ACUTE UNDIFFERENTIATED FEBRILE ILLNESS AMONG ADULTS – A HOSPITAL BASED OBSERVATIONAL STUDY

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ABSTRACT. BACKGROUND: Fever is a burning issue in the tropics and the most common cause of morbidity. Quite frequently this fever goes undiagnosed because of many reasons like the lack of diagnostic facilities, insufficient epidemiological data available on causes of fever, and so on. This research study was aimed to find out the etiology and clinical markers of Acute Undifferentiated Febrile Illness [AUFI] among the rural population of Southern India. **METHODOLOGY:** This prospective, observational study was conducted at Government Villupuram Medical College and Hospital, a rural tertiary care centre in Tamil Nadu, India. Consecutive hospitalised adult patients [>16 years] with AUFI[5-14 days fever] were enrolled into the study from August 2010 to February 2012 [18 months].Upon enrollment, detailed history was recorded, physical examination done and basic blood tests including biochemical examination, smear study for malaria, blood cultures and serology for the commonly encountered infections were done according to study protocol. The patients were followed up until clinical recovery and convalescence. The data were entered in MS excel and analyzed using Epi-info software 2008 version. **RESULTS:** A total of 403 patients were included in the study . The distribution of AUFI included Malaria 133[33%], Typhoid 83[20.59%], Dengue 42[10.4%], Leptospirosis 25[6.2%], and other causes 36[8.9%] and unknown cause 84[20.84%]. Malaria patients were significantly associated with jaundice, altered mentation, travel outside the district, elevated AST/ALT levels, thrombocytopenia and splenomegaly. Typhoid fever was associated with longer fever duration, abdominal pain, coated tongue, relative bradycardia, normal platelet counts and low leucocyte count. Dengue fever could be predicted by rash, pruritis, petechiae ,retro-orbital pain and low platelet counts. Leptospirosis patients showed significant association with conjunctival suffusion, muscle tenderness and subconjunctival hemorrhage. Weil's disease was noticeably rare. **Conclusion:** Post monsoon upsurge of AUFI should be anticipated and preventive measures at personal and community levels planned. Clinical prediction of AUFI is possible with proper physical examination and judicious use of laboratory.

KEYWORDS: Acute Undifferentiated Febrile Illness, Malaria, Typhoid, Dengue, Leptospirosis, Jaundice, Thrombocytopenia, Defervescence time, Hospital stay.

INTRODUCTION: Fever is a common symptom of any systemic illness and one of the most important causes of morbidity in tropics. The term Acute Undifferentiated Febrile Illness [AUFI] connotes fever of <14 days duration without any evidence of organ or system specific etiology[1]. Unlike the Western world, in the developing nations the differential diagnosis for AUFI includes potentially significant illnesses such as Malaria, Dengue fever, Enteric fever, Leptospirosis, Rickettsiosis, Hantavirus, and Japanese encephalitis[2]. Most febrile illnesses are not specified as to their cause and treatment is rather generic, typically with antipyretics and antibiotics[3]. Because of this, clinical decision making is compromised, since evidence based epidemiologic data on fever is far from sufficient in this part of the world[4]. Hence, this study was done with the aim of providing the basic data on common causes of AUFI and its predominant clinical markers of the diseases causing AUFI.

OBJECTIVES:

1. To find out the causes of AUFI among hospitalized adults over a period of 18months.
2. To identify the important clinical markers associated with the various causes of AUFI.

MATERIALS AND METHODS: This was conducted as a prospective, observational study over a period of 18 months between August 2010 and February 2012 at Government Villupuram Medical College and Hospital, a 500 bedded tertiary care teaching institute in Villupuram district, Tamil Nadu. This is a fertile place with an average recorded rainfall of 80-100 cms/year. The district spans 7190 sq kms and is fed by 2 monsoons, namely the Southwest monsoon [Jun – Sept] and the Northeast monsoon [Oct- Nov]. **Study population:** All patients with more than 16 years of age, hospitalized with fever of 5-14 days duration [oral temperature of 101*F at least once during admission] and no evidence of organ specific disease on initial clinical evaluation were included in the study. Immuno-compromised patients [HIV] and those with hematological malignancies were excluded. **Data collection and analysis:** On admission, eligible patients were identified, detailed history elicited and physical examination done. This was followed by basic laboratory investigations which included Blood counts, Blood basic biochemistry, Liver function tests, Urine basic investigations and Chest X-ray as per study protocol **[Figure.1]**. The treatment was entirely at the discretion of the treating physician. The patients were followed up till clinical recovery and convalescence. Upon discharge, selected patients [whose diagnoses were unclear] were asked to return after 4 weeks for convalescent serology. Others were followed up by telephone calls and review OP visit, if necessary. Data were analyzed using Epi-Info version 3.5.1, 2008. Two-sided *P* values were calculated using the chi-square test or Fisher's exact test for (qualitative) dichotomous and ordinal variables. Continuous (quantitative) variables were compared using a two-sided Wilcoxon rank sum test and the unpaired student's *t*-test. Variables were analyzed in a stepwise manner and final associations were recorded as odds ratios (ORs) with 95% confidence intervals. **Ethical considerations:** The study was approved by the Institutional Review Board of the Government Villupuram Medical College and Hospital, Villupuram. All patients in the study gave written informed consent.

RESULTS: This study revealed that the causes of AUFI included Malaria 133 [33%], Typhoid 83 [20.59%], Dengue 42 [10.42%], Leptospirosis 25 [6.2%], Alternate diagnosis 36 [8.9%] and unknown diagnosis 84[20.84%] **[Figure.1].** The clinical presentation of AUFI showed that the majority were reporting headache 71.5%, followed by chills 55.1%, myalgia 47.1%,

nausea/vomit 44.9%, constipation 33.7%, diarrhea 11.4% and arthralgia 9.4%. **[Table 1].** Physical examination revealed hepatomegaly 53.1%, splenomegaly 24.3%, anemia 24.6%, jaundice 10.4%, lymphadenopathy 8.9% and coated tongue 6.5% as prominent clinical findings. The important laboratory findings included mean Hemoglobin [11.23gm%], Total count [8037/cu mm] and Thrombocytopenia [platelets <1.5 lakhs/cu mm],which occurred in 38% of cases. Other important laboratory findings included AST/ALT elevations in 57% and acute kidney injury [serum creatinine >1.5 mg%] in 3.5% of cases **[Table.1].** Among the 403 study subjects, AUFI occurred predominantly during and post monsoons [Jun-Nov] 243 cases [60.3%] [Figure.2]. The mean age of occurrence of AUFI was 28.3 years, mean fever duration at presentation was 7.7 days. Men were predominantly affected with male to female ratio being 1.9:1. Approximately 79.2% had a confirmed diagnosis and 96.5% [389 cases] were cured. The relapse rate was 1.9%[8 cases], with malaria and typhoid causing 1% relapse each . 37[9.2%] patients required ICU care , 4[1%] died during the study period .Most [75%] of the deaths were attributable to malaria. The mean time to defervescence was 3.5 days and mean hospital stay was 5.5 days.

Among the study population 8.9% [36 cases] were those whose initial evaluation using the study protocol did not reveal the diagnosis. However on further evaluation using investigations such as urine culture, IgM ELISA for Scrub Typhus, IgM ELISA for Chikungunya antibody, CT scan chest, sputum AFB staining, sputum culture and ECHO cardiography, the etiology was ascertained. They were classified as “Alternate diagnosis” group. The breakup for this group included Urinary tract infection 10[2.5%], Tuberculosis 7[1.7% of AUFI], Scrub typhus 7[1.7%], Intra abdominal abscesses 4[1%], Upper respiratory tract infection 3[0.7%], SLE 1[0.2%],Infective endocarditis 1[0.2%], Pneumonia 2[0.5%] and Chickungunya infection 1[0.2%].

ANALYSIS: The statistical association between the variables and the disease outcome were analyzed using Chi-square and t test. The clinical and lab findings which were associated with occurrence of Malaria were travel history ($p < 0.0001$), presence of splenomegaly ($p < 0.0001$), jaundice ($p < 0.0001$) and altered mentation (0.004), thrombocytopenia [$p<0.001$], AST/ALT elevations [$p<0.001$],serum bilirubin elevation [‘p’ <0.001] as frequent occurrence in malaria, as compared with others.**[Table.2]**. Typhoid patients were significantly associated with abdominal pain [p <0.001], constipation [0.002], coated tongue [$p<0.002$], myalgia [$p<0.001$] and relative bradycardia $p<0.0001$], low WBC counts [0.00001], low polymorphs count [$p = 0.00001$], low lymphocyte count [$p = 0.000001$], Serum bilirubin levels [$p = 0.0029$], AST/ALT levels[$p = 0.000001$], Alkaline phosphatase levels[$p = 0.000001$] and Serum creatinine [$p = 0.0053$] **[Table.3]**. Dengue showed significant association with petechiae [$p<0.0001$], pruritis [$p<0.0001$], rash [$p = 0.001$], retro-orbital pain [$p<0.0001$], arthritis [$p<0.0001$], bleeding manifestations [$p<0.001$], leucopenia [$p<0.001$], thrombocytopenia [$p<0.0001$] and elevated AST/ALT levels [$p<0.0001$] **[Table.4.].** Leptospirosis patients were associated with abdominal pain [$p<0.001$], arthralgia [$p=0.01$], conjunctival suffusion [$p<0.0001$], muscle tenderness [$p<0.0001$] and subconjunctival hemorrhage [$p<0.0001$]. Laboratory associations were differential count [$p< 0.001$], alkaline phosphatase elevation [$p <0.01$] and elevated serum creatinine values [$p<0.001$] **[Table .5].**

DISCUSSION: In our study, AUFI occurred most commonly during and post monsoons 60.3%. It affected males twice as that of females and that in the most productive age group. The study

revealed the heavy burden of tropical infections such as malaria, typhoid, dengue, leptospirosis in the study population. Previous studies in Northern and Southern parts of the country have paved the path for organized research on AUFI[1,2,5]. Similar to others, this study showed the occurrence of AUFI predominantly in the young and middle aged productive population .Male preponderance [2:1] was observed, as had been noted in many studies across the country1,5. This sexual parity was probably because of travel and occupational exposures. Seasonal upsurge in fever is also a well known documentation in other studies[5,6,7].

MALARIA: Malaria constituted 1/3rd of AUFI in our study. In central India majority of the cases (88%) had non-malarial acute undifferentiated fever, whereas in another South Indian study, it constituted 17.1% [1,5]. According to official estimates in India, although about 100 million individuals are investigated for malaria by microscopy every year, fewer than 2% of them are slide-positive[8].In our study the high yield of malaria is due to referral bias and microscopy supported by HRP based Rapid Diagnostic Tests. Clinical features of malaria were documented in other studies too, which revealed significant associations such as jaundice, altered mentation and splenomegaly[5,9]. In a previous study in Northwestern India, the relapse rate of vivax infection was estimated as upto 30%.[10]. In our study relapse occurred only in 2% of vivax +ve malaria, probably due to the institution of timely radical treatment .In our study ,the mortality for malaria was 2.2%,whereas in others the range was 7.9- 30% 11.The low mortality could be explained by the low prevalence of falciparum infection in our state[<10%][11].

TYPHOID: Typhoid constituted 20.59% of AUFI in our study. Salmonella, the commonest bloodstream bacterial infection accounted for 1/10th of AFI in a North Indian study[1]. .In our study typhoid had a sudden upsurge in January and February 2012, which can be attributed to the natural disaster Thane cyclone in December 2011. Younger age, relative bradycardia, abdominal pain, low total count and longer fever duration at presentation were some of the reliable associations, as substantiated in other studies[12,13]. In contrast to other studies, we identified constipation rather than diarhoea to be frequenting typhoid[5,13].

DENGUE: In our study dengue contributed 10.42% of cases to the fever burden. The proportion of dengue fever among all fever cases has been estimated to be 14% in a population-based study in rural South India and 48% in a hospital based study in urban North India[1,5]. Younger age significantly predicted for acute dengue in previous case studies[3,14] . Similar to ours, another study done in Chennai, India, documented frequent presence of petechiae, rash, bleeding manifestation and arthralgia in adults with dengue[15] .Unlike a few other studies anemia and hepatosplenomegaly were not very significant associations here, probably due to the confounding effect of malaria and typhoid[15]. Earlier studies have shown that significantly elevated hepatic transaminase levels are common in dengue infections[5,14] .

LEPTOSPIROSIS: Leptospirosis caused 6.2% of AUFI in our study. Compared with others these patients suffered abdominal pain, arthralgia, conjunctival suffusion, muscle tenderness and subconjunctival hemorrhage more frequently. The incidence of Weil's disease was low[8%]. In the absence of AST/ALT rise, moderate Alkaline phosphatase elevations and serum creatinine rise was commonly associated with leptospirosis. In our study there were no deaths probably because of the low numbers. Leptospirosis is known to cause upto 1/3rd of AUFI in a previous estimate[16].It is most common in the coastal regions like Chennai and Kolkatta[17]. The occurrence

of leptospirosis has got a strong correlation with rainfall and floods,most outbreaks occurring during October to November[17,18]. In our study too, leptospirosis peaked during monsoons with almost nil transmission during winters. Similar to our study, moderate Alkaline phosphatase elevation and jaundice were associated with severe disease in previous studies[17] .

In our study further 20.84 % of AUFI went without a diagnosis, despite extensive evaluation. In many other studies the diagnosis could not be ascertained in 8- 50% of cases depending upon study centre and work up protocols[2,5]. In our study, the high percentage of unknown cases occurred because the study did not incorporate viral diagnostic methods.

This study identified areas for future focused research like microbial sensitivity pattern of the prevalent pathogens .Outcome based studies should be designed in this setup to materialise rational, protocol based management of fever. This would be the first step to fight irrational and unwarranted usage of antimicrobials in the hospital setting. Such studies should be periodically repeated for surveillance purpose to detect newer and potentially serious pathogens causing changing fever patterns. Considering the burden of local infections, it is strongly recommended that an Infectious Diseases Team be constituted at every district to anticipate outbreaks and design protocols for Infectious Disease management.

Limitations

1. This study was not powered to make an exhaustive search into all the causes of fever since viral studies were not available in our institute.
2. The focus was on hospitalized patients and hence could not be generalized to predominantly milder forms of AUFI which occur in the community. Hence, it may underestimate the true burden.

CONCLUSION: Our study clearly identified the predominant causes and provided some basic epidemiological data on AUFI. It was proven in our study that majority of the AUFI could be reliably predicted using proper history, good physical examination and simple laboratory tests. We herein stress the need for establishment of accurate epidemiologic database of causes of AUFI in every region to anticipate epidemic, prioritize resource allocation and optimize health care delivery.

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Table.1 Clinical Features of AUFI in Tropical India

VARIABLE	N=403(%)
Age[mean (SD in years)]	28.32(9.5)
Mean fever [mean(SD in days)]	7.72(2.6)
Defervescence[mean(SD in days)]	3.53(1.3)
Hospital Stay[mean(SD in days)]	55.46(1.8)
Male/female ratio	1.96/1
Symptom Analysis	
Headache n(%)	288(71.5)
Chills n(%)	222(55)
Cough n(%)	193(47.9)
Myalgia n(%)	190(47)
Nausea/vomit n(%)	181(44.9)
Constipation n(%)	136(33.7)

Dyspnoea n(%)	84(20.8)
Diarhoea n(%)	46(11.4)
Jaundice n(%)	42(10.4)
Abdominal pain n(%)	37(9.2)
Rash n(%)	37(9.2)
Arthralgia n(%)	38(9.4)
Altered mentation n(%)	20(5)
Bleeding manifestations n(%)	16(4)
Retro orbital pain n(%)	15(3.7)
Pruritis n (%)	12(3)
H/o travel n(%)	81(60.9)
H/o contact	18(4.5)
Clinical signs.	
Hepatomegaly n(%)	214(53.1)
Splenomegaly n(%)	98(24.3)
Anemia n(%)	98(24.3)
Icterus n(%)	37(9.2)
Lymphadenopathy n(%)	36(8.9)
Coated tongue n(%)	26(6.5)
Arthritis n(%)	20(5)
Relative bradycardia n(%)	20(5)
Conjunctival suffusion n (%)	10(2.5)
Herpes labialis n(%)	11(2.7)
Muscle tenderness n(%)	8(2)
Neck stiffness n(%)	8(2)
Shock n(%)	8(2)
Laboratory tests	
Hb%[mean(SD in gm/dl)]	11.23(1.9)
Platelet count[mean(SD 1 x 100,000)]	1.60(0.41))
DC[mean (SD in %)]	8037(2726)
Polymorphs[mean(SDin %)]	59.53(5.9)
Lymphocytes[mean(SDin %)]	35.63(6)
Serum bilirubin[mean (SD in mg/dl)]	1.42(0.86)
AST[mean(SD in IU/L)]	70.01(51.6)
ALT[mean(SD in IU/L)]	70.4(39.6)
ALP[mean(SD in IU/L)]	127.37(50.9)
Ser creatinine[mean (SD in mg/dl)]	1.04(0.29)

Table.2 Clinical Associations of Malaria

Variable	Malaria	Others	Chi square	'P' value	OR	CI
Age[mean (SD in years)]	29.2(8.8)	27.9(9.7)		0.165(NS)		

Mean fever [mean(SD indays)]	8.35(2.61)	7.41(2.6)		.0008(HS)		
Defervescence[mean(SD indays)]	3.44(1.3)	3.57(1.27)		0.34(NS)		
Hospital Stay[mean(SD indays)]	5.466(2.17)	5.46(1.60)		0.98(NS)		
Male/female ratio	3.3/1					
Myalgia n(%)	38(28.5)	152	26.38	0.000001	0.31	0.19—0.48
Jaundice n(%)	29(21.8)	13	25.76	0.000001	5.51	2.75—11.02
H/o travel n(%)	81(60.9)	89	27.39	0.000001	3.17	2.06—4.87
Rash n(%)	0	37	18.46	0.00002	0	undefined
H/o contact	0	18	7.78	0.005	0	undefined
Clinical signs						
Hepatomegaly n(%)	75(56.6)	139	0.676	0.41	1.218	0.80---1.85
Splenomegaly n(%)	49(36.8)	49	15.92	0.00006	2.63	1.65—4.20
Anemia n(%)	31(23.3)	67	0.04	0.835	0.92	0.56—1.49
Icterus n(%)	31(23.3)	6	45.01	0.0000	13.37	5.41—33.00
Altered mentation n(%)	13(9.7)	7	8.28	0.004	4.07	1.58---10.46
Shock n(%)	4(3)	4	0.43	0.51	2.06	0.51—8.38
Laboratory tests						
Hb%[mean(SD in gm/dl)]	11.26(1.97)	11.21(1.85)		0.8(NS)		
Platelet count[mean(SD 1 x 100,000)]	1.417(0.34)	1.7(0.4)		0.0001(HS)		
DC[mean (SD in %)]	8146.6(2670)	7983.3(27.57)		0.57(NS)		
Polymorphs[mean(SDin %)]	58.7(3.9)	59.9(6.6)		0.069(NS)		
Lymphocytes[mean(SDin %)]	36.5(4.66)	35.2(6.5)		0.04(s)		
Serum bilirubin[mean (SD in mg/dl)]	1.78(1.24)	1.24(0.49)		0.000001(HS)		
AST[mean(SD in	77.5(33)	66.3(58.3)		0.0410(S)		

IU/L)]						
ALT[mean(SD in IU/L)]	83.2(37.8)	64(38.9)		<.0.0001(HS)		
ALP[mean(SD in IU/L)]	136.9(39.4)	122.7(55.18)		0.0082(HS)		
Ser creatinine[mean (SD in mg/dl)]	1.06(0.33)	1.03(0.25)		0.3325(NS)		

Table.3.Clinical Associations of Typhoid

Variable	Typhoid	Others	CHI Square	P	OR	CI
Age[mean (SD in years)]	26.04(7.89)	28.9(9.77)		0.014(S)		
Mean fever [mean(SD indays)]	8.6(2.73)	7.5(2.6)		0.001(S)		
Defervescence[mean(SD indays)]	3.68(1.6)	3.49(1.18)		0.2395(NS)		
Hospital Stay[mean(SD indays)]	5.65(2.02)	5.41(1.74)		0.2923(NS)		
Male/female ratio	1:1.06					
Constipation n(%)	40(48)	96	8.959	0.0027	2.17	1.326—3.55
Myalgia n(%)	57(68.6)	133	18.3687	0.00001	3.08	1.84—5.155
Jaundice n(%)	3(3.6)	39	4.31	0.378	0.270	0.08—0.8973
H/o travel n(%)	28(33.7)	142	2.638	0.104	0.6382	0.38—1.058
Diarhoea n(%)	10(12)	36	0.0001	0.99	1.08	0.512—2.279
Abdominal pain n(%)	22(26.5)	15	35.05	0.000000	7.33	3.599—14.93
Rash n(%)	4(4.8)	33	1.77	0.183	0.44	0.151—1.28
Clinical signs						
Hepatomegaly n(%)	49(59)	165	1.1933	0.274	1.353	0.8299---2.208
Splenomegaly n(%)	16(19.2)	82	1.1187	0.2902	0.6931	0.38—1.26
Icterus n(%)	0	37	9.225	0.002	0	

Altered mentation n(%)	2(2.4)	18	0.8434	0.3584	0.414	0.09---1.822
Coated tongue n(%)	12(14.4)	14	9.49	0.002	3.69	1.638—8.33
Relative bradycardia n(%)	18(21.6)	2	57.60	0.000000	44.03	9.97—194.04
Rose spot n(%)	3(3.6)	0	7.274	0.0069	0	
Laboratory tests						
Hb%[mean(SD in gm/dl)]	11.03(1.96)	11.28(1.88)		0.2974(NS)		
Platelet count[mean(SD 1 x 100,000)]	1.89(0.22)	1.53(0.41)		0.000001(HS)		
DC[mean (SD in %)]	6697.6(1560)	8384.7(2856)		0.000001(HS)		
Polymorphs[mean(SDin %)]	55.2(5.88)	60.6(5.39)		0.000001(HS)		
Lymphocytes[mean(SDin %)]	39.6(5.47)	34.6(5.7)		0.000001(HS)		
Serum bilirubin[mean (SD in mg/dl)]	1.17(0.28)	1.48(0.94)		0.0029(S)		
AST[mean(SD in IU/L)]	45.4(12.3)	76.3(55.8)		0.000001(HS)		
ALT[mean(SD in IU/L)]	50.49(15.66)	75.55(42.2)		0.000001(HS)		
ALP[mean(SD in IU/L)]	103.6(27)	133.5(53.8)		0.000001(HS)		
Ser creatinine[mean (SD in mg/dl)]	0.996(0.13)	1.06(0.31)		0.0053(S)		

Table.4.Clinical Associations of Dengue

Variable	Dengue	Others	Chi Square	P value	OR	CI
Age[mean (SD in years)]	22.4(6.76)	29(9.52)		0.00001(HS)		
Mean fever [mean(SD indays)]	5.54(0.7)	7.97(2.67)		0.0001(HS)		
Defervescence[mean(SD indays)]	3.34(.930	3.55(1.31)		0.311(NS)		
Hospital Stay[mean(SD indays)]	4.9(1.14)	5.52(1.86)		0.0341(HS)		
Male/female ratio	2/1					
Myalgia n(%)	19(45.2)	171	0.0097	0.921	0.92	0.48-1.74
Dyspnoea n(%)	3(7)	81	4.45	0.03	0.27	0.08-

						0.88
Arthalgia n(%)	9(21.4)	29	6.41	0.011	3.12	1.36-7.15
Bleeding manifestation n(%)	8(19)	8	23.72	0.000002	10.38	3.66-29.41
Retro orbital pain n(%)	14(33.3)	1	105.68	0.000000	180	22.83-1419.23
Pruritis n(%)	12(28.5)	0	96.64	0.0000000	undef	Undef
Rash n(%)	10(23.8)	27	10.15	0.001	3.86	1.72-8.7
Petechiae n(%)	5(12)	1	27.21	0.000001	48.64	5.53-427.6
Clinical signs						
Hepatomegaly n(%)	17(40.4)	197	2.46	0.12	0.57	0.295-1.08
Splenomegaly n(%)	5(12)	93	3.208	0.073	0.389	0.148-1.02
Anemia n(%)	8(19)	90	0.42	0.51	0.71	0.32-1.59
Arthritis n(%)	9(21.4)	11	23.19	0.000002	8.68	3.35-22.45
Shock n(%)	4(9.5)	4	9.7112	0.001	9.3947	2.257-39.08
Laboratory Tests						
Hb%[mean(SD in gm/dl)]	11.36(1.78)	11.21(1.9		0.63(NS)		
Platelet count[mean(SD 1 x 100,000)]	1.009(.280	1.68(0.36)		0.000001(HS)		
DC[mean (SD in %)]	5373.8(1805)	8347(2647)		0.000001(HS)		
Polymorphs[mean(SDin %)]	62.04(5.070	59.23(5.94)		0.0034(HS)		
Lymphocytes[mean(SD in %)]	32.6(4.92)	35.9(6.02)		0.0006(HS)		
Serum bilirubin[mean (SD in mg/dl)]	1.48(0.66)	1.42(.087		0.6807(NS)		
AST[mean(SD in IU/L)]	169.2(87.5)	58.4(28.6)		0.000001(HS)		
ALT[mean(SD in IU/L)]	121.2(55.4)	64.48(32.6)		0.000001(HS)		
ALP[mean(SD in IU/L)]	195.7(74.60	119.4(40.6		0.00000(HS		
Ser creatinine[mean (SD in mg/dl)]	1.09(.37)	1.03(.27		0.202(NS)		

Table.5.Clinical associations of Leptospirosis

Variable	Leptospirosis (n=25)	Others (n=378)	Chi square	P value	OR	CI
Age[mean (SD in years)]	26(8.58)	28.47(9.52)		0.0065(NS)		
Mean fever [mean(SD indays)]	6.1(1.1)	7.82(2.68)		0.0022(S)		
Defervescence[mean(SD indays)]	3.52(1.38)	3.53(1.28)		0.9625(NS)		
Hospital Stay[mean(SD indays)]	5.44(2.10)	5.46(1.79)		0.9455(NS)		
Male/female ratio	1.5/1					
Myalgia n(%)	19(76)	171	8.90	0.002	3.83	1.49—9.812
Jaundice n(%)	3(12)	39	0.071	0.789	1.853	0.339—4.1413
H/o travel n(%)	6(24)	164	3.613	0.05	0.412	0.1609—1.055
Arthalgia n(%)	6(24)	32	6.62	0.01	3.414	1.272—9.159
Abdominal pain n(%)	8(32)	29	16.644	0.00004	5.66	2.25---14.236
Bleeding manifestation n(%)	2(8)	14	1.135	0.286	2.2609	0.484—10.55
Rash n(%)	5(20)	32	3.74	0.05	2.70	0.95—7.68
Conjunctival suffusion n(%)	7(28)	3	71.72	0.00000	48.61	11.60—203.70
Clinical signs						
Hepatomegaly n(%)	11(44)	203	0.8866	0.3463	0.6773	0.2998—1.5305
Splenomegaly n(%)	7(28)	91	0.196	0.657	1.22	0.496—3.029
Sub conjunctival hemorrhage n(%)	4	0	61.08	0.00000	Undefined	Undefined
Anemia n(%)	4(16)	94	1.001	0.316	0.575	0.192—1.719
Icterus n(%)	2(8)	35	0.0446	0.832	0.8522	0.192—3.766
Arthritis n(%)	3(12)	17	2.7986	0.09	2.8957	0.788—10.63
Muscle tenderness n(%)	8(32)	0	123.40	0.00000	Undefined	Undefined
Neck stiffness n(%)	2(8)	6	4.95	0.02	5.39	1.03—28.20
Laboratory Tests						
Hb%[mean(SD in	11.4(1.62)	11.2(1.9)		0.5893(NS		

gm/dl)]				)		
Platelet count[mean(SD 1 x 100,000)]	1.64(0.31)	1.6(0.41)		0.6178(NS)		
DC[mean (SD in %)]	8996(1624)	7973(2773)		0.06994(N S)		
Polymorphs[mean(SD in %)]	63.8(6.3)	59.2(5.78)		0.0002(HS)		
Lymphocytes[mean(S Din %)]	31.6(6.01)	35.9(5.9)		0.0006(HS		
Serum bilirubin[mean (SD in mg/dl)]	1.35(0.6)	1.42(0.87)		0.0028(NS)		
AST[mean(SD in IU/L)]	58.9(26.9)	70.7(52.7		0.267(NS)		
ALT[mean(SD in IU/L)]	70.7(37.2)	70.4(39.8)		0.9706(NS)		
ALP[mean(SD in IU/L)]	155.08(59. 6)	125.54(49. 80		0.0048(S)		
Ser creatinine[mean (SD in mg/dl)]	1.25(0.43	1.03(0.270		0.0002(HS)		

Figure – 1 (Study Protocol for Workup of Acute Undifferentiated Febrile Illness Patients)

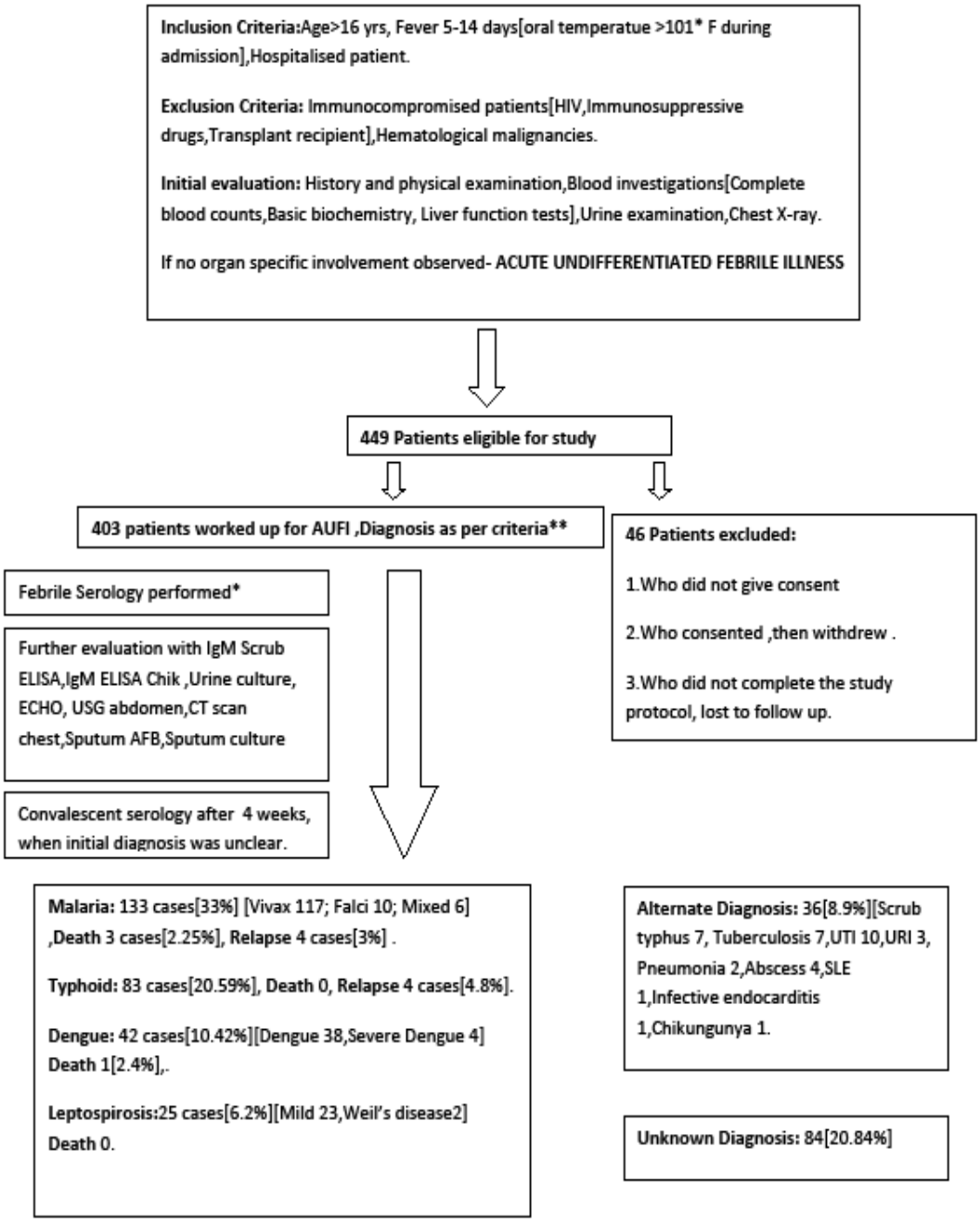

Figure – 2 – (Distribution of various infections causing Acute Undifferentiated Febrile Illness in Villupuram District).

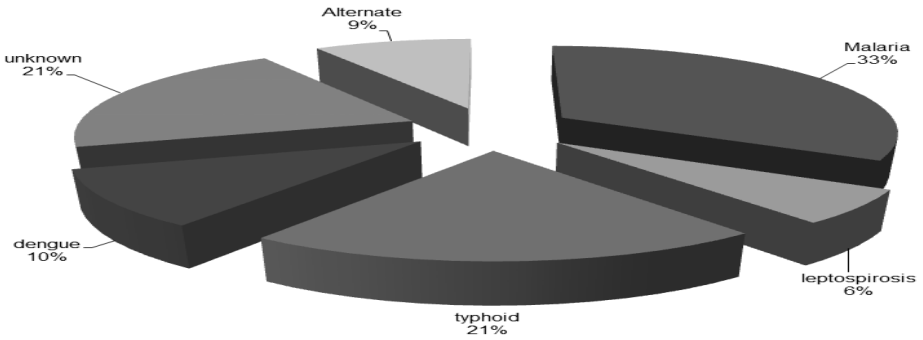

Figure – 3 Seasonal variation of acute undifferentiated fever showing peak occurrence during and post monsoons [June –December]