, pallor rash, splenomegaly and anaemia on the likelihood that participants have Malaria.

Presence of rigors was 57.128 times more likely to associated with malaria than when rigors absent. Splenomegaly present were 48.747 times more likely to exhibit malaria than splenomegaly absent.

Anaemia present were 10.160 times more likely to exhibit malaria than anaemia absent. Chills present were 4.049 times more likely to exhibit malaria than chills absent.

Pain abdomen present were 4.314 times more likely to exhibit malaria than pain abdomen absent.

Vomiting, myalgia, headache and flushing was associated with a reduction in the likelihood of exhibiting Malaria.

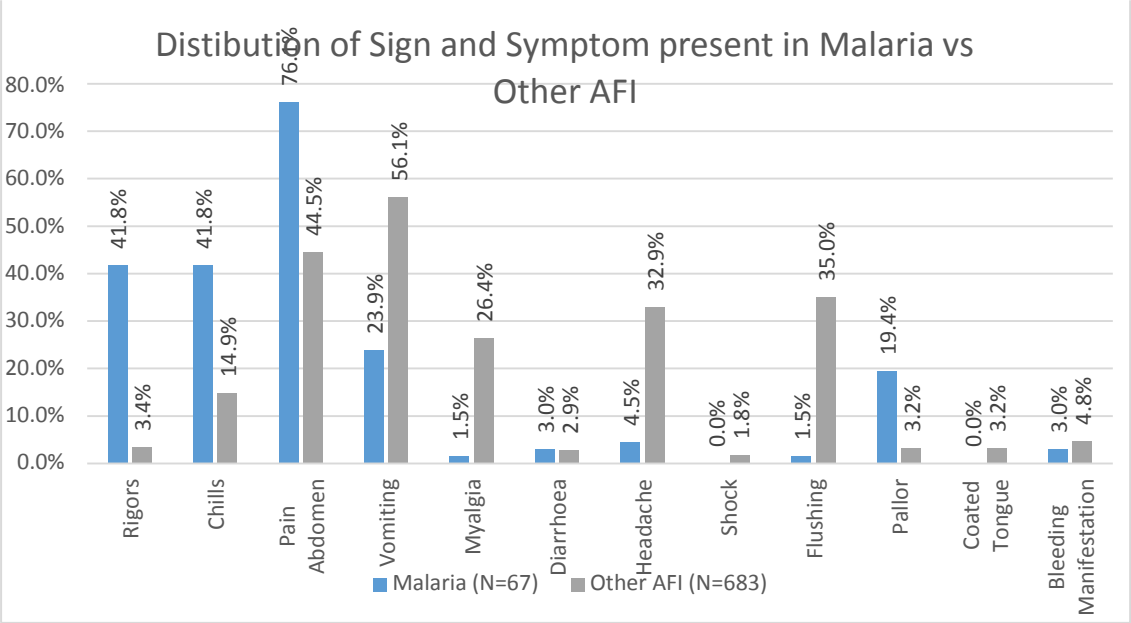


Figure 16a: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF MALARIA AND OTHER AFI CASES

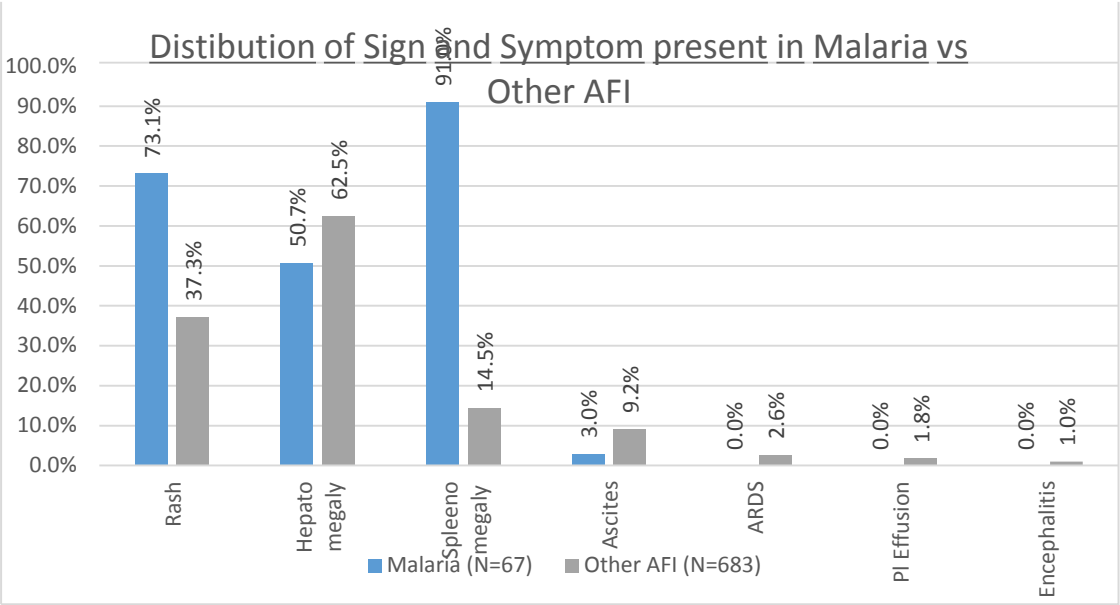


Figure 16b: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF MALARIA WITH OTHER AFI CASES

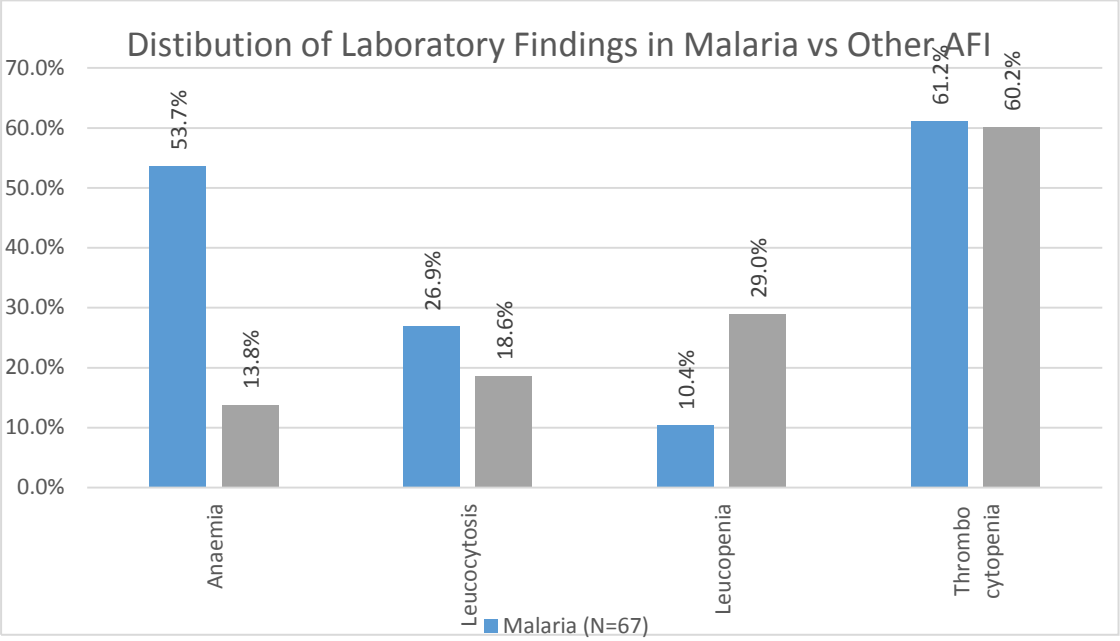


Figure 16c: BAR DIAGRAM SHOWING COMPARISON OF LABORATORY PARAMETERS OF MALARIA WITH OTHER AFI CASES

Table 16: ANALYSIS OF SIGNIFICANT PARAMETERS IN RICKETTSIAL DISEASE

	Rickettsial fever (N=80)		Other AFI (N=670)		P value	Adjusted Odds Ratio*	95% CI	
	N	%	n	%			Lower	Upper
Rigors	0	0.0%	51	7.6%	0.011			
Chills	0	0.0%	130	19.4%	<0.001			
Pain Abdomen	42	52.5%	313	46.7%	0.327			
Vomiting	29	36.3%	370	55.2%	0.001			
Myalgia	8	10.0%	173	25.8%	0.002			
Diarrhoea	0	0.0%	22	3.3%	0.100			
Headache	36	45.0%	192	28.7%	0.003	6.071	3.307	11.147
Shock	0	0.0%	12	1.8%	0.228			
Flushing	0	0.0%	240	35.8%	<0.001			
Pallor	1	1.3%	34	5.1%	0.125			
Coated Tongue	0	0.0%	22	3.3%	0.100			
Bleeding Manifestation	2	2.5%	33	4.9%	0.331			
Rash	73	91.3%	231	34.5%	<0.001	22.801	9.060	57.381
Hepatomegaly	66	82.5%	395	59.0%	<0.001	2.544	1.243	5.207
Spleenomegaly	30	37.5%	130	19.4%	<0.001	1.938	1.083	3.468
Ascites	4	5.0%	61	9.1%	0.217			
ARDS	1	1.3%	17	2.5%	0.477			
Pl Effusion	1	1.3%	11	1.6%	0.792			
Encephalitis	1	1.3%	6	0.9%	0.358			
Anaemia	4	5.0%	126	18.8%	0.002			
Leucocytosis	31	38.8%	114	17.0%	<0.001			
Leucopenia	5	6.3%	200	29.9%	<0.001	0.230	0.100	0.526
Thrombocytopenia	33	41.3%	419	62.5%	<0.001			

*Logistic Regression

A logistic regression was performed to ascertain the effects of headache, rash, hepatomegaly, splenomegaly and leucopenia the likelihood that study subjects have Rickettsial disease.

Children with rash were 22.801 times more likely to exhibit rickettsial disease than those without rash.

Children with of hepatomegaly and splenomegaly would likely to have rickettsial disease 2.544 and 1.938 times respectively.

Leucopenia was associated with a reduction in the likelihood of exhibiting rickettsial disease.

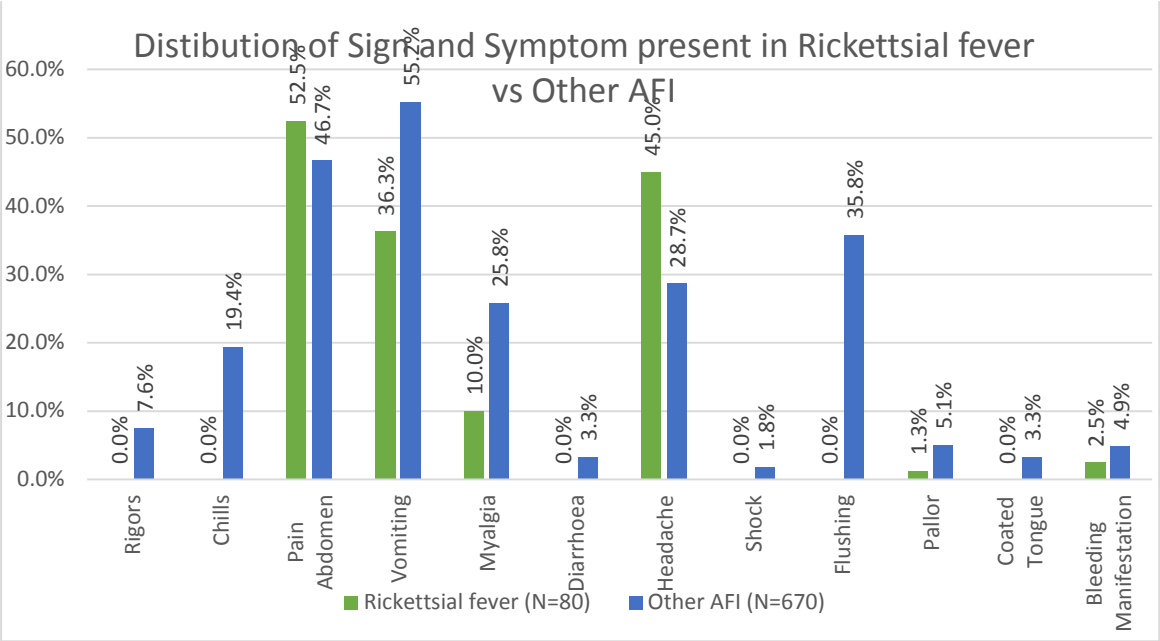


Figure 17a : BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF RICKETTSIAL FEVER WITH OTHER AFI CASES

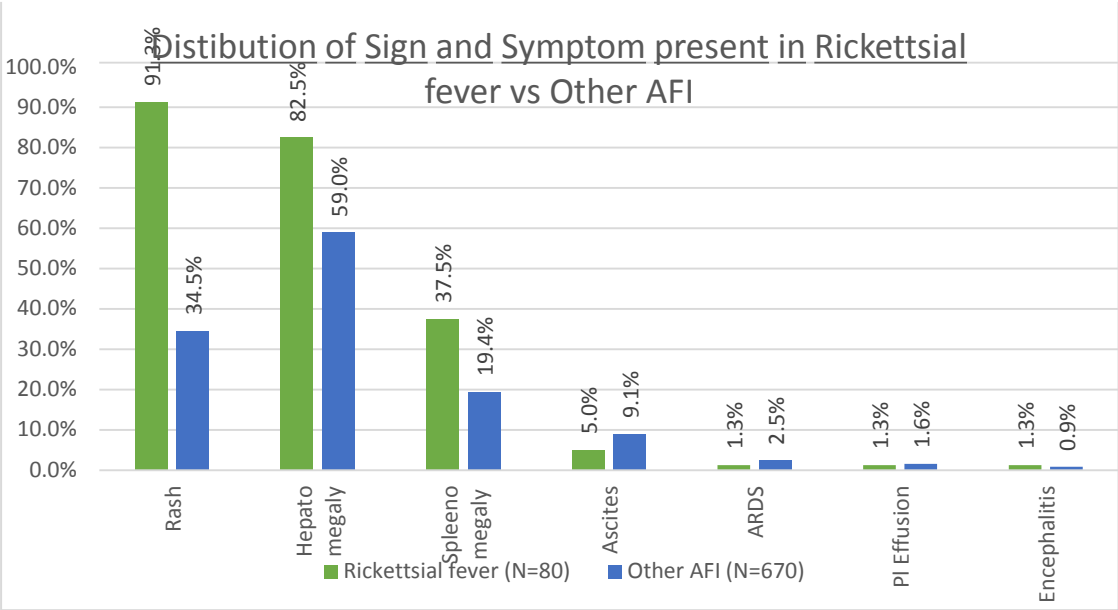


Figure 17b : BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF RICKETTSIAL FEVER WITH OTHER AFI CASES

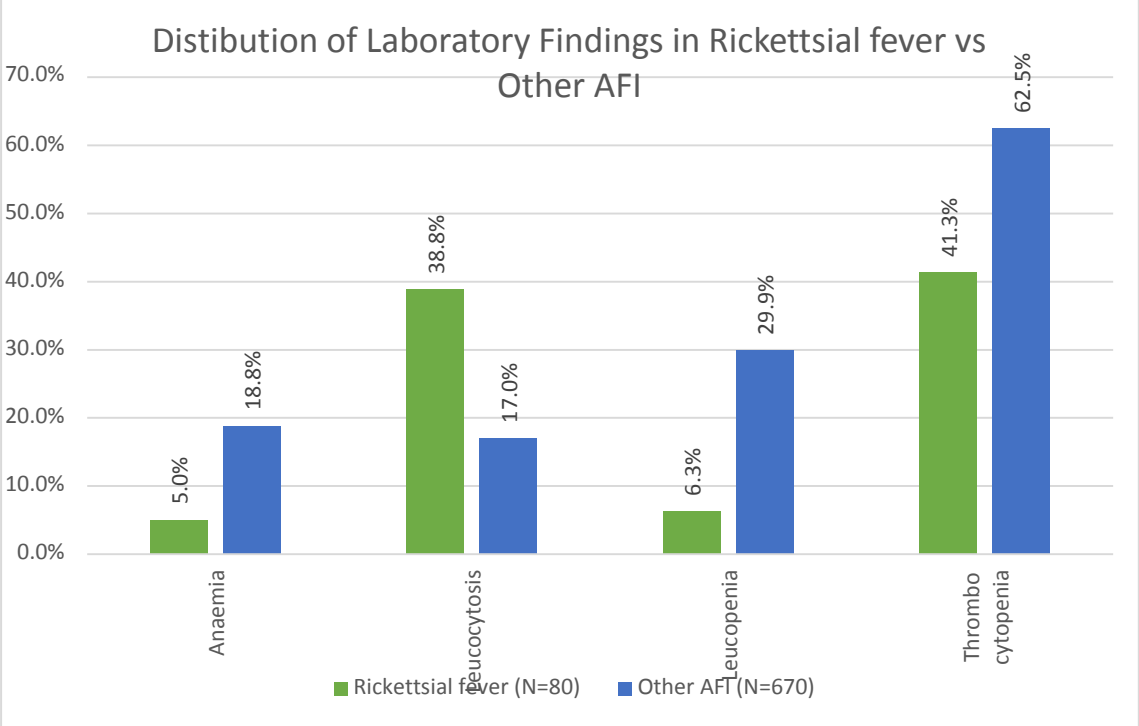


Figure 17c : BAR DIAGRAM SHOWING COMPARISON OF LABORATORY PARAMETERS OF RICKETTSIAL FEVER WITH OTHER AFI CASES

Table 17: ANALYSIS OF SIGNIFICANT PARAMETERS IN ENTERIC FEVER

	Enteric fever (N=94)		Other AFI (N=656)		P value	Adjusted Odds Ratio*	95% CI	
	N	N	n	%			Lower	Upper
Rigors	0	0.0%	51	7.8%	0.005			
Chills	0	0.0%	130	19.8%	<0.001			
Pain Abdomen	42	44.7%	313	47.7%	0.582			
Vomiting	64	68.1%	335	51.1%	0.002	1.991	0.957	4.141
Myalgia	16	17.0%	165	25.2%	0.085			
Diarrhoea	1	1.1%	21	3.2%	0.251			
Headache	12	12.8%	216	32.9%	<0.001	0.427	0.174	1.047
Shock	0	0.0%	12	1.8%	0.186			
Flushing	3	3.2%	237	36.1%	<0.001	0.243	0.078	0.755
Pallor	4	4.3%	31	4.7%	0.840			
Coated Tongue	16	17.0%	6	0.9%	<0.001	177.086	14.398	2177.979
Bleeding Manifestation	2	2.1%	33	5.0%	0.212			
Rash	18	19.1%	196	29.8%	<0.001			
Hepatomegaly	88	93.6%	373	56.9%	<0.001	9.578	3.087	29.718
Splenomegaly	15	15.9%	125	19.1%	<0.001			
Ascites	1	1.1%	64	9.8%	0.005			
ARDS	0	0.0%	18	2.7%	0.104			
Pl Effusion	0	0.0%	12	1.8%	0.186			
Encephalitis	0	0.0%	7	1.0%	0.314			
Anaemia	19	20.2%	111	16.9%	0.430			
Leucocytosis	76	80.9%	69	10.5%	<0.001	13.479	6.727	27.008
Leucopenia	0	0.0%	205	31.3%	<0.001			
Thrombocytopenia	26	27.7%	426	64.9%	<0.001	0.515	0.256	1.034

*Logistic Regression

A logistic regression was performed to ascertain the effects of vomiting, headache, flushing, coated tongue, hepatomegaly, leucocytosis and thrombocytopenia on the likelihood that study subjects have enteric fever.

Presence of coated tongue in children with AFI was 177.086 times more likely to exhibit enteric fever than absence of coated tongue.

Children with hepatomegaly were 9.578 times more likely to exhibit enteric fever than hepatomegaly being absent.

Presence of leucocytosis on hemogram was 13.479 times more likely to exhibit enteric fever than absence of leucocytosis.

Headache, flushing and thrombocytopenia was associated with a reduction in the likelihood of exhibiting enteric fever.

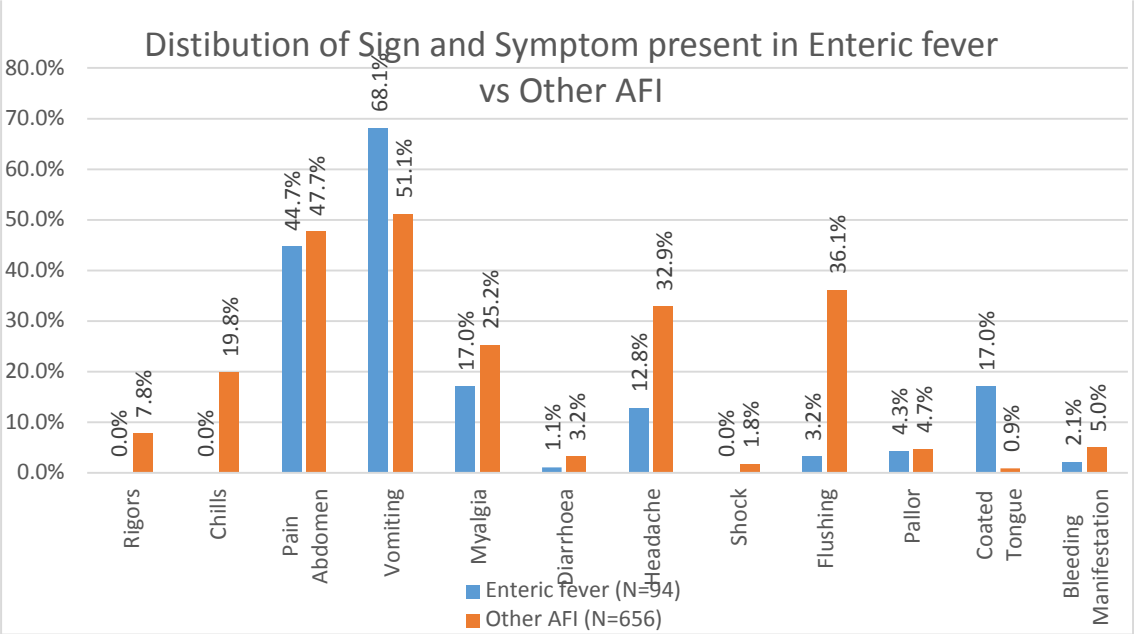


Figure 18a: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF ENTERIC FEVER WITH OTHER AFI CASES

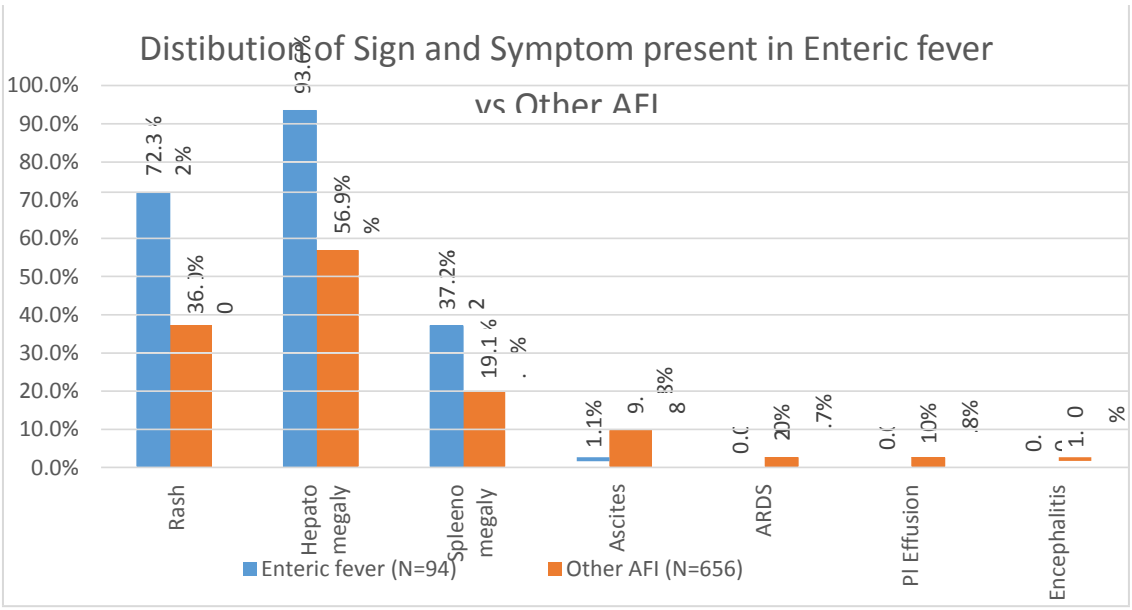


Figure 18b: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF ENETRIC FEVER WITH OTHER AFI CASES

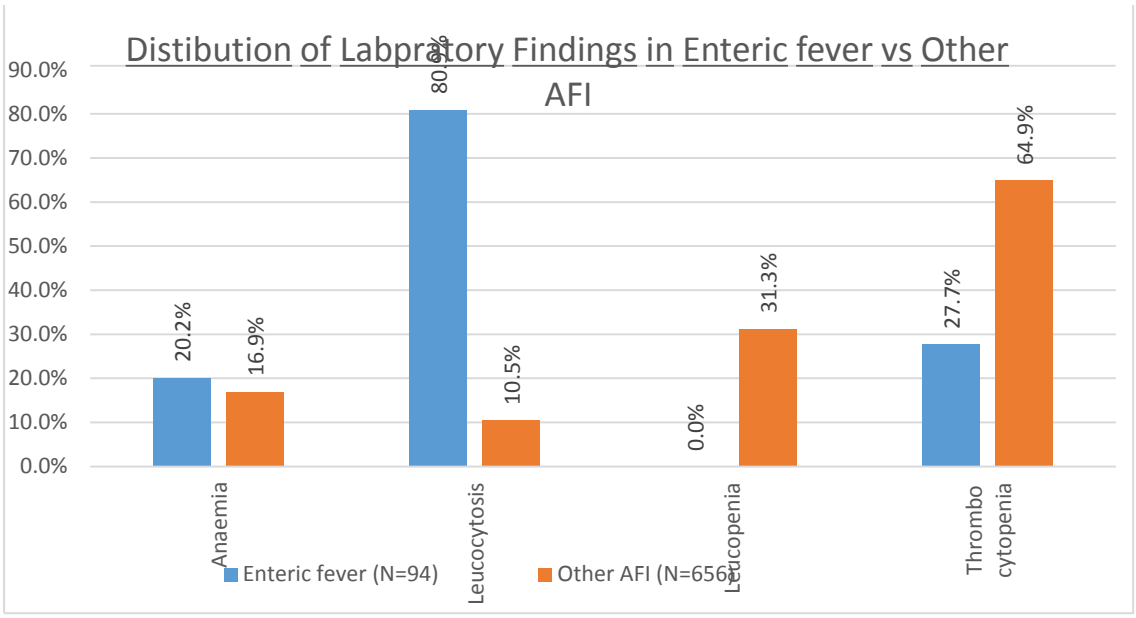


Figure 18c: BAR DIAGRAM SHOWING COMPARISON OF LABORATORY PARAMETERS OF ENTERIC FEVER WITH OTHER AFI CASES

Table 18: ANALYSIS OF SIGNIFICANT PARAMETERS IN DENGUE FEVER

	Dengue (N=216)		Other AFI (N=670)		P value	Adjusted Odds Ratio*	95% CI	
	N	N	N	%			Lower	Upper
Rigors	0	0.0%	51	9.6%	<0.001			
Chills	8	3.7%	122	22.8%	<0.001	0.046	0.012	0.178
Pain Abdomen	147	68.1%	208	39.0%	<0.001	1.960	0.990	3.881
Vomiting	129	59.7%	270	50.6%	0.023			
Myalgia	31	14.4%	150	28.1%	<0.001			
Diarrhoea	2	0.9%	20	3.7%	0.038	0.043	0.007	0.247
Headache	111	51.4%	117	21.9%	<0.001	4.587	2.125	9.902
Shock	12	5.6%	0	0.0%	<0.001			
Flushing	142	65.7%	98	18.4%	<0.001	9.835	4.658	20.763
Pallor	3	1.4%	32	6.0%	0.007			
Coated Tongue	1	0.5%	21	3.9%	0.011			
Bleeding Manifestation	22	10.2%	13	2.4%	<0.001	19.387	3.320	113.203
Rash	73	33.8%	231	43.3%	0.017			
Hepatomegaly	196	90.7%	265	49.6%	<0.001	5.264	2.493	11.114
Splenomegaly	24	11.1%	136	25.5%	<0.001			
Ascites	44	20.4%	21	3.9%	<0.001			
ARDS	11	5.1%	7	1.3%	0.002			
Pl Effusion	6	2.8%	6	1.1%	0.102			
Encephalitis	6	2.8%	1	0.2%	0.001			
Anaemia	11	5.1%	119	22.3%	<0.001	0.170	0.054	0.537
Leucocytosis	3	1.4%	142	26.6%	<0.001	0.113	0.026	0.495
Leucopenia	136	63.0%	69	12.9%	<0.001	8.790	4.185	18.464
Thrombocytopenia	207	95.8%	245	45.9%	<0.001	21.111	8.330	53.498

*Logistic Regression

A logistic regression was performed to ascertain the effects of chills, pain abdomen, diarrhoea, headache, flushing, pallor rash, bleeding manifestation, leucocytosis. Leukopenia, thrombocytopenia and anaemia on the likelihood that study participants have Dengue.

Children with AFI associated with headache and flushing were 4.587 and 9.835 times more likely to exhibit dengue fever than their absence.

Presence of hepatomegaly in children with AFI was 5.264 times more likely to exhibit dengue than hepatomegaly absent.

Bleeding manifestation in children with AFI were 19.387 times more likely to exhibit dengue than bleeding manifestation absent.

Thrombocytopenia and leucopenia on hemogram of children with AFI were 21.111 and 4.185 times respectively more likely to exhibit dengue than absence of thrombocytopenia and leucopenia..

Children with Pain abdomen were 1.960 times more likely to exhibit dengue than pain abdomen absent.

Chills, diarrhoea, anaemia and leucocytosis was associated with a reduction in the likelihood of exhibiting Dengue.

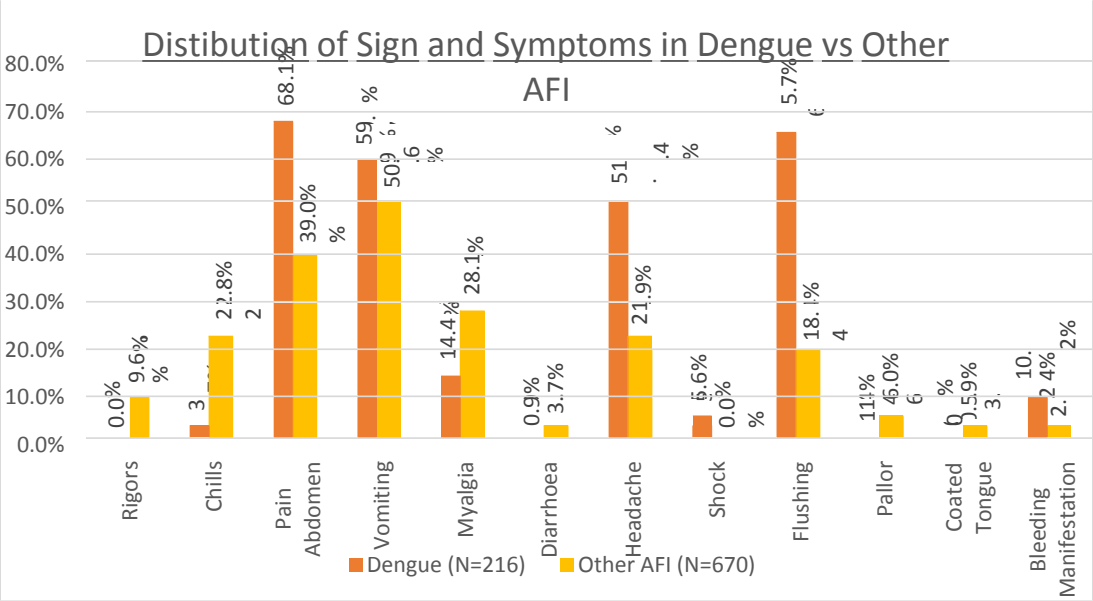


Figure 19a: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF DENGUE FEVER WITH OTHER AFI CASES

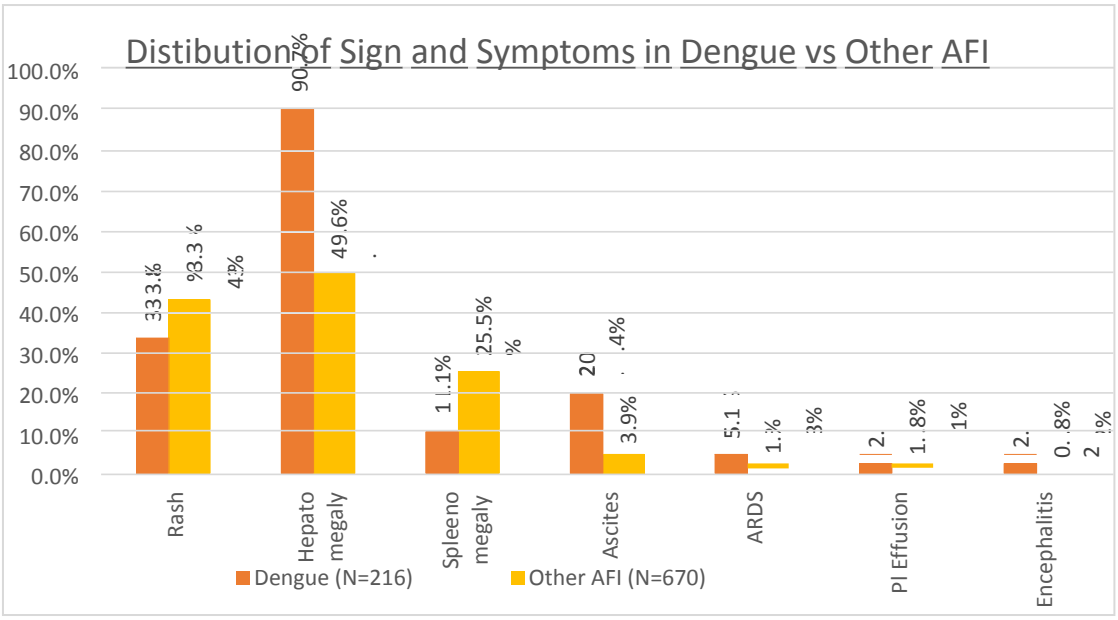


Figure 19b: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF DENGUE FEVER WITH OTHER AFI CASES

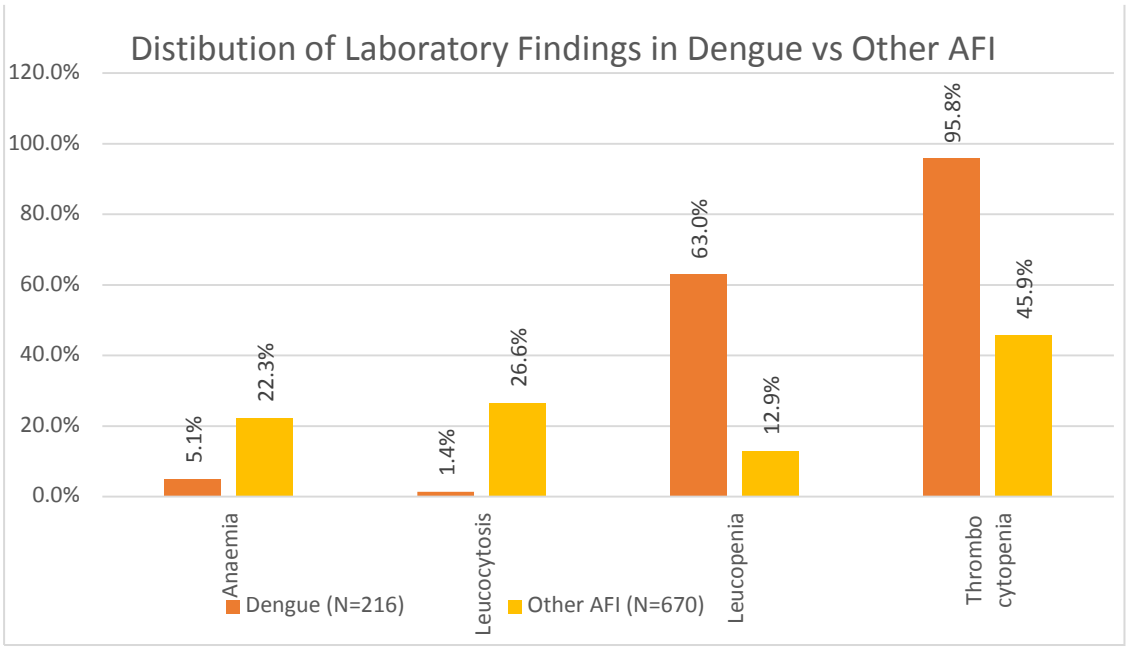


Figure 19c: BAR DIAGRAM SHOWING COMPARISON OF LABORATORY PARAMETERS OF DENGUE FEVER WITH OTHER AFI CASES

Table 19: ANALYSIS OF SIGNIFICANT PARAMETERS IN UNCLASSIFIED AFI

	Unclassified Fever (N=287)		Other AFI (N=463)		P value	Adjusted Odds Ratio*	95% CI	
	N	n	n	%			Lower	Upper
Rigors	18	6.3%	33	7.1%	0.651			
Chills	89	31.0%	41	8.9%	<0.001	6.624	3.205	13.690
Pain Abdomen	67	23.3%	288	62.2%	<0.001	0.325	0.193	0.546
Vomiting	156	54.4%	243	52.5%	0.618			
Myalgia	120	41.8%	61	13.2%	<0.001	1.875	0.989	3.555
Diarrhoea	12	4.2%	10	2.2%	0.111			
Headache	61	21.3%	167	36.1%	<0.001	0.307	0.171	0.552
Shock	0	0.0%	12	2.6%	0.006			
Flushing	92	32.1%	148	32.0%	0.979			
Pallor	9	3.1%	26	5.6%	0.118			
Coated Tongue	1	0.3%	21	4.5%	0.001			
Bleeding Manifestation	2	0.7%	33	7.1%	<0.001	0.138	0.025	0.750
Rash	41	14.3%	263	56.8%	<0.001	0.147	0.084	0.258
Hepatomegaly	71	24.7%	390	84.2%	<0.001	0.155	0.094	0.256
Splenomegaly	9	3.1%	151	32.6%	<0.001	0.074	0.029	0.186
Ascites	11	3.8%	54	11.7%	<0.001			
ARDS	1	0.3%	17	3.7%	0.004			
Pl Effusion	0	0.0%	12	2.6%	0.006			
Encephalitis	0	0.0%	7	1.5%	0.036			
Anaemia	59	20.6%	71	15.3%	0.066			
Leucocytosis	12	4.2%	133	28.7%	<0.001	0.178	0.080	0.393
Leucopenia	55	19.2%	150	32.4%	<0.001	0.392	0.210	0.732
Thrombocytopenia	141	49.1%	311	67.2%	<0.001	0.334	0.195	0.572

*Logistic Regression

A logistic regression was performed to ascertain the effects of chills, pain abdomen, diarrhoea, myalgia, headache, rash, bleeding manifestation, hepatomegaly,

splenomegaly, leucocytosis. Leucopenia and thrombocytopenia on the likelihood that study participants have unclassified fever.

Children with AFI associated with chills and myalgia were 6.624 and 1.875 times more likely to exhibit unclassified fever than their absence.

Pain abdomen, diarrhoea, headache, rash, bleeding manifestation, hepatomegaly, splenomegaly, leucocytosis, leucopenia and thrombocytopenia was associated with a reduction in the likelihood of exhibiting unclassified fever.

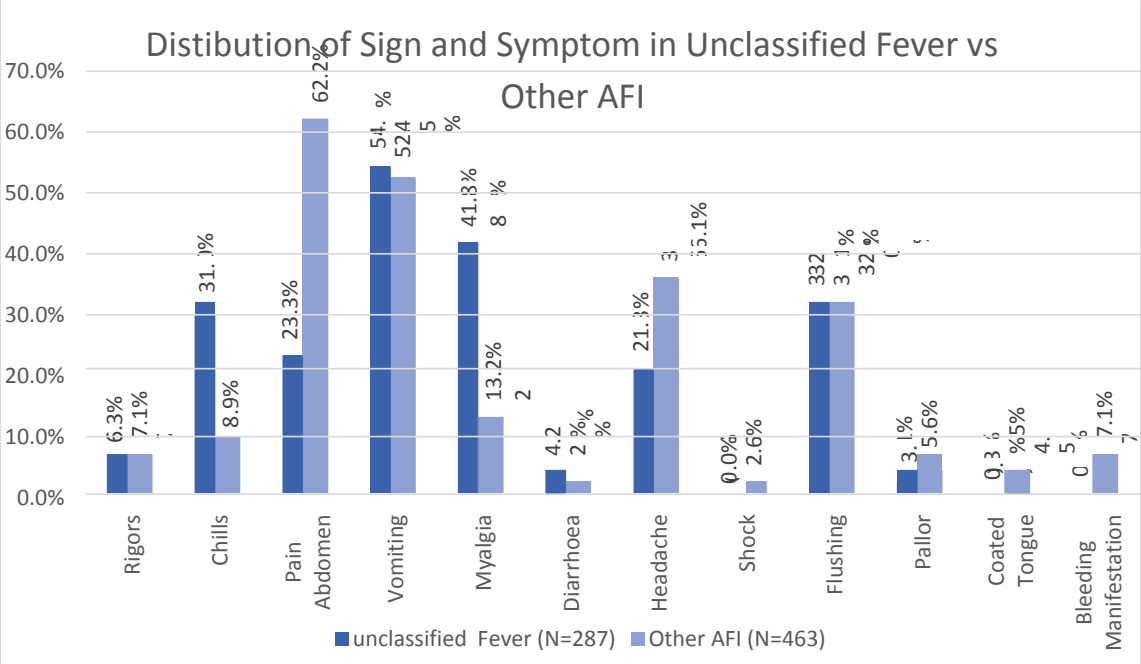


Figure 20a: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF UNCLASSIFIED FEVER WITH OTHER AFI CASES

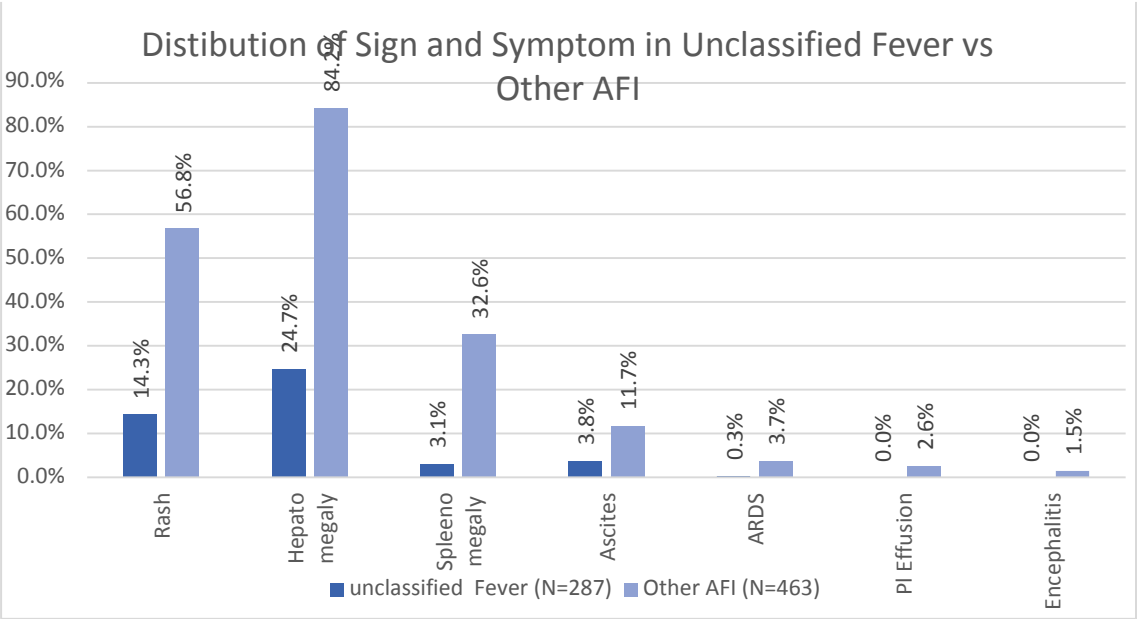


Figure 20b: BAR DIAGRAM SHOWING COMPARISON OF SIGNS AND SYMPTOMS OF UNCLASSIFIED FEVER WITH OTHER AFI CASES

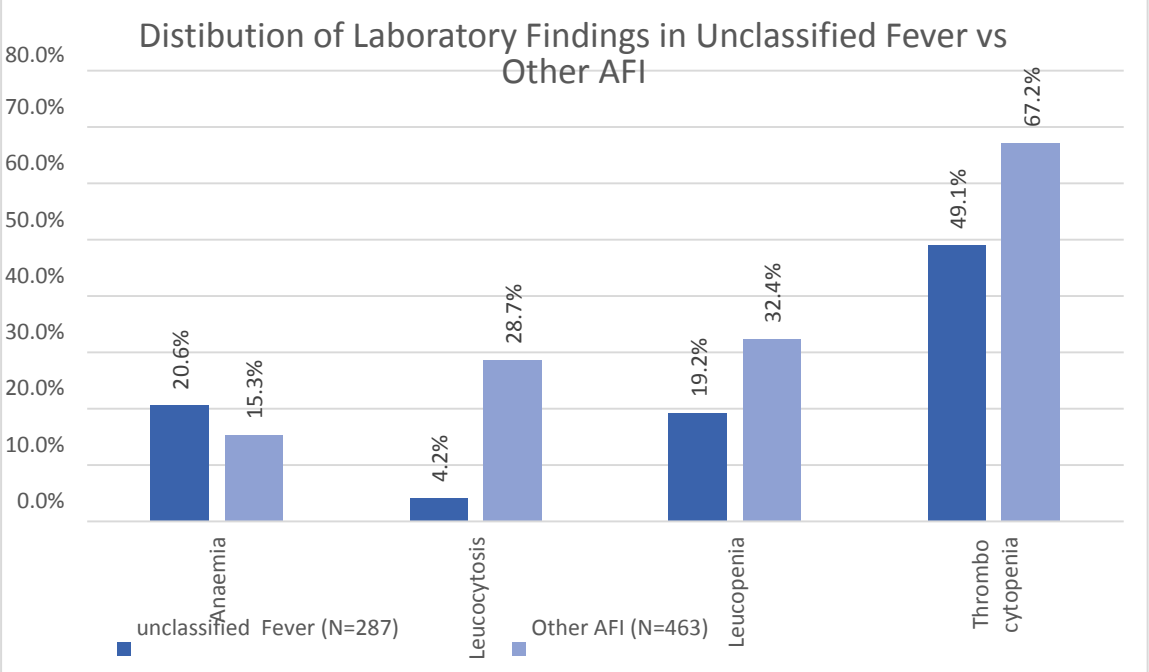


Figure 20c: BAR DIAGRAM SHOWING COMPARISON OF LABORATORY PARAMETERS OF UNCLASSIFIED FEVER WITH OTHER AFI CASES

**Logistic regression models were not created for the small patient cohorts with leptospirosis.

DISCUSSION

DISCUSSION

Fever is an ancient adaptive compensatory defence mechanism which causes activation of immune system, decrease in bacterial and viral growth rate, and improve host survival in response to invasion by foreign antigens[4]. Acute febrile illness is defined as fever of less than two weeks duration with no identifiable cause on clinical examination[2,5] . Fever commonly accompanies a wide range of childhood illnesses and if not managed appropriately, can lead to potentially serious outcomes including death [43]. Infectious diseases are an important cause of morbidity and mortality in children with AFI in the developing countries. Due to the overlapping manifestations of the febrile illness in the acute phase, lack of knowledge of the locally prevalent disease and limitation in the availability of the diagnostic facility poses a diagnostic and therapeutic challenge to the treating physician[9,44,59] . There is supportive evidence from the literatures that, there is need for knowledge of locally prevalent diseases for syndromic based management of the AFI. The following findings of our study tries to delineate the clinico- etiological profile of the common infectious diseases in our region.

Demographic details

In our study, 750 subjects between 1month to 18 years of age were included, the median age of children hospitalised with AFI was 84months (7years). Infants, toddlers and preschool children accounted for 57. 9%, 40.3% were school going children and 11.9% were in the adolescent age group (table 4a). Similarly, Capeding M R et al[6] reported in their multicentre active surveillance study including 1500 subjects aged between 2 to 14years, the median age of presentation of children with

AFI was 7years. In contrast to Crump J A et al[45] and Chheng K et al[44] in their study observed median age of children with AFI was 2years.

Out of 750 subjects 389 (53.1%) were males and 352(46.9%) were females (table 3). Chheng K et al[44] similarly reported 54.5% of their study subjects with AFI were male.

In our study, it was observed that there was male preponderance seen in children with AFI with etiological diagnosis of malaria, rickettsial disease, enteric fever and unclassified illness. Whereas, female preponderance was seen in cases of dengue fever and leptospirosis (table 5b).

Majority of our study subjects were Hindus, accounting to 644 (85.9%), followed by 92(12.3%) and 14(1.9%) were Muslims and Christians respectively. There was no significant statistical association noted (table 6). Analysis of socio-economic status among the studied families revealed almost half of the families belonging to Class II. Class III and Class IV combined constituted nearly the remaining half (table 8).

Duration of fever and AFI

In our study, 712 (94.9%) hospitalised children with AFI had fever of less than 1 week duration (table 9a). The median duration of illness prior to admission in children with AFI was 4days. Capeding M Ret al[6] have reported similarly in their study that 96.5% of the subjects presented with fever of less than 5 days. Chheng Ket al[44] in their study observed median duration of illness being 3days before admission.

In the study, duration of fever of greater than 1week at presentation was seen in cases of leptospirosis, rickettsial fever accounting to 33.3.% and 21.3% and only 2.3% of the dengue fever presented with second week of fever.

Clinical profile of AFI

In our present study, vomiting (53.2%), pain abdomen (47.3%), headache (30.4%) and myalgia (24.1%) were the common nonspecific symptoms at presentation in children with AFI.(table 9). Major signs observed were hepatomegaly and flushing accounting for 461(61.5%), and 240(32.0%) respectively. Splenomegaly, rash, pallor and coated tongue were the rare clinical signs noted (table 12). Kasper R M et al [45] in their study reported most common symptoms of enrolled patients were headache (69.5%), cough (57.5%), sore throat (46.6%), chills (48.1%) and malaise (46.8%).

Out of 67 subjects with **malarial disease,** pain abdomen (76.1%), fever with chills and rigors (41.8%) and vomiting (23.9%) were the common symptoms. Fever with chills and rigors typical of malarial illness was seen only in 41.8% of our subjects. Major identified signs in malaria were splenomegaly 61(91%), hepatomegaly 34(50.7%) and pallor 13 (19.4%). Other uncommon signs observed were rash, ascites and bleeding manifestation in the form of epistaxis. Analysis by logistic regression (table 13) noted that presence of fever with rigors and splenomegaly was consistent with malaria.

Major symptoms noted in 80 children with **rickettsial disease** (table 16) were pain abdomen in 52.5%, headache, myalgia and vomiting were the other associated nonspecific symptoms. Most common sign observed in the study subjects was rash in 91.3%, which was the typical maculo papular rash involving the palms and soles. There were 2 cases with purpura fulminans. Other signs noted were hepatomegaly in 82.5% and splenomegaly in 37.5%. Complications such as ascites, pleural effusion and ARDS were all noted in 1 case and encephalitis was noted in another case. Analysis suggested that presence of the typical rash showed higher probability of

rickettsial disease (table 14). Eschar typical of the disease was not seen in any of the cases in our study. In a study by Prabhu M and others[42], on children with rickettsioses clinical characteristics reported were nonspecific which did not clearly aid in distinguishing other febrile illness. But, they have also mentioned presence of clinical hepatitis would give a diagnostic clue.

Common complaints at presentation among 94 children with **enteric fever** were gastrointestinal symptoms such as vomiting, pain abdomen accounting for 68.1%, and 44.1% respectively. Headache, diarrhoea and myalgia were noted in less than 20% of the cases. The observed clinical signs in our study, hepatomegaly (93.6%) was the major association on analysis, rash which was uncommon and nonspecific was noted only in 19.1%, which was in hand with the literature data available[33]. Logistic regression analysis showed (table 15) Coated tongue though seen in only 17.1%, its presence increased the probability of enteric fever. Splenomegaly was uncommonly observed in 37.5% cases.

In 216 children diagnosed with **dengue**, associated common nonspecific symptoms were pain abdomen 68.1%, vomiting 59.7% and headache 51.4%. Myalgia, fever with chills and diarrhoea were the less frequently associated symptoms noted in less than 15% of the cases. The recorded clinical signs in children with dengue were abdominal tenderness, hepatomegaly, flushing in more than 50 % of the cases, rash and splenomegaly were less commonly noted. Signs observed in cases of dengue with warning signs and severe dengue were ascites, bleeding manifestations (malena (21), petechiae (16), hematemesis (5), epistaxis (9)), shock and pleural effusion were seen in 20.4%, 10.2%, 5.6% and 2.8% of cases respectively. Five cases of severe dengue had ARDS and 6 had dengue encephalitis. On univariate and multivariate analysis (table 16) of the various signs and symptoms in our study headache, flushing, pain

abdomen, hepatomegaly and bleeding manifestations were more likely to suggest dengue in a child with AFI. Similarly in a study by Reller E Met al[59] to define the epidemiology of dengue in Southern Sri Lanka noted the most frequent symptom was headache accounting to 75.9% and more than half of their patients presented with lethargy, muscle and joint pain. Other infrequent symptoms noted were cough and sore throat and lymphadenopathy. They observed hepatomegaly and abdominal tenderness were the frequently noted signs.

In the study there were 6 cases of leptospirosis**,** all of them presented with pain abdomen and more than half of the cases had fever with chills, vomiting and myalgia as nonspecific symptoms. Only 1 case had diarrhoea, conjunctival congestion and jaundice. Hepatomegaly was the consistent sign seen in all cases. Complications such Ascites and pleural effusion were observed in half of the cases and ARDS was noted in 2 cases. Analysis of the association of signs and symptoms with leptospirosis could not be done due to the small patient cohort. Andrews MA and others[8] in their study reported the major symptoms in patients with leptospirosis were conjunctival congestion, myalgia and jaundice. They mentioned that pulmonary syndrome was the major cause of mortality.

In our study, **unclassified fever** which was presumed as viral fever accounting for 287 subjects, vomiting (54.4%) and myalgia (41.8%) were the common associated nonspecific symptoms. Fever with chills, pain abdomen and headache were the rare associations. Flushing, hepatomegaly and rash were the identified signs in 32.1%, 24.7% and 14.3% respectively. Rarely bleeding manifestation such as epistaxis and malena attributed to viral haemorrhagic fever. Other complications such as ascites, pleural effusion were in infrequently noted in the subjects with unclassified fever. There was no clear association of signs noted with unclassified fever other than

fever with chills which is a very nonspecific symptom on statistical analysis (table 19).

Laboratory characteristics of AFI

i. Haemogram :

Thrombocytopenia was the most common haematological abnormality noted in children with AFI (table 13).

Haemogram in **malarial** cases showed thrombocytopenia and anaemia in more than 50% of the cases. Leucocytosis was noted in 26% of the cases.

In the study subjects with **rickettsial fever** haemogram showed thrombocytopenia and leucocytosis in 41.3% and 38.8% cases respectively. Less frequently anaemia and leucopenia were also noted. There was no significant association seen with the lab parameters with rickettsial disease. In contrast to our finding Prabhu M and others[42] in their study reported leucopenia being the associated haematological abnormality in cases of SFGR.

Leucocytosis was the most frequently associated finding on hemogram in cases with **enteric fever,** which was seen in 80.9% of cases. Leucopenia and anaemia was less commonly associated finding.

In cases of **leptospirosis,** leucocytosis and thrombocytopenia was noted in nearly 70% of the cases.

Thrombocytopenia and leucopenia was the most frequently noted lab finding in 95% and 66% respectively on the hemogram of patients with **dengue**. Similar results were reported in the study by Reller M E et al[59]. Anaemia and leucocytosis were rarely noted and these findings decreased the possibility of dengue.

In cases of **unclassified fever,** haemogram showed thrombocytopenia, anaemia in more than half of the cases but could not help in differentiating from other AFI.

In our study, analysis of various parameters on hemogram by logistic regression suggested that anaemia increased the probability of malaria. Leucocytosis was suggestive of enteric fever. Thrombocytopenia and leucopenia increased the likelihood of dengue. There were no statistically significant association noted with lab parameters of rickettsioses and unclassified fever. Analysis for leptospirosis was not done due to small subject cohort.

ii. **Specific investigations**

On all 750 cases of AFI, specific laboratory investigations for dengue, malaria, enteric, rickettsial and leptospirosis were done to identify the aetiology.

In our study there were 216 cases of **dengue**, all were diagnosed on the basis of serological positivity. There were 43% of NS1 Ag positive cases, 33.8% of IgM positive cases and 23.2% of the cases had both Ns1Ag and IgM positive. Proportion of serologically positive cases was higher than NS1Ag positive cases which has been supported by the study by Capending et al [6.]

Laboratory evidence for **malaria** was seen in only 23.88% of the 67 cases. All rapid card for malarial parasite positive cases were confirmed by smear examination. In contrast to Pondel et al [9] and Mabunda et al[60] reported nearly 50% slide positive cases.

In the present study positive slide for malaria were mostly of Plasmodium falciparum followed by Pl vivax. There was 1 case with both Pl falciparum and vivax positive.

Enteric fever was diagnosed in 94 cases, serological confirmation was noted in only 67% with nonspecific widal positivity, done in 2nd week of fever. There was on 4.25% of cases with blood culture positive. All the cultures yielded Salmonella typhi.

Similarly Kasper[45] and others have stated that blood culture yield was low accounting for only 6.3% of their study subjects.

In the study of 80 cases with **rickettsioses**, 66.25% of cases showed serological positivity by Weil Felix test.

Among the 6 cases of leptospirosis, 66.7% of cases showed positive for IgM leptospira.

iii. Convalescent sera

Examination of convalescent sera was done to identify the four fold rise in antibody titres. Testing of convalescent sera could be done in only 15 cases with diagnosis of rickettsioses (9), enteric fever (6) and raising titres noted in 13 cases. Testing of convalescent sera though essential could not be done in all our cases this was due to mainly parental disagreement for pricking the child again after recovery and few were due to lost to follow up.

Etiology of AFI

In our study, among the 750 children with AFI admitted to our hospital common etiological agents identified on the basis of the case definitions were dengue (28.8%), enteric fever (12.5%), rickettsioses (10.67%), malaria (8.9%) and leptospirosis (0.8%). Capending et al[6] and Tam Iroh et al[3] in their studies reported that chikungunya, S typhi, leptospitrosis, dengue and rickettsioses as the common etiologies of AFI in Asian children.

In the present study, one third of the cases of AFI accounting to 38.3% were presumed as unclassified fever due to the absence of clinical or laboratory evidence.

In contrast, studies done by Crump et al[2] and Mahende et al[43] cause of fever as unidentified in only 7.5% of the cases. Andrew et al[8] reported that 63.54% of the cases of fever diagnosis could not be established.

Available reports in literature and results of our study of clinico etiological profile of the common infectious diseases, would be helpful in developing a suitable algorithm with an syndromic approach of the children presenting with acute febrile illness in our region.

CONCLUSION

CONCLUSION

- Majority of the children with AFI presenting to hospital were of school going age group (mean 7 yrs) in the study.
- Mean duration of fever among children presented was 3.8 days.
- In our study 61.7% of the cases had etiological diagnosis. 38.3% of the cases were unclassified fever.
- Children with etiological diagnosis, 76.02% was supported by laboratory confirmation and 23.98% were diagnosed by clinical evaluation.
- Results from this study show that common etiological cause of AFI in children presenting to our centre are dengue(28.8%) followed by enteric fever (12.5%), rickettsial fever (10.7%), malaria (8.9%) and leptospirosis (0.8%).
- Headache, flushing, hepatomegaly and thrombocytopenia with leucopenia were more commonly associated with dengue fever in the subjects.
- Subjects with presence of rigors, splenomegaly and anaemia have increased likelihood of suffering from malaria.
- Rickettsial disease was more commonly associated rash, hepatomegaly and splenomegaly.
- In this study presence of coated tongue, hepatomegaly and leucocytosis on blood picture was commonly associated with enteric fever.
- Children with AFI with no definitive etiological diagnosis due to non specific signs and symptoms and no confirmatory laboratory evidence accounted to 38.3%.
- Our study had no significant symptoms and signs associated with unclassified fever.

- Complications such as
  - Anaemia was associated more with malaria,
  - Ascites, pleural effusion, ARDS, hypotension and bleeding manifestations were observed more frequently among subjects with dengue fever,
  - Encephalitis was noted in children with dengue and rickettsial fever.
- Significant proportion of the children presenting with AFI have been labelled as unclassified fever in the study, indicating the need for widening the spectrum of laboratory tests such as viral and other etiological agents to aid for better management.
- The study demonstrates that, identifying the common etiological agents of AFI help in developing a region Specific epidemiological profile and collective perception of nonspecific symptoms, clinical signs and laboratory parameters helps in syndromic evaluation of the children presenting with AFI which in turn would aid in early initiation of the treatment and management protocol.

LIMITATIONS OF THE STUDY

- Small sample size and short duration of the study
- Not an exact reflection of the population
- Many potential pathogens (influenza virus, hantan virus, and chikungunya virus) were not routinely tested, and samples were not subjected to a broader battery of serologic testing due to financial constraints.
- Lost to follow up for second visit, hence convalescent-phase serum samples could not be analysed to confirm the diagnosis.

SUMMARY

SUMMARY

- The study was a hospital-based observational cross sectional study conducted at R L Jalappa hospital.
- Cases were children from 1 month to 18 years of age attending the department of Paediatrics with fever of less than 2 weeks duration.
- After obtaining written informed consent from the parents of the patient, detailed history was taken, clinical examination was done and entered in a semi-structured proforma. Blood samples were collected for various haematological and microbiological analysis.
- Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software.
- A total of 750 children with AFI comprised the study group.
- In the study, majority (40.3%) of patients belonged to school going age group (7 to 13 years) with a median age of presentation being 84months i.e. 7 years, with a male (53.1%) predominance in the study group.
- Majority (85.4%) of the subjects belonged to Hindu religion and most (83.6%) of the study subjects were from a nuclear family.
- Study of distribution according to socioeconomic status showed maximum (48.4%) subjects belonged to Class II and minority belonging to Class V (0.8%).
- Fever of less than I week was noted in 94.9% of the subjects with AFI and the mean duration of fever at admission was 3.8days.
- In our study, 38.3% of the subjects had no confirmed etiological diagnosis and were diagnosed as unclassified fever followed by cases dengue (28.8%),

enteric fever (12.5%), rickettsial fever (10.7%), malaria (8.9%) and leptospirosis (0.8%).

- Vomiting (53.2%) and pain abdomen (47.3%) were the common non specific symptoms among the subjects presenting with AFI and the least common symptom was diarrhoea (2.9%).
- 61.5% of the subjects with AFI had hepatomegaly.
- Haemogram demonstrated thrombocytopenia in majority of the subjects.
- Cases of malaria presented commonly with pain abdomen (76.1%) and chills and rigors (41.8%). 91.1% of the cases had splenomegaly, 50% had associated hepatomegaly with 13% of the cases had clinical pallor on examination. Thrombocytopenia (61.2%) and anaemia (53.7%) were the common findings on the haemogram.
- Majority of the subjects with rickettsial fever had pain abdomen (52.5%) and headache (45%) as the presenting complaint. The typical maculopapular rash (91.3%) was the most common sign followed by hepatomegaly (82.5%). On hemogram, leucocytosis (83.3%) and thrombocytopenia (66.6%) were the common findings.
- In subjects with enteric fever, vomiting and pain abdomen were the common symptoms with majority of the subjects having hepatomegaly (93.6%). Leucocytosis (80.9%) was the common association on hemogram.
- All study subjects with leptospirosis cases were associated with pain abdomen and hepatomegaly. 83.3% of the subjects had leucocytosis and thrombocytopenia on the hemogram.
- In the subjects with dengue, 50% of the cases presented with pain abdomen, vomiting and headache. Majority (90.7%) had hepatomegaly and

thrombocytopenia (95.8%) and leucopenia (63%) were the common hemogram findings.

- In the study, it was observed that complications such as bleeding manifestations, ARDS, hypotension, encephalitis were more commonly associated with dengue
- Etiological diagnosis was delinated in 38.3% of the subjects, considered as unclassified fever. Majority presented with vomiting (54.4%) and myalgia (41.8%). There was no consistent sign observed in these subjects. Thrombocytopenia and anaemia were the features commonly noted on hemogram.
- Results from the study showed that common etiological cause of AFI in children was dengue (28.8%) followed by enteric fever (12.5%), rickettsial fever (10.7%), malaria (8.9%) and leptospirosis (0.8%).
- Significant proportion of the children presenting with AFI have been labelled as unclassified fever in the study, which suggests the need for widening the spectrum of laboratory tests such as viral and other etiological agents to aid for better management.
- Hence, as demonstrated by the study we conclude that, identifying the common etiological agents of AFI help in developing a region specific epidemiological profile and collective perception of nonspecific symptoms at presentation, clinical signs and laboratory parameters helps in syndromic evaluation of the children presenting with AFI which in turn would aid in early initiation of the treatment and management protocol.

BIBLIOGRAPHY

BIBLOGRAPHY

1. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. Lancet. 2005;365:1147-52.
2. Crump JA. Time for a comprehensive approach to the syndrome of fever in the tropics. Trans R Soc of Trop Med and Hyg. 2014;108.
3. Iroh Tam,K Stephen Obaro, Storch. Challenges in the Etiology and Diagnosis of AcuteFebrile Illness in Children in Low- and Middle-Income Countries. JPIDS 2016;1-16.
4. Atkins E: Pathogenesis of fever. Physiol Rev 40:580, 1960 (PMID: 13794961)
5. Kashinkunti MD, Gundikeri SK, Dhananjaya M. Acute undifferentiated febrile illness-clinical spectrum and outcome from a tertiary care teaching hospital of north Karnataka. Int J Biol Med Res 2013;4:3399-3402.
6. Capeding M.R, Chua M.N, Hadinegoro S.R., Hussain I. I. H. M, Nallusamy R, Pitisuttithum P, et al. Dengue and other common causes of acute febrile illness in asia: an active surveillance study in children. *PLoS Negl. Trop. Dis.* 2013; 7:e2331.
7. Zaidi AK, Awasthi S, deSilva HJ. Burden of infectious diseases in South Asia. BMJ 2004;328:811–15.
8. MA Andrews, Aleena Elizabeth, Pravinlal Kuttichira, Clinical Profile of acute undifferentiated febrile illness in patients admitted to a teaching hospital in Kerala; Health Science 2014;1(3):IS001D8.
9. Pondei K, Kunle-Olowu E O, PetersideO Patterns of acute febrile illness in children in a tertiary health institution in the Niger Delta region of Nigeria. J Med. Med. Sci:2012; 734-740.

10. Singh R, Singh SP, Ahamd N.A Study of Etiological Pattern in an Epidemic of Acute Febrile Illness during Monsoon in a Tertiary Health Care Institute of Uttarakhand, India.J Clin Diagn Res. 2014; 8:MC01-MC03.

11. Joshi R, Colford JM, Reingold AL, Kalantri S: Nonmalarial acute undifferentiated fever in a rural hospital in central India: diagnostic uncertainty and overtreatment with antimalarial agents. Am J Trop Med Hyg. 2008, 78: 393-399.

12. Neild L.S, Kamat D. Nelson Textbook Of Pediatrics First South Asian Edition: Elsevier; 2016. Ch 176, Fever: p1277-79.

13. Dinarello C.A, Porat R. Harrison's Principles of Internal Medicine. 19th ed. New York. Mc Graw- Hill Education. 2015. Figure 23.1 Chronology of Events required for the induction of fever: p 125.

14. Ogoina D: Fever, fever patterns and diseases called _fever'–a review. J Infect Public Health. 2011, 4 (3): 108-124.

15. Salah E.T, Ahmed E, Elhussien M, Salah T. The use of vital signs as predictors of serious bacterial infections in children with acute febrile illness in pediatric emergency setting in Sudan. Sudan J Paediatr. 2014;14: 35-40.

16. Cunha BA. The diagnostic significance of fever curves. Infect Dis Clin North Am. 1996;10:33–44.

17. Dechovitz A.B,Moffet H.L.Classification of Acute Febrile Illness In Childhood.Clin Pediatr:1968;649-53.

18. Dye C. After 2015: infectious diseases in a new era of health and development. Philos Trans R Soc Lond B Biol Sci 2014;369:20130426.

19. T. Dikid, S.K. Jain,A. Sharma,A. Kumar,and J.P. Narain Emerging & re-emerging infections in India: An overview Indian J Med Res. 2013 Jul; 138(1): 19–31.

20. Combating emerging infectious diseases in the South-East Asia Region. New Delhi: World Health Organization, WHO SEARO; 2005. World Health Organization, Regional Office for South East Asia Region.

21. World Health Organization. Guidelines for the Treatment of Malaria. 3rd ed. 2015.Available from: [Cited on May 2, 2017.] *http://www.who.int/malaria/publications/atoz/9789241549127/en.*

22. Bhakta S. Textbook of Pediatric Infectious Diseases.1st ed: Jaypee Brothers Medical Publisher(P) Ltd;2013.Ch 6.1 Malaria in Children:p346-50.

23. Kundu R. PG Texbook Of Pediatrics. 1st ed. India:Jaypee Brothers Medical Publisher(P) Ltd; 2015. Ch 32.2, Malaria: p1232-37.

24. John C.C. Nelson Textbook Of Pediatrics First South Asian Edition: Elsevier; 2016. Ch 288,Malaria (Plasmodium): p1709-22.

25. Dumler J.S, Reller M.E. Nelson Textbook Of Pediatrics First South Asian Edition: Elsevier; 2016. Ch 228, Rickettsial Infections: p1497-1504

26. Rathi N. PG Texbook Of Pediatrics. 1st ed.India:Jaypee Brothers Medical Publisher (P) Ltd; 2015. Ch 34.1, Epidemology, Classification and Approach to Diagnosis of Rickettsial Infections: p1306-09

27. Kulkarni AA. PG Texbook Of Pediatrics. 1st ed.India:Jaypee Brothers Medical Publisher(P)Ltd; 2015. Ch 34.2 , Spotted Fevers: p 1309-12

28. Rathi N, Rathi A, Goodman MH, Aghai ZH. Rickettsialdiseases in Central India: proposed clinical scoring system for early detection of spotted fever. Indian Pediatr. 2011;48:867-72.

29. Arthi P, Bagyalakshmi R, Krishna M, Krishna M, NitinM, Madhavan HN, et al. First case series of emerging Rickettsial neonatal sepsis identified by PCR based DNAsequencing. Indian J Med Microbiol. 2013;31:343-8.

30. Rathi N, Kulkarni A, Yewale V. For Indian Academy of Pediatrics Guidelines on Rickettsial Diseases in Children Committee. IAP guidelines on rickettsial diseases in children. Indian Pediatr. 2017;54:223–229.

31. World Health Organization. Background document: The diagnosis, treatment and prevention of typhoid fever.2003.Available from : *http://www.who.int/rpc/TFGuideWHO.pdf* . Accessed on May 17, 2017.

32. Karla A, Shah A.K. Textbook of Pediatric Infectious Diseases.1st ed: Jaypee Brothers Medical Publisher(P) Ltd;2013.Ch 4.1Salmonella Infections:p217-24

33. Ghosh A, Mitra M. PG Texbook Of Pediatrics. 1st ed.India:Jaypee Brothers Medical Publisher(P) Ltd; 2015. Ch 29.6 ,Typhoid Fever: p1088-92

34. Bhutta Z.A. Nelson Textbook Of Pediatrics First South Asian Edition: Elsevier; 2016. Ch 198, Salmonella: p1382-93.

35. Government of India. Ministry of Health and Family Welfare. National Vector Borne Disease Control Program. National guidelines for Clinical Management of Dengue Fever[Document on internet]. New Delhi. 2014. Available from: *http://pbhealth.gov.in/Dengue-National-Guidelines-2014%20Compressed.pdf.* Accessed on February 18, 2017.

36. Halstead S.B. Nelson Textbook Of Pediatrics First South Asian Edition: Elsevier; 2016. Ch 269, Dengue Fever and Dengue Hemorrhagic Fever: p1629-32.

37. Gupta P, Dabas A. PG Texbook Of Pediatrics. 1st ed.India:Jaypee Brothers Medical Publisher(P)Ltd; 2015. Ch 31.16 ,Dengue: p1203-10

38. Shivakumar S. Leptospirosis – Indian Data 2013 Available from: *https://www.researchgate.net/publication/260750253*. Accessed September 9, 2017.

39. Shivakumar S. Medicine Update.18ed.API.2008.Ch 106. Leptospirosis: Current Scenario in India: 799-809.

40. Sankar J. PG Texbook Of Pediatrics. 1st ed.India: Jaypee Brothers Medical Publisher(P) Ltd; 2015. Ch 29.14 , Leptospirosis: p 1112-14

41. Davies H.D, Simonsen K.A. Nelson Textbook Of Pediatrics First South Asian Edition: Elsevier; 2016. Ch 220, Leptospira: p1480-81.

42. Prabhu M, Nicholson WL, Roche AJ, Kersh GJ, Fitzpatrick KA, Oliver LD, et al. Q fever, spotted fever group and typhus group rickettsioses among hospitalized febrile patients in northern Tanzania. Clin Infect Dis 2011;53: e8-15.

43. Crump JA, Morrissey AB, Nicholson WL, Massung RF, Stoddard RA, Galloway RL,et al. Etiology of severe non-malaria febrile illness in Northern Tanzania: a prospective cohort study. PLoS Negl Trop Dis 2013: 7: e2324.

44. Chheng K, Carter MJ, Emary K, Chanpheaktra N, Moore CE, Stoesser N et al. A prospective study of the causes of febrile illness requiring hospitalization in children in Cambodia. *PLoS One* 2013: 8: e60634

45. Kasper M R, Blair P J,Touch S, Sokhal B, Yasuda C Y, Williams M et al. Infectious Etiologies of Acute Febrile Illness among Patients Seeking Health Care in South-Central Cambodia. Am. J. Trop. Med. Hyg. 2012; 86: 246–253.

46. Mueller TC, Siv S, Khim N, Kim S, Fleischmann E, Ariey F, et al. Acute undifferentiated febrile illness in rural Cambodia: A 3-year prospective observational study. PLoS One. 2014;9: e95868.

47. Mahende C, Ngasala B, Lusingu J, Butichi A, Lushino P, Lemnge M, Premji Z. Aetiology of acute febrile episodes in children attending Korogwe District Hospital in north-eastern Tanzania. PLoS One 2014; 9:e104197; PMID:25090651; http://dx.doi.org/10.1371/journal.pone.0104197

48. Lorenzi O. D., Gregory C. J., Santiago L. M., Acosta H., Galarza I. E., Hunsperger E., et al. 2013. Acute febrile illness surveillance in a tertiary hospital emergency department: comparison of influenza and dengue virus infections. Am. J. Trop. Med. Hyg. 88, 472–480.

49. Manock SR, Jacobsen KH, de Bravo NB, Russell KL, Negrete M, Olson JG, et al. Etiology of acute undifferentiated febrile illness in the Amazon basin of Ecuador. Am. J. Trop. Med. Hyg. 2009;81:146–51.

50. Gowri Veligandla, Ezhilvanan, E. Padmavathi and Bhaskar, M. 2017. Etiological Spectrum and Prevalence of Acute Undifferentiated Febrile Illness (AUFI) in Fever Cases Attending our Tertiary Care Centre. Int.J.Curr.Microbiol.App.Sci. 2017: 954-962.

51. Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S. Etiologies of acute undifferentiated febrile illness in Thailand. J Med Assoc Thai. 2004;87:464–72.

52. Kawthalkar S.M. Essntials of Clinical Pathology.India: Jaypee Brothers Medical Publisher(P) Ltd; 2017. Ch 32. Automation in Hematology. p319-326.

53. World Health Organization. Basic Malaria Microscopy. 2nd ed. 2010. Available from: *http://apps.who.int/iris/bitstream/10665/44208/1/9789241547826_eng.pdf.* Accessed on February 9, 2017

54. Vasudevan J, Mishra A Kumar, Singh Z. An Update On BG Prasad's socioeconomic scale: May 2014 A commentry. Int J Res Med, 2016; 4:4183-6.

55. Bun HF, Anemia. In: Harrisons Principles of Internal Medicine, 11th ed. Eds. Brounwald E, Isselbacher KJ, Petersdorf RG, Wilson JD, Maston JB, Fauci AS, New York, McGraw Hill Book Company, 1987; 262-266.

56. Arvind R. Physical Diagnosis in Paediatrics. 3rd ed. Jaypee Brothers Medical Publisher (P) Ltd; 2007. Ch 09. Examination of Alimentary System: p125-147

57. Chrispal A,Boorugu H, Gopinath K G, Chandy S, Prakash JAJ,Thomas EM et al. Acute Undifferentiated Febrile Illness in Adult Hospitalized Patients: the Disease Spectrum and Diagnostic Predictors – an Experience from a Tertiary Care Hospital in South India. *Trop Doct* 2010**:**230-234.

58. Dhingra B.Mishra D. Early Diagnosis of Febrile Illness: The Need of the hour.Indian Pediatr. 2011: 48:845-49

59. Reller ME, Bodinayake C, Nagahawatte A, Devasiri V, Kodikara-Arachichi W, Strouse JJ, et al.Unsuspected dengue and acute febrile illness in rural and semi-urban southern Sri Lanka. Emerg Infect Diseases. 2012;18(2):256–63.

60. Mabunda S, Aponte JJ, Tiago A, Alonso P. A country-wide malaria survey in Mozambique. II. Malaria attributable proportion of fever and establishment of malaria case definition in children across different epidemiological settings. Malar J. 2009;8:74. doi: 10.1186/1475-2875-8-74.

ANNEXURE

ANNEXURE 1

PROFORMA OF THE STUDY

1) Name:

2) Age:

3) Sex:

4) Address:

5) Religion: Hindu / Muslim / Christian / others

6) Type of family: Nuclear / Joint

7)) Socioeconomic classification (ACCORDING TO BG PRASAD CLASSIFICATION)

No. of family members

Type of housing

Per capita income

8) Chief complaints :

FEVER

Duration ≤ 1 week

1 week – 2 weeks

Frequency

Type Continuous/ Intermittent

Night time fever spike

Chills / rigors

Associated complaints :

9) General physical examination:

- Vital signs: PR ……. RR …… TEMP……. BP…….
- Anthropometry :

Height :

Weight :

BMI:

Head Circumference:

Grade :

Head to toe examination

Eye

Pallor

Icterus

Congestion

Lymphadenopathy

Oral cavity

Nails

Skin

Rashes

10) Systemic examination

Per abdomen :

Hepatomegaly

Splenomegaly

Cardiovascular system:

Respiratory system :

Central nervous system :

Provisional diagnosis:

Investigations

1. Routine investigations :
    - CBC
    - CRP
    - Urine routine

2. In First week of Fever
    - Blood culture
    - Peripheral smear for MP
    - Rapid card
    - Dengue serology

3. In Second week of Fever
    - Widal test
    - Weil felix
    - Lepto IgM ELISA
    - Standard agglutination test for brucella

FINAL DIAGNOSIS :

ANNEXURE 2

PATIENT INFORMATION SHEET

Study title: A Study of Clinico-Etiological Profile of Acute Febrile Illness in Paediatric Patients Admitted to Tertiary Care Centre in South India.

Study site: R.L Jalappa hospital, Tamaka, Kolar.

Aim: 1) To outline the disease specific clinico- epidemiological profile of children presenting with AFIs.

2) To determine common infectious agents as a cause for AFIs.

The most common reason for admission to hospital in children is fever. Causes of fever due to locally prevalent diseases is less known. Hence , in our study we are trying to identify the common causes of fever in our admissions to help develop a rational treatment policy.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study we will collect information (as per proforma) from you. Routine (CBC, CRP, Urine Routine) and Relevant blood investigations (Blood c/s, PS and rapid card for MP, Dengue serology, Widal, Weil Felix, IgM Leptospira, Standard Agglutination test) will be carried out if required. This information collected will be used for dissertation and publication only.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don‘t wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification you can contact the study investigator:

Dr. Shruti Appaji

Mobile no: 9535148325

E-mail id: appajishruti@yahoo.com

ANNEXURE 3

CONSENT FORM

Study title: A Study of Clinico-Etiological Profile of Acute Febrile Illness in Paediatric Patients Admitted to Tertiary Care Centre in South India.

Chief researcher/ PG guide's name: Dr. Krishnappa J

Principal investigator: Dr.Shruti Appaji

Name of the subject:

Age :

Address :

a. I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out and photographs to be taken.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that I may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's parent signature :

Signature of the witness: Date:

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

ಒಪ್ಪಿಗೆ ಪತ್ರ

Study Title: A Study of Clinico-Etiogical Profile of Acute Febrile illness in Paediatric Patients Admitted to Tertiary Care Centre in South India.

ಮುಖ್ಯ ಸಂಶೋದಕರು/ಮಾರ್ಗದರ್ಶಕರು : ಡಾ॥ ಕೃಷ್ಣಪ್ಪ.ಜೆ

ಮುಖ್ಯ ಸಂಶೋದಕರು : ಡಾ॥ ಶೃತಿ ಅಪ್ಪಾಜಿ
ಭಾಗವಹಿಸುವತ ಹೆಸರು :
ವಯಸ್ಸು :
ವಿಳಸ :

ಅ. ನನ್ನ ಮಾತೃ ಭಾಷೆಯಲ್ಲಿ ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ತಿಳಿಸಲಾಗಿದೆ, ಹಾಗೂ ಇದಕ್ಕೆ ಸಂಬಂಧ ಪಟ್ಟ ಪರೀಕ್ಷೆಗಳನ್ನು ಮತ್ತು ಭಾವ ಚಿತ್ರಗಳನ್ನು ತೆಗೆಯುವ ಬಗ್ಗೆ ಮಾಹಿತಿ ನೀಡಿಲಾಗಿದೆ. ಈ ಅಧ್ಯನದ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯು ಸಾಂಸ್ಥಿಕ ದಾಖಲೆಯಾಗಿದ್ದು ಗೌಪ್ಯತೆ ಕಾಪಾಡಿಕೊಂಡಿರುತ್ತದೆಂಬುದನ್ನು ನಾನು ಅರ್ಥ ಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಆ. ಚಿಕಿತ್ಸೆಗೆ (ವೈದ್ಯಕೀಯಕ್ಕೆ) ಸಂಬಂಧ ಪಟ್ಟ ಈ ಮಾಹಿತಿಯು ಈ ಸಂಸ್ಥೆಯ ದಾಖಲೆಗಳಾಗಿರುತ್ತದೆ ಮತ್ತು ಅದರ ಗೌಪ್ಯತರಯನ್ನು ಕಾಪಾಡುವುದಾಗಿ ತಿಳಿಸಿರುತ್ತಾರೆ.

ಇ. ನಾನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸ್ವಇಚ್ಛೆಯಿಂದ ಭಾಗವಹಿಸುತ್ತೇನೆ. ಯಾವುದೇ ಸಂದರ್ಭದಲ್ಲಿ ಬೇಡವೆನಿಸಿದಾಗ ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ಹಿಂಪಡೆಯ ಬಹುದಾಗಿಯೂ ಮತ್ತು ಇದರಿಂದ ಈ ಸಂಸ್ಥೆಯಲ್ಲಿ ನನಗೆ ನೀಡಬೇಕಾದ ಚಿಕಿತ್ಸೆ/ಆರೈಕೆಗೆ ಯಾವುದೆ ತೊಂದರೆ ಇಲ್ಲದೆ ದೊರಕುವ ನಂಬಿಕೆಯಿದೆ.

ಈ. ಈ ಅಧ್ಯಯನದಿಂದ ಹೊರಬರುವಂತಹ ಯಾವುದೇ ಮಾಹಿತಿಯು ವೈಜ್ಞಾನಿಕ ಅಧ್ಯಯನಕ್ಕೆ ಉಪಯೋಗಿಸಿಕೊಳ್ಳಲು ಇದಕ್ಕೆ ನಿರ್ಭಂದಿಸದಂತೆ ಒಪ್ಪಿಗೆ ಕೊಟ್ಟಿರುತ್ತೇನೆ.

ಉ. .....(ಸ್ನಾತಕೋತರ ಪದವೀಧರರ ಹೆಸರು) ಈ ಸಂಶೋದನೆಯ ಉದ್ದೇಶದ ಮಾಹಿತಿಯನ್ನು , ಕೈಗೊಳ್ಳುವ ವಿಧಾನಗಳನ್ನು, ಇದರಿಂದ ನಾನು ಎದರಿಸಬೇಕಾದ ಅನಾನುಕೂಲಗಳ ವಿವರವನ್ನು ಆಡುಭಾಷೆಯಲ್ಲಿ ತಿಳಿಯ ಪಡಿಸುತ್ತಾರೆ. ಈ ಮೇಲಿನ ಎಲ್ಲಾ ವಿಚಾರಗಳನ್ನು ಮನದಟ್ಟು ಮಾಡಿಕೊಂಡು. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಮ್ಮತಿಸುತ್ತೇನೆ.

ಪೋಷಕರ ಸಹಿ :

ಸಾಕ್ಷಿದಾರರ ಸಹಿ: **ದಿನಾಂಕ:**

ನಾನು ಈ ಸಂಶೋದನೆಯಿಂದ ಆಗಬಹುದಾದ ಅನುಕೂಲಗಳು/ಅನಾನುಕೂಲಗಳನ್ನು ಭಾಗವಹಿಸುತ್ತಿರುವವರೆಗೆ ಕೂಲಂಕುಶವಾಗಿ ನನ್ನ ತಿಳುವಳಿಕೆಯ ಅನುಸಾರ ವಿವರಿಸಿರುತ್ತೇನೆ.

ಮುಖ್ಯ ಸಂಶೋದಕರು/ಮಾರ್ಗದರ್ಶಕರ ಸಹಿ: **ದಿನಾಂಕ:**

MASTER CHART

Sl No	Name	Age	al-1 female	IP no.	Religion(H	Family type	SES (BG pra	e week, 2	-tinous, 2-	Night spike	Chills,	g-V, mayalg	Pulse	BP	brile -F, afe	RR	Head to toe ex	present / A	Hepatome	Spleenome	Ascites(1-p	CVS		RS		CNS		, SEPSIS-4,	ANAEMIA-1	CRP (1-pos	UR:NORM	GROWTH-	Smear for	Rapid card	Ns1AG -1,	Widal(titres	Weil felix	IgM Lepto(	Agglutinat	ongue		Widal	Weil	kettsial-4.I
1	subramani	4y	1	240258	H	N	3	1	2	N	N	P	100	N	F	24	FLUSHING	A	1	2	2	0		0		0		1	1,3	1	1	2	N	N	4	0	0	0	0	0	0	0	1
2	balachandr	3y	1	241475	H	N	2	1	2	N	N	V	90	N	AF	24	FLUSHING	P	2	2	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
3	abhi	1.2y	1	240460	H	N	3	2	2	N	N	N	110	N	AF	29		P	1	1	2	0		0		0		1	3	1	1	2	N	N	4	0	0	0	0	0	0	0	1
4	irshad	7y	1	241368	M	J	3	1	2	N	N	N	118	N	F	24		A	2	2	2	0		0		0		4	1,2,4	1	1	2	N	N	4	0	0	0	0	0	0	0	4
5	bhanu	12y	1	240541	H	N	2	1	2	N	N	M,H	87	N	AF	22	MACULOPAPU	P	2	2	2	0		0		0		1	3,4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
6	veerendra	12y	1	241393	H	J	3	2	2	N	N	M	113	N	F	22		A	2	2	2	0		0		0		2	3,4	2	1	2	N	N	1	0	0	0	0	0	0	0	2
7	veena	14y	2	240038	H	N	3	2	2	N	N	V,P	110	N	F	21	FLUSHING	A	2	2	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
8	akshaya	5y	2	242253	H	N	1	1	2	N	N	P	127	N	F	23		A	1	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
9	bindu	2y	2	241988	H	N	3	1	2	P	N	V	132	N	F	26		A	2	1	2	0		0		0		7	5	1	1	2	N	N	4	0	0	0	0	0	0	0	7
10	babu	13y	1	242261	H	J	2	2	2	N	N	P,M	86	N	AF	21	PALLOR	P	1	2	2	0		0		0		1	3,4	2	1	2	N	N	1	0	0	0	0	0	0	0	1
11	vandana	3y	2	241725	H	N	3	1	2	P	N	V	119	N	F	25		P	1	2	2	0		0		0		4	2,4	2	1	2	N	N	4	0	0	0	0	0	0	0	4
12	jeevitha	6y	2	241860	H	N	4	1	2	N	N	N	120	N	F	23		A	2	2	2	0		0		0		2	4	1	1	2	N	N	1	0	0	0	0	0	0	0	2
13	vinutha	8y	2	242234	H	N	3	1	2	P	N	N	100	N	F	22	FLUSHING	A	2	2	2	0		0		0		2	4	1	1	2	N	N	2	0	0	0	0	0	0	0	2
14	kruthika	3y	2	245318	H	N	3	1	2	N	N	N	120	N	F	25		P	1	2	2	0		0		0		4	1,2	2	1	2	N	N	4	0	0	0	0	0	0	0	4
15	syed jawad	4m	1	242956	M	N	3	1	2	N	N	N	165	N	F	32	FLUSHING	P	2	2	2	0		0		0		1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
16	sania	14y	2	246266	H	N	3	2	1	N	N	M,H	82	N	AF	22		A	1	2	2	0		0		0		1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
17	varsha	2y	2	247154	H	N	2	1	2	N	N	N	99	N	AF	29		A	1	2	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
18	madiya	6y	2	247552	H	N	3	2	2	N	N	P	117	N	F	24	FLUSHING	A	2	2	1	0		0		0		2	4	1	1	2	N	N	3	0	0	0	0	0	0	0	2
19	likith gowd	5y	1	248783	H	J	3	1	2	N	N	N	125	N	F	23		A	2	2	2	0		0		0		3	1,2	2	1	2	N	N	4	0	0	0	0	0	0	0	3
20	sumanth	10y	1	248789	H	J	1	2	2	N	P	N	133	N	F	22		P	2	2	2	0		0		0		1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
21	sumith	5y	1	249571	H	N	3	1	2	N	N	N	119	N	F	24	PALLOR	A	2	2	2	0		0		0		4	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	4
22	bindushree	1y	2	250306	H	N	2	1	2	N	N	N	146	N	F	28		A	1	2	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
23	sadananda	1y	1	248791	H	N	3	1	2	P	N	N	103	N	AF	29		P	1	1	2	0		0		0		7	5	2	1	2	N	N	4	0	0	0	0	0	0	0	7
24	b/o nandin	1m	1	248937	H	J	2	2	2	P	N	N	110	N	AF	36		P	1	2	2	0		0		0		4	2,3	1	1	2	N	N	4	0	0	0	0	0	0	0	4
25	shaeen	7y	1	248567	M	N	2	1	2	P	N	V	95	N	AF	21	FLUSHING	P	2	2	2	0		0		0		2	4	1	1	2	N	N	1	0	0	0	0	0	0	0	2
26	sufiya ibsun	5y	2	231470	M	N	3	2	2	P	N	N	98	N	AF	23	CONJCTIVALCO	A	2	2	2	0		0		0		1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
27	saboni	5y	2	231546	C	N	3	2	1	P	N	N	118	N	F	26		P	2	2	2	0		0		0		4	5	1	1	2	N	N	4	0	0	0	0	0	0	0	4
28	tejaswini	11y	2	248672	H	N	3	1	1	P	P	P	121	N	F	22		A	1	1	2	0		0		0		3	2	1	1	2	N	N	4	0	0	0	0	0	0	0	3
29	murali	11y	1	250317	H	N	2	2	2	P	P	P	110	N	F	18	MACULOPAPU	P	1	1	2	0		0		0		4	4	1	1	2	N	N	4	0	0	0	0	0	0	0	4
30	pavithra	17y	2	248881	H	N	3	1	2	P	P	V,P	86	N	AF	18		A	2	1	2	0		0		0		7	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	7
31	manasmith	4y	2	252592	H	N	3	2	2	N	N	P	100	N	AF	24	PETECHIAE	A	2	2	2	0		0		0		2	4	1	1	2	N	N	3	0	0	0	0	0	0	0	2
32	ranjith	4y	1	253121	H	J	3	1	2	N	N	N	121	N	F	26		A	2	2	2	0		0		0		1	1,3,4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
33	naman kna	3y	1	251773	M	J	2	1	2	N	N	N	116	N	F	22		A	1	1	2	0		0		0		7	1	2	1	2	N	N	4	0	0	0	0	0	0	0	7
34	gayathri	16y	2	251835	H	N	3	1	2	P	N	H	100	N	F	19	PALLOR	P	2	1	2	0		0		0		7	1,5	2	1	2	N	N	4	0	0	0	0	0	0	0	7
35	ghomenda	13y	1	255832	H	N	3	1	1	P	N	M	87	N	AF	22		A	1	2	2	0		0		0		1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
36	punith	4y	1	256063	H	N	3	2	2	N	N	N	126	N	F	24		A	1	1	2	0		0		0		4	5	1	1	2	N	N	4	0	0	0	0	0	0	0	4
37	helsitha	7y	2	258069	C	J	1	1	2	N	P	V	113	N	F	21		P	2	2	2	0		0		0		1	1,4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
38	kusuma	8y	2	255474	H	N	3	2	2	N	N	V,P	100	N	F	22		A	2	1	2	0		0		0		3	2	1	1	2	N	N	4	0	0	0	0	0	0	0	3
39	vedhashre	2y	2	255482	H	N	3	1	2	N	N	N	103	N	AF	27	ANASARCA	A	1	2	1	0		0		0		2	4	1	1	2	N	N	2	0	0	0	0	0	0	0	2
40	arvind	9y	1	255492	H	N	3	2	2	N	N	V	106	N	F	22	ANASARCA	A	2	2	1	0		0		0		2	4	2	1	2	N	N	2	0	0	0	0	0	0	0	2
41	harikrishna	4y	1	256801	H	J	3	1	2	P	N	P	97	N	AF	24		A	1	1	2	0		0		0		3	5	1	1	2	N	N	4	0	0	0	0	0	0	0	3
42	pravalika	4y	2	259849	H	N	3	1	2	N	N	P	100	N	AF	25		P	2	2	2	0		0		0		1	2,4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
43	numha	3y	1	260425	M	N	2	1	2	P	N	N	99	N	AF	26	FLUSHING	A	1	2	2	0		0		0		1	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
44	geona	2y	2	263612	C	N	2	2	2	N	N	N	112	N	F	27		P	2	2	2	0		0		0		1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
45	satvika	3m	2	236917	H	N	3	1	2	N	N	N	154	N	F	33	FLUSHING	A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
46	mohan	8y	1	263233	H	J	2	1	2	P	N	N	112	N	F	23	MACULOPAPU	A	1	2	2	0		0		0		4	1,4	1	1	2	N	N	4	0	0	0	0	0	0	0	4
47	nagamani	16y	2	264769	H	N	2	2	2	P	N	P	100	N	F	18		P	2	2	2	0		0		0		7	1	2	1	2	N	N	4	0	0	0	0	0	0	0	7
48	anil kumar	17y	1	264475	H	N	2	1	2	N	N	H	80	N	AF	19	COATED TONG	A	1	1	2	0						3	2,4	1	1	2	N	N	4	0	0	0	0	0	0	0	3
49	afreen taj	1.6y	2	266500	M	N	3	1	2	N	N	N	144	N	F	28	FLUSHING	A	1	2	2	0		0		0		2	1,4	1	1	2	N	N	3	0	0	0	0	0	0	0	2
50	srishakthi	13y	2	267353	H	N	3	2	1	P	P	N	84	N	AF	21	FLUSHING	A	1	2	2	0		0		0		1	3,4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
51	mimona	8y	2	267729	M	N	2	1	2	P	N	P,V	123	N	F	22	PETECHIAE	A	2	1	2	0	ARDS		0		0		2	4	2	1	2	N	N	1	0	0	0	0	0	0	0	2
52	abhilash	7y	1	268017	H	N	3	2	2	P	N	N	114	N	F	23		A	1	1	2	0		0		0		3	2	2	1	2	N	N	4	0	0	0	0	0	0	0	3
53	hemanth ga	4y	1	268976	H	N	2	1	2	P	N	N	115	N	F	26	FLUSHING	A	1	2	2	0		0		0		1	1,4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
54	ameena	16y	2	268102	M	N	3	2	2	N	N	P	84	N	AF	21	PALLOR	P	2	2	1	0		0		ENCEPHAL		2	4	1	1	2	N	N	2	0	0	0	0	0	0	0	2
55	sudeep	6y	1	269402	H	J	3	1	2	P	N	N	124	N	F	23		P	2	1	2	0		0		0		7	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	7
56	hemanth	2y	1	272071	H	N	2	1	2	P	N	V	100	N	AF	27	FLUSHING	A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
57	poorvika	2y	2	270689	H	N	2	1	2	N	N	N	99	N	AF	25		A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
58	pooja	6y	2	270824	H	N	2	1	2	P	N	V	114	N	F	23	PALLOR	A	2	1	2	0		0		0		7	5	2	1	2	N	N	4	0	0	0	0	0	0	0	7
59	charan tej	1y	1	273263	H	N	3	1	2	N	N	V	134	N	F	28		A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
60	kujel	2y	1	276119	M	J	3	1	2	N	N	N	99	N	AF	29		P	2	2	2	0		0		0		1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
61	nitharika	9y	2	273511	H	J	3	2	2	P	P	P	111	N	F	22	FLUSHING	A	1	2	1	0		0		0		2	2,4	2	1	2	N	N	2	0	0	0	0	0	0	0	2
62	hamsa	2y	2	273115	H	N	3	1	2	N	N	N	100	N	AF	28		P	1	1	2	0		0		0		3	2	2	1	2	N	N	4	0	0	0	0	0	0	0	3
63	mithun	9y	1	276392	H	N	3	1	2	P	P	P,V	87	N	AF	21		P	1	2	2	0		0		0		4	2	1	1	2	N	N	4	0	0	0	0	0	0	0	4
64	shafiya	14y	2	276484	M	N	3	2	2	P	N	M	100	N	F	22	MALENA	A	1	2	1	0		0		0		2	4	1	1	2	N	N	3	0	0	0	0	0	0	0	2
65	mahendra	6y	1	280487	H	N	3	1	2	N	P	P,V	98	N	AF	24		A	1	2	2	0		0		0		2	4	1	1	2	N	N	1	0	0	0	0	0	0	0	2
66	chandu	3y	1	279433	H	N	3	1	2	N	N	V	100	N	AF	26		A	1	1	2	0		0		0		4	4	2	1	2	N	N	4	0	0	0	0	0	0	0	4
67	jaswanth	6y	1	279229	H	N	3	1	2	P	N	N	112	N	F	23	MACULOPAPU	P	1	1	2	0		0		0		3	2	1	1	2	N	N	4	0	0	0	0	0	0	0	3
68	sowjanya	10y	2	281471	H	J	2	2	2	N	P	N	103	N	F	20		P	2	2	2	0		0		0		2	4	2	1	2	N	N	3	0	0	0	0	0	0	0	2
69	divya s	10m	2	283305	H	N	2	1	2	N	N	V	134	N	F	28		A	2	2	2	0		0		0		2	1,4	1	1	2	N	N	3	0	0	0	0	0	0	0	2
70	gopika	17y	2	282735	H	N	2	1	2	N	P	P,V,H	100	N	F	20	FLUSHING	A	2	2	2	0		0		0		2	4	1	1	2	N	N	1	0	0	0	0	0	0	0	2
71	vivan	1y	1	282834	H	N	2	1	2	N	N	N	103	N	AF	31		A	2	2	2	0		0		0		2	5	1	1	2	N	N	1	0	0	0	0	0	0	0	2
72	madhushr	15y	2	282736	H	N	2	2	2	N	P	V,P	108	N	F	22	EPISTAXSIS	A	1	2	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
73	charan	7m	1	283762	H	J	3	1	2	P	N	V	154	N	F	29	FLUSHING	A	1	2	2	0		0		0		1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
74	hemashree	7y	2	283914	H	J	3	1	2	P	N	P	95	N	AF	22		A	2	2	2	0		0		0		1	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
75	dilip kumar	8m	1	280211	H	J	3	1	2	N	N	N	104	N	AF	29		P	1	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
76	afreen	7y	2	286486	M	N	3	1	2	N	N	N	114	N	F	23	FLUSHING	A	2	2	2	0		0		0		2	4	2	1	2	N	N	2	0	0	0	0	0	0	0	2
77	aliya	1.8y	2	286536	M	N	2	2	2	N	N	N	128	N	F	27		A	1	2	2	0		0		0		3	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	3
78	varsha,	4y	2	288222	H	N	3	1	2	P	N	P	98	N	AF	25		P	2	2	2	0		0		0		1	2	1	1	2	N	N	4	0	0	0	0	0	0	0	1
79	dhanush	7y	1	289627	H	N	2	2	1	N	N	V,P	94	N	AF	23		A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
80	mavaneet	15y	1	288631	H	N	2	1	2	N	P	P	115	N	F	21		A	1	1	2	0		0		0		3	4	2	1	2	N	N	4	0	0	0	0	0	0	0	3
81	preetham	3y	1	128297	H	N	3	1	2	P	N	N	127	N	F	25	FLUSHING	P	1	1	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
82	likitha	3y	2	128360	H	N	3	2	2	N	N	N	113	N	F	25		A	1	2	2	0		0		0		2	4,3	2	1	2	N	N	1	0	0	0	0	0	0	0	2
83	chanukya	7y	1	290905	H	N	3	2	2	P	N	H,P	92	N	AF	22		A	2	2	2	0		0		0		2	4	2	1	2	N	N	1	0	0	0	0	0	0	0	2
84	supriya	2y	2	288902	H	N	1	1	2	N	N	V	102	N	AF	27	PETECHIAE	P	1	1	1	0		0		0		3	2,4	1	1	2	N	N	4	0	0	0	0	0	0	0	3
85	farad pash	4y	1	294864	M	N	2	2	2	N	N	P	126	N	F	26	PALLOR	A	2	1	2	0		0		0		7	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	7
86	dikshith m	7y	1	295370	H	N	2	2	2	P	N	P,V,H	114	N	F	23		A	2	2	2	0		0		0		1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
87	shravani	3.6y	2	294781	H	N	3	2	2	P	N	V	98	N	AF	24	FLUSHING	P	1	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
88	sudharsha	1y	1	296473	H	N	3	1	2	P	N	N	103	N	AF	27		P	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
89	sayeed	1y	2	290869	M	J	3	1	2	N	N	V	110	N	AF	28		P	2	2	2	0		0		0		1	1,4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
90	manjula	8m	2	299297	H	N	3	1	2	P	N	N	155	N	F	31	FLUSHING	A	1	2	1	0		0		0		2	4	2	1	2	N	N	1	0	0	0	0	0	0	0	2
91	komala	8y	2	298821	H	N	3	1	2	N	N	P	133	N	F	23		A	1	2	2	0		0		0		1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
92	divya	9m	2	299628	H	N	4	1	2	N	N	N	154	N	F	30	FLUSHING	A	2	2	2	0		0		0		1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
93	vishnuvard	9y	1	299681	H	N	3	1	2	N	N	P	121	N	F	23		A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
94	shama	3y	1	300979	M	N	3	1	2	N	N	V	127	N	F	26		A	2	2	2	0		0		0		1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
95	balaraj	17y	1	302315	H	N	3	2	1	N	N	P,V	124	N	F	21		A	2	2	2	0		0		0		1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
96	somasheka	6m	1	302321	H	N	3	2	2	P	N	N	112	N	AF	29	PALLOR	A	1	1	2	0		0		0		3	1,4	2	1	2	N	N	4	P		0	0	0	0	0	0	3
97	kashifa kha	12y	2	301896	M	N	2	1	2	N	N	V,H	87	N	AF	20		A	1	2	1	0		0		0		2	4	1	1	2	N	N	2	0	0	0	0	0	0	0	2

| | | |

| | | |

| | | |

392	mahanthes	1y5m	1	340002	H	J	2	2	2	P	P	P,H,D	110	N	AF	27	FLUSHING	P	1	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
393	abdul rahan	12y	1	339961	M	N	3	1	2	P	N	P,H	110	N	F	24		P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	2	0	0	0	0	0	0	0	2
394	anushka	4y	2	342083	H	N	2	2	2	N	P	V,M	99	N	AF	25	FLUSHING	A	1	2	2	0	0	0	1	1,3		1	1	2	N	N	4	0	0	0	0	0	0	0	1
395	janani	4y	2	342198	H	N	3	1	2	N	N	P	88	N	AF	22		A	2	2	2	0	0	0	1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
396	nikhil	10y	1	343404	H	J	2	2	2	P	N	V	112	N	F	23	RASH	P	1	1	2	0	0	0	3	2,4		1	2	2	N	N	4	P		0	0	0	0	0	0	3
397	deekshitha	15y	1	339984	H	N	3	1	2	P	N	V,P	102	N	AF	24		P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	2	0	0	0	0	0	0	0	2
398	harshitha	7y	2	321654	H	N	3	1	2	P	N	P,H	110	N	F	24	FLUSHING	P	1	2	2	0	0	0	1	4	1	1	2	N	N	1	0	0	0	0	0	0	0	2
399	rajesh	8y	1	340903	H	N	1	2	2	P	N	V	112	N	F	23	RASH	P	1	2	2	0	0	0	3	2	1	2	2	N	N	4	P		0	0	0	0	0	0	3
400	prajwal	3y6m	1	340305	H	J	2	2	2	P	N	V	104	N	AF	27	RASH	P	1	1	2	0	0	0	3	2,4		1	2	2	N	N	4	P		0	0	0	0	0	0	3
401	nagendra	14y	1	339958	H	N	1	2	2	P	N	V	93	N	AF	20		P	1	2	2	0	0	0	3	2	1	1 SALMONE	2	N	N	4	P		0	0	0	0	0	0	3
402	suni	13y	1	342633	H	N	1	1	2	P	N	P,V	84	N	AF	22	FLUSHING	P	1	2	2	0	0	0	1	4	1	1	3	N	N	1	0	0	0	0	0	0	0	2
403	arjun	11y	1	344786	H	N	3	1	2	P	N	P,H	110	N	F	24		P	1	1	2	0	0	0	1	3,4		1	1	2	N	N	3	0	0	0	0	0	0	0	2
404	sanjay	6y	1	413939	H	N	2	2	2	P	N	P,V,H	90	N	AF	24	FLUSHING	P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	1	0	0	0	0	0	0	0	2
405	prajwal	12y	1	412835	H	N	2	1	2	P	N	P,V	86	N	AF	22	FLUSHING	P	1	2	2	0	0	0	1	3,4		1	1	3	N	N	2	0	0	0	0	0	0	0	2
406	chandu	17y	1	441258	H	N	2	1	2	P	N	V	90	N	AF	24	RASH	P	1	2	2	0	0	0	3	1,2		1	2	2	N	N	4	P		0	0	0	0	0	0	3
407	sanosh	13y	1	442615	H	N	3	2	2	P	P	P,V	104	N	F	23		A	2	1	2	0	0	0	2	2,4		2	1	2	N	N	4	0	0	0	0	0	0	0	7
408	abhishek	8y	1	442098	H	N	2	1	2	P	N	V	110	N	F	24		P	2	2	2	0	0	0	1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
409	jameela	13y	2	442148	M	N	3	1	2	N	P	P,H	92	N	AF	22	MACULOPAPUL	P	1	1	2	0	0	0	7	5	1	1	2	N	N	4	0	P		0	0	0	0	0	4
410	charan	12y	1	442059	H	J	2	1	2	P	N	V,H	90	N	AF	24	RASH	P	1	2	2	0	0	0	3	1,2		1	2	2	N	N	4	P		0	0	0	0	0	0	3
411	md rayaan	4y	1	411861	M	N	2	2	2	N	P	P	145	N	F	26		A	1	0	2	0	0	0	2	4	2	1	2	P	P	4	0	0	0	0	0	0	0	7
412	arman	6y	1	410519	M	N	1	2	2	P	P	P	116	N	F	23		P	1	1	2	0	0	0	2	1,2,4		2	1	2	N	N	4	0	0	0	0	0	0	0	7
413	vinayashree	5y	2	412556	H	N	3	2	2	P	P	P	102	N	F	24	FLUSHING	P	1	1	2	0	0	0	1	3,4		1	1	2	N	N	1	0	0	0	0	0	0	0	2
414	pawana	2y	1	412730	H	N	2	1	2	P	N	V	99	N	AF	27		A	2	2	2	0	0	0	1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
415	anu	4y	2	413329	H	N	2	1	2	N	P	P,H	92	N	AF	22	MACULOPAPUL	P	1	1	2	0	0	0	7	5	1	1	2	N	N	4	0	P		0	0	0	0	0	4
416	meghana	1y5m	2	413133	H	N	1	1	2	N	P	V	114	N	AF	29	MACULOPAPUL	P	1	2	2	0	0	0	7	2,4		1	1	2	N	N	4	0	P		0	0	0	0	0	4
417	karthik	5y	1	342561	H	N	2	2	2	N	P	V,M	99	N	AF	20	FLUSHING	A	1	2	2	0	0	0	1	3,4		1	1	2	N	N	4	0	0	0	0	0	0	0	1
418	ranali	8y	2	342311	H	N	3	1	2	P	P	P	83	N	AF	22		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
419	sahana	1y2m	2	343355	H	J	2	1	2	P	N	V	110	N	AF	26		P	2	2	2	0	0	0	1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
420	dheeraj	8y	1	342113	H	N	3	2	2	P	P	V,H	90	N	AF	22	MACULOPAPUL	P	1	2	2	0	0	0	7	2,4		1	1	2	N	N	4	0	P		0	0	0	0	P	4
421	pavan	6y	1	342013	H	J	2	1	2	P	N	V	90	N	AF	24	RASH	P	1	2	2	0	0	0	3	1,2		1	2	2	N	N	4	P		0	0	0	0	0	0	3
422	arbiya	11y	2	342107	H	N	3	1	2	P	N	V,P	90	N	AF	22		P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	2	0	0	0	0	0	0	0	2
423	lakshmipat	10y	1	341080	H	N	2	2	2	N	P	V,M	99	N	AF	20	FLUSHING	A	2	2	2	0	0	0	1	1,3		1	1	2	N	N	4	0	0	0	0	0	0	0	1
424	abhishek	13y	1	343617	H	N	3	1	2	N	N	H,M	92	N	AF	22		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
425	tasmiya bes	3y	2	343575	H	N	2	1	2	P	P	P,V,H	90	N	AF	24	FLUSHING	P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	3	0	0	0	0	0	0	0	2
426	vanathi	4y	2	343435	H	N	2	2	2	N	P	V,M	99	N	AF	20	FLUSHING	A	2	2	2	0	0	0	1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
427	nadiya	8y	2	343315	H	N	3	1	2	P	N	H,M	92	N	AF	22		A	1	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
428	meenakshi	13y	2	413592	M	J	2	1	2	N	P	P,V,H	88	N	AF	22		A	2	2	2	0	0	0	1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
429	prabha	8y	2	412404	H	J	3	1	2	P	P	H,M	110	N	F	26	PALLOR	A	2	2	2	0	0	0	1	3,4		2	1	2	N	N	4	0	0	0	0	0	0	0	1
430	charan	7y	1	412465	H	N	2	2	2	N	P	V,M	99	N	AF	26	FLUSHING	A	2	2	2	0	0	0	1	1,3		1	1	2	N	N	4	0	0	0	0	0	0	0	1
431	sanjay	6y	1	413939	H	N	2	2	2	P	N	P,V,H	90	N	AF	24	FLUSHING	P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	1	0	0	0	0	0	0	0	2
432	jeevika	4y	2	342132	H	N	3	2	2	P	P	P,V	90	N	AF	24	COATED TONG	A	1	2	2	0	0	0	3	5	1	2	2	N	N	4	P		0	0	0	0	0	0	3
433	trishal	4y	1	343483	H	N	2	1	2	P	P	P	114	N	F	26		P	1	1	2	0	0	0	2	1	2	1	2	N	N	4	0	0	0	0	0	0	0	7
434	prajwal	12y	1	412835	H	N	2	2	2	P	P	V	110	N	F	23		P	2	2	2	0	0	0	1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
435	praveen	4y	1	343472	H	N	3	1	2	N	P	V	102	N	AF	26	MACULOPAPUL	P	1	1	2	0	0	0	7	4	1	1	2	N	N	4	0	P		0	0	0	0	0	4
436	charanya	7y	2	343567	H	J	3	1	2	P	N	V	126	N	F	25	RASH, COATED	P	1	1	2	0	0	0	3	2,4		1	2	2	N	N	4	P		0	0	0	0	0	0	3
437	gangadhar	6y	1	413241	H	N	3	1	2	P	N	P,V	110	N	F	26		P	2	2	2	0	0	0	1	3,4		1	1	2	N	N	4	0	0	0	0	0	0	0	1
438	md pashal	10y	1	342066	M	N	2	1	2	P	P	V,M	99	N	F	24	FLUSHING	A	1	2	2	0	0	0	1	5	1	1	2	N	N	4	0	0	0	0	0	0	0	1
439	md razai	12y	1	344281	M	N	3	1	2	N	N	H,M	92	N	AF	22		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
440	ganavi	10y	2	414199	H	N	3	1	2	P	P	P	112	N	F	24	FLUSHING	P	1	1	2	0	0	0	1	1,3,4		1	1	2	N	N	1	0	0	0	0	0	0	0	2
441	chandrika	15y	2	414268	H	N	2	1	2	N	P	V	99	N	AF	20		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
442	ajay kumar	10y	1	344208	H	N	2	2	2	N	P	P	104	N	F	25		P	1	1	2	0	0	0	2	1,2,4		1	1	2	N	N	4	0	0	0	0	0	0	0	7
443	srikanta	12y	1	344331	H	N	2	1	2	P	P	P,V	113	N	F	25	EPISTXSIS	P	1	2	1	0	0	0	1	3,4		2	1	2	N	N	2	0	0	0	0	0	0	0	2
444	divya	11y	2	342381	H	N	3	2	2	P	N	H,M	124	N	F	23		P	1	2	2	0	0	0	3	2	2	1	2	N	N	4	P		0	0	0	0	0	0	3
445	b/o kavya	1y	2	345876	H	N	3	2	2	P	N	V	112	N	AF	27	MACULOPAPUL	P	1	0	2	0	0	0	2	3,4		1	1	2	N	N	4	0	P		0	0	0	0	0	4
446	venu	1y	1	345594	H	N	3	1	2	P	N	V	92	N	AF	22		A	1	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
447	surya tej	7y	1	414198	H	N	2	2	2	P	P	V,M	134	N	F	27		P	1	1	2	0	0	0	2	4	2	1	2	N	N	4	0	0	0	0	0	0	0	7
448	jaswanth	3y	1	410284	H	N	3	1	2	P	N	P	102	N	AF	26	FLUSHING	P	1	1	2	0	0	0	1	3,4		1	1	2	N	N	1	0	0	0	0	0	0	0	2
449	sahid	10y	1	412356	M	N	2	1	2	N	P	V	99	N	AF	20		A	2	2	2	0	0	0	1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
450	lokesh	10y	1	344883	H	N	2	2	2	N	P	P	78	N	AF	23		P	2	1	2	0	0	0	2	3,4		2	1	2	N	N	4	0	0	0	0	0	0	0	7
451	karthik	3y	1	343137	H	N	2	2	2	P	N	V	112	N	AF	23	RASH	P	1	1	2	0	0	0	3	2,4		1	1	2	N	N	4	P		0	0	0	0	0	0	3
452	ganavi	3y	2	415315	H	N	3	1	2	P	N	P	102	N	F	26	FLUSHING	P	1	1	2	0	0	0	1	3,4		1	1	2	N	N	3	0	0	0	0	0	0	0	2
453	nithin	10y	1	346588	H	N	2	1	2	P	P	V	99	N	AF	26		A	2	2	2	0	0	0	1	5	2	1	2	N	N	4	0	0	0	0	0	0	0	1
454	varun	11y	1	346239	H	N	3	2	2	N	P	P,H	90	N	AF	20	MACULOPAPUL	P	1	1	2	0	0	0	7	2	1	1	2	N	N	4	0	0	0	0	0	0	0	4
455	ayan	4y	1	414581	H	N	1	1	2	P	P	P	112	N	F	26	FLUSHING	P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	2	0	0	0	0	0	0	0	2
456	balkuthulla	7y	1	344394	H	J	2	1	2	P	N	P,H,V	90	N	AF	23	COATED TONG	P	1	2	2	0	0	0	3	2	1	1	2	N	N	4	P		0	0	0	0	0	0	3
457	abhilash	3y	1	345334	H	N	3	1	2	P	N	P,V	104	N	AF	25		P	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
458	tejaswini	2y	2	416194	H	N	3	1	2	N	P	V	92	N	AF	24	MACULOPAPUL	P	2	2	2	0	0	0	7	4	1	1	2	N	N	4	0	P		0	0	0	0	0	4
459	chetan	14y	1	344724	H	N	3	1	2	P	N	V	87	N	AF	22	MACULOPAPUL	P	1	1	2	0	0	0	7	5	1	1	2	N	N	4	0	P		0	0	0	0	0	4
460	hemanth	3y	1	345803	H	J	2	1	2	P	N	V	90	N	AF	24	RASH	P	1	2	2	0	0	0	3	1,2		1	1	2	N	N	4	P		0	0	0	0	P		0	3
461	swathi	7y	2	415889	H	N	2	1	2	N	P	P	104	N	AF	23		P	2	1	2	0	0	0	2	5	2	1	2	N	N	4	0	0	0	0	0	0	0	7
462	gayathri	7y	2	346237	H	N	3	2	2	N	P	V	90	N	AF	22	PURPURA	P	1	1	2	0	0	0	7	2,4		1	1	2	N	N	4	0	P		0	0	0	0	0	4
463	harshavard	1y	1	347135	H	N	3	1	2	P	N	V	102	N	AF	26	FLUSHING	P	1	2	2	0	0	0	1	3,4		1	1	2	N	N	1	0	0	0	0	0	0	0	2
464	vaibhav gow	4y	1	416244	H	N	2	1	2	N	P	P,M	99	N	AF	20		A	2	2	2	0	0	0	1	3	2	1	2	N	N	4	0	0	0	0	0	0	0	1
465	nikhil	5y	1	346691	H	N	2	1	2	N	P	P	99	N	AF	23	FLUSHING	A	1	2	2	0	0	0	1	1,3		1	1	2	N	N	4	0	0	0	0	0	0	0	1
466	shaikarbaz	5y	1	346676	H	N	3	1	2	N	N	H,M	92	N	AF	22		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
467	manasvi	3y	2	416261	H	N	3	1	2	P	N	P	114	N	F	26	FLUSHING	P	1	1	2	0	0	0	1	3,4		1	1	2	N	N	3	0	0	0	0	0	0	0	2
468	sadam	12y	1	347655	H	N	2	1	2	N	P	H,M	99	N	AF	20		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
469	ankith	8y	1	346731	H	N	3	1	2	N	P	V	100	N	AF	23	MACULOPAPUL	P	1	1	2	0	0	0	7	3,4		1	1	2	N	N	4	0	P		0	0	0	0	P	4
470	nayan	7y	1	415618	H	N	2	2	2	P	P	P	114	N	F	23		P	1	1	2	0	0	0	2	1,4		2	1	2	P	P	4	0	0	0	0	0	0	0	7
471	bhanupriy	12y	2	345876	H	N	2	2	2	P	N	V	112	N	F	23	RASH	P	1	1	2	0	0	0	3	2,4		1	1	2	N	N	4	P		0	0	0	0	0	0	3
472	gayathri	13y	2	349558	H	J	2	2	2	P	N	P,H	132	N	F	24	RASH, COATED	P	1	2	2	0	0	0	3	2	1	2	2	N	N	4	P		0	0	0	0	0	0	3
473	suma	5y	2	349546	H	N	2	2	2	N	P	V,M	99	N	AF	20	FLUSHING	A	2	2	2	0	0	0	1	1,3		1	1	2	N	N	4	0	0	0	0	0	0	0	1
474	arfa	5y	2	349234	M	N	3	1	2	N	N	P,V	110	N	F	24		A	2	2	2	0	0	0	1	4	2	1	2	N	N	4	0	0	0	0	0	0	0	1
475	gowtham	9y	1	348069	H	N	3	1	2	N	P	V	90	N	AF	29	MACULOPAPUL	P	1	2	1	0	PL EFFUSIO	0	7	3,4		1	1	2	N	N	4	0	P		0	0	0	0	0	4
476	srikanth	12y	1	416220	H	N	2	1	2	P	P	P,M	102	N	F	26	EPISTAXSIS	P	1	1	2	0	0	0	1	3,4		1	1	2	N	N	3	0	0	0	0	0	0	0	2
477	nandan gow	12y	1	344624	H	N	3	1	2	P	N	P,V,M	112	N	F	20	COATED TONG	P	1	2	2	0	0	0	3	2	1	1	2	N	N	4	P		0	0	0	0	0	0	3
478	diyashree	6y	2	349251	H	N	2	1	2	P	P	P,V	102	N	AF	24	FLUSHING	A	2	2	2	0	0	0	1	3	1	1	2	N	N	4	0	0	0	0	0	0	0	1
479	owais	1y6m	1	417120	C	J	3	1	1	P	N	V	134	N	F	26	FLUSHING, MA	P	1	2	1	0	0	0	1	4	1	1	2	N	N	2	0	0	0	0	0	0	0	2
480	hemashree	1y5m	2	347423	H	N	2	2	2	P	N	V	103	N	AF	28	FLUSHING	P	1	2	2	0	0	0	1	3,4		2	1	2	N	N	1	0	0	0	0	0	0	0	2
481	jeevanashr	12y	2	348025	H	N	2	1	2	P	P	P	104	N	F	23		P	1	1	2	0	0	0	2	1,2,4		2	1	2	N	N	4	0	0	0	0	0	0	0	7
482	yusuf	6m	1	418875	M	N	2	1	2	P	N	V	102	N	AF	28	FLUSHING	A	2	2	2	0	0	0	1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
483	rajkshitha	12y	2	348693	H	N	3	2	2	P	N	P,M	112	N	F	20	COATED TONG	P	1	1	2	0	0	0	3	2,4		1	1	2	N	N	4	P		0	0	0	0	0	0	3
484	keerthik ya	4y	1	344656	H	N	2	1	2	P	N	P,V	110	N	AF	26		P	2	2	2	0	0	0	1	4	1	1	2	N	N	4	0	0	0	0	0	0	0	1
485	umar	3y8m	1	348945	M	N	2	2	2	P	N	V	92	N	AF	22	MACULOPAPUL	P	1	2	1	0	0	0	7	2,4		1	1	2	N	N	4	0	P		0	0	0	0	0	4
486	rakesh dha	3y	1	348065	H	N	3	2	2	N	P	P,V	123	N	F	24	MACULOPAPUL	P	1	1	2	0	0	0	7	4	2	1	2	N	N	4	0	0	0	0	0	0	0	4
487	ramakrishn	4y	1	356871	H	N	2	1	2	P	P	P	92	N	AF	26		P	1	2	2	0	0	0	7	5	1	1	2	N	N	4	0	P		0	0	0	0	0	4
488	mannath	4y	1	417908	H	N	2	2	2	N	P	P	114	N	F	23		P	1	1	2	0	0	0	2	4	2	1	2	P	N	4	0	0	0	0	0	0	0	7
489	sudeep kum	7y	1	349656	H	N	2	1	2	P	N	V	90	N	AF	25	FLUSHING	A	2	2	2	0	0	0	1	3	2	1	2	N	N	4	0	0	0	0	0	0	0	1

| | | |

| | | |

| | | |