Acute Kidney Injury in Acute Febrile Illness

A dissertation submitted to the
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CHRISTIAN MEDICAL COLLEGE, VELLOR

BONAFIDE CERTIFICATE

This is to certify that the work presented in this dissertation titled "**Acute Kidney Injury in Acute Febrile Illness**" done towards fulfillment of the requirements of the **Tamil Nadu Dr. M.G.R. Medical University, Chennai for the D.M. (Branch–III) (Nephrology)** exams to be conducted in August 2011, is a bonafide work of the candidate **Dr. Pratish Jacob George**, Senior Post Graduate student in the Department of Nephrology, Christian Medical College, Vellore, under my guidance and supervision. This dissertation has not been submitted, fully or in part to any other board or University.

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Acknowledgement

All praise and thanks be to God for His guidance and sustenance from conception to submission of this work. This study seeks to improve lives for people suffering from acute febrile illness, which frequently results in acute kidney injury and death. The patients, many of whom succumbed to their illness, exhibited selflessness by participating in this study. This work is dedicated to each one of them.

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Contents

Abbreviations

ADQI	Acute Dialysis Quality Initiative
AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network
AIN	Acute interstitial nephritis
ARF	Acute renal failure
ATN	Acute tubular necrosis
CKD	Chronic kidney disease
DF	Dengue Fever
DHF	Dengue Hemorrhagic Fever
DIC	Disseminated intravascular coagulation
DSS	Dengue Shock Syndrome
ESRD	End-stage renal disease
GFR	Glomerular filtration rate
ISN	International Society of Nephrology
MDRD	Modification of diet in renal disease
MODS	Multi organ dysfunction syndrome
NKF	National Kidney Foundation
RIFLE	Risk, Injury, Failure, Loss, and End-stage kidney disease
RRT	Renal replacement therapy
WHO	World Health Organization

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ABSTRACT

AIM: To study the clinical features, prognosis and outcomes of acute kidney injury (AKI) in patients presenting with scrub typhus, malaria, dengue fever, typhoid, leptospirosis and undifferentiated fever particularly to identify patients at high risk of developing AKI and mortality related to AFI, aiming to identify mechanisms for effective management using the RIFLE criteria and testing the utility of Cystatin C as a biomarker for diagnosis of AKI.

PATIENTS AND METHODS: Consecutive in-patients with AFI were enrolled prospectively after admission to a tertiary care referral hospital. They were studied based on etiology of AFI. AKI in these patients was investigated and graded using the RIFLE criteria. Their presentation and course during hospital stay was studied to estimate morbidity, severity of AKI, dialysis requirement, mortality and evaluated for prognostic indicators.

RESULTS: 163 patients were enrolled in the study and 136 patients were studied based on inclusion criteria. The mean age was 40.9 ± 15.6 (16 to 77 years) and sex ratio 2:1 (male 91: female 45). AKI was observed in 71.3% and was graded using the RIFLE criteria as Risk (R) in 19.9%, Injury (I) in 15.4% and Failure (F) in 36%. 10 (7.4%) patients had hospital associated AKI. Undifferentiated fever had the highest incidence of AKI (94.7%) with dialysis requirement in 26.3% and death in 52.6%, while in the differentiated fevers AKI was commonest in malarial infection by *P. falciparum* (100%). Maximum dialysis requirement was noted in in mixed malarial infection (27.8%) and highest mortality in dengue fever (42.7%). Overall 26.5% patients died during hospital

stay with 33% mortality in AKI as compared to 10.3% in the non AKI group. RIFLE criteria was identified as a sensitive tool for diagnosis of AKI in AFI and patients have worse prognosis and outcomes from R through I and F stages in terms of organ support, dialysis requirement and death. RIFLE staging using Cystatin C appears to be sensitive in diagnosing AKI in AFI earlier and may be a useful adjunct for early management. Fractional excretion of sodium (FENa) was useful in identifying early AKI. The Liano scoring at admission identified high risk patients and may be useful for triage to high dependency care. Renal Failure Index (RFI) was higher in those who underwent dialysis and died. Hemodialysis was initiated in 18.4% of whom 48% required SLED. Mortality in patients initiated on hemodialysis was 64% with 100% mortality in those requiring SLED.

CONCLUSION: AKI has a high incidence in AFI. Application of the RIFLE criteria shows incremental risk for morbidity, dialysis requirement and mortality. Patients requiring hemodialysis have high mortality. Cystatin C has promise as a biomarker for early identification and management of AKI in AFI.

Introduction

Acute renal failure has dominated the attention of Nephrologists for decades, with focused research aiming at reducing the morbidity and mortality related to the entity. Despite advances in diagnostics, management and dialysis related interventions the results have been disappointing with no significant mortality differences in last five decades.(1) The importance of this quest to reduce mortality and renal morbidity is amplified by the fact that 60% critically ill patients die during hospitalization and 13% of the survivors become dialysis dependent (1). In patients who recover from acute renal failure after variable periods of renal replacement therapy, renal insufficiency is observed in 41% and five year survival is about 50%. (2) This puts an additional burden on health infrastructure and economy. (3)

Infectious disease resulting from established as well as novel bacterial and viral diseases are increasing with 13 million deaths annually. In developing countries infectious disease account for 50% deaths, as a result of growth of these diseases and poor care health infrastructure. (4) Most of these diseases are sub optimally managed in the community, often presenting with complications to higher centers. Alternately long hours spent in travel to health care centers contribute to deterioration in organ function and reserve.

Acute renal failure has interested renal care physicians in the tropics owing to a heavy burden of disease related to infectious disease. Care for these patients involves an aggressive combination of infectious disease and clinical nephrology.

In India it has been an understudied area with no cumulative national data on incidence of these diseases and related complications. Available literature has been restricted to a few centers of excellence on specific diseases of interest. Recent data citing renal failure in

41.3% with mortality of 12.1% in scrub typhus, typhoid, leptospirosis, malaria, dengue fever and acute undifferentiated febrile illness (5) emphasizes a need to improve care and reduce in-hospital mortality and morbidity related to renal failure. The benefits of early diagnosis and appropriate health care interventions as a possible solution to this complex problem is currently undergoing intense scrutiny by the renal as well as infectious disease community.

This study aims to study morbidity and mortality, identify risk factors, validate standard criteria for diagnosis and identify steps to improve care for patients admitted to hospitals in India with acute renal failure in acute febrile illness.

Review of Literature

Infection is a major cause for death in South Asia and India in particular. This situation has been ascribed to poverty, crowding, ill hygiene, illiteracy, malnutrition, poor access to clean drinking water, sanitation and appropriate health care. Malaria, typhoid and dengue fever are common causes of morbidity and death. In the presence of poor reporting and indiscriminate antibiotic use, the magnitude and burden of disease are unreliable. Tackling the problem at the community level is further hampered by antibiotic resistance. (6)

The National Commission on Macroeconomics and Health identified infection and vector borne disease to be a significant health problem in India, with 1.6% of the total burden of disease and 4200 disability adjusted life years (DALYS) lost in 1996. Comparatively tuberculosis was reported at 2.8% with 7577 DALYS. This translates to huge numbers related to malaria and other vector borne diseases like dengue fever, which are prominently mentioned in the report.(7)

Acute febrile illness (AFI) is commonly seen in the community and managed by local health care practitioners, empirically with anti-malarials and antibiotics in most cases. Thereafter they are referred to or find their way to higher centers especially if unresponsive to these medications. Acute undifferentiated fever constitute about 30-50% of these patients presenting to hospitals with fever. They do not have a localizing cause for fever and remain undiagnosed after a standard work up for fever using blood counts, liver enzymes, chest roentgenogram, ultrasound and blood smears for malaria, which are usually available at most local centers.

Diagnosis and management require a stepwise approach with careful blood film microscopy, serological testing and cultures of blood and available fluid. Investigating these require an intricate knowledge of loco-regional diseases to improve diagnosis and reduce costs related to investigation and better outcomes as a result of early appropriate interventions.

In a study during the monsoons of 2006 in Mumbai 2214 patients with AFI were investigated and 53.75% had undifferentiated fever. Amongst the others 22.5% had malaria, 21.8% had leptospirosis and 1.88% had dengue. 160 patients died of whom 23.12% had acute renal failure (ARF) with acute respiratory distress syndrome (ARDS), 15% had ARDS with hepatorenal failure, 11.25% had hepatorenal failure and 15.62% had isolated ARF. (8)

Data from Vellore, Tamil Nadu, has highlighted a significant burden of disease related to undifferentiated AFI and a diagnostic algorithm was proposed for diagnosis of these patients. Scrub typhus, malaria, dengue fever, typhoid, leptospirosis, spotted fever rickettsiosis and Hanta virus infection was diagnosed in 47.5%, 17.1%, 7%, 8%, 3%, 1.8% and 0.3% respectively with an overall mortality of 12.1%. (9)

Scrub typhus presented with multi organ dysfunction characterized by leucocytosis with transaminitis, tell tale eschar, febrile defervesence with doxicycline, aseptic meningitis and respiratory embarrassment progressing to ARDS. Malaria presented with varying grades of clinical severity, splenomegaly, thrombocytopenia and hepatorenal decompensation characterized by mixed hyperbilirubinemia, transaminitis and renal failure. Dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock

syndrome (DSS) presented with bleeding manifestations, leucopenia, thrombocytopenia and overt bleeding. Typhoid fever presented with diarrhea and leucopenia.(9)

Evidence based diagnostic and management algorithms offer scope for better management of patients at a secondary level, where multiorgan dysfunction and renal failure, often result in death.

ARF has been commonly described in malaria, leptospirosis, melioidosis, shigellosis, cholera and diarrheal disease from tropical countries.(10) The incidence of infection related ARF has been increasing in India in the past few decades, (11) infective causes like sepsis, leptospirosis and malaria accounting for 9.3, 7.8% and 7.5% respectively. (12) This contrasts to childhood diarrhea which has improved in terms of incidence and mortality as a result of community based health programs and awareness by governmental as well as non governmental organizations.(13)

Malaria, leptospirosis, dengue fever and malaria related ARF are a major cause of morbidity and death. (14)(15) Emergence of new diseases, particularly zoonotic and vector borne diseases, along with better diagnostic and surveillance facilities, has added to this burden in India. (16)

Infection related ARF has a high rate of complications despite optimal management. Moderate to severe ARF occurs in 1.5 % hospital admissions in India. (17) In-hospital mortality in ARF is higher than for those without ARF (42.7% versus 13.4%) (18) and deaths related to ARF in sepsis far exceed those not resulting from sepsis (74.5% versus 45.2%). (19) Intervention with dialysis is required in 69% and persistent dialysis-dependent renal failure in 8.18% patients. (12) However, data on ARF in infectious

disease in India continues to be sparse, especially their incidence, outcomes and intervention, particularly so in zoonotic and vector borne diseases.

A concomitant study group of the Vellore study evaluated renal manifestations and interventions for those presenting with acute kidney injury (AKI) in AFI. This study for the first time utilized the RIFLE criteria and validated its utility in patients presenting with AFI and ARF. It generated a baseline glomerular filtration rate (GFR) from the Modification of Diet in Renal Disease (MDRD) equation (whenever a baseline creatinine was unavailable) and utilized serial creatinine measurements to track AKI during the admission and period of hospital stay. (5)

AKI was observed in falciparum malaria, scrub typhus, typhoid fever, mixed malarial infection, dengue, and leptospirosis in 63.2%, 42.6%, 8.7%, 7.6%, 6.5% and 3.3% respectively. Overall 41.1% patients had AKI. 17.4%, 9.3% and 14.4% of these patients were categorized to Risk (R), Injury (I) and Failure (F) of the RIFLE classification of AKI respectively with an incremental risk for death and requirement for dialysis seen across the groups from R to F. While the overall mortality was 12.3% the risk of death based on initial RIFLE category was unavailable.(5)

Renal involvement in AFI is not clearly elucidated and pathophysiology of AKI in AFI is an evolving area of interest. An understanding of the disease and related pathophysiology enables early identification, appropriate management and early intervention.

Scrub typhus

Scrub typhus is an endemic febrile illness with a multisystemic presentation characterized by rash, fever, localized lymphadenopathy and an eschar at the site of the bite of a chigger (larva stage) thrombiculid mite transmitting *Orientia tsutsugamushi*.

The incubation period ranges from 7-15 days. *Rickettsial* proliferation on small vessel endothelium damages its integrity leading to endothelial dysfunction, cytokine release and a polymorphic response. This results in platelet aggregation, micro infarction and gangrene. (20) This focal or diffused vasculitis/perivasculitis causes pulmonary, hepatic, neural, cardiac and splenic manifestations.

Till recently ARF in scrub typhus has been infrequently reported with predominant renal involvement in the disease attributed to pre renal causes like sepsis/hypovolemia and secondary to increased vascular permeability and hypoalbuminemia. (21) Vasculitis and interstitial nephritis are other proposed pathophysiological mechanisms. (22) A case report has documented direct invasion by the *O. tsutsugamushi* cocobacillus in the renal interstitium and acute tubular necrosis with tubular deposition. Glomerular involvement in scrub typus is not reported and is an area of evolving interest. (23)

Whenever available diagnosis is confirmed by Weil-Felix heterophile antibody testing to *Proteus mirabilis,* which may be negative in about 50% patients. Microagglutination testing (MAT), immunoflourescent antibody testing (IFAT), enzyme linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) are the other alternatives. Contiguous presence of hepatic transaminitis, thrombocytopenia and high leucocyte counts is predictive of scrub typhus with specificity and sensitivity of 80%. The

case fatality rate is 14% with renal dysfunction (creatinine >1.4 mg%) being a predictor of death (relative risk 43.99). (24)

Scrub typhus responds to an empirical course of doxicycline. Early recognition and treatment with doxicycline, tetracycline, azithromycin or telithromycin is life saving. Rifampicin is a suitable alternative in unresponsive patients.(25) Prophylaxis with weekly doxicycline especially for medical personnel in endemic areas should be considered.(20) In the Vellore data 42.6% patients had AKI. R was seen in 20.2%, I in 21% and F in 11.2%, with dialysis requirement in 5.9% patients and mortality in 13.3%. (5) Renal failure should be managed early in the pre renal failure with aggressive hydration and dialysis support when indicated by standard indications.

Malaria

Malaria is endemic in India with 80.5% of the population at risk for the disease. The National Vector Borne Control Program reports about 1.5 million cases in India of which 53 % are reported as falciparum malaria.(26) The speculative low number of cases reflects wide distribution, poor access to patients and under reporting of the disease. Malaria is caused by infestation of the *Plasmodium* species transmitted by the bite of anopheles mosquito. Malarial infection is caused by the four species *Plasmodium vivax, Plasmodium falciparum, Plasmodium malariae and Plasmodium ovale*, either alone or in combination. In combination the disease is referred to as mixed malarial infection.

The anopheline mosquito transmits sporozoites to the blood stream during its blood meal and within hours sporozoites invade hepatocytes, dividing into exoerythrocytic merozoites. These leave the liver, invade red blood cells (RBC s) developing into ring shaped, vacuolated trophozoites. These divide into merozoites which lyse the RBC s and

invade other unaffected RBC s in a process referred to as blood schizogony. This process occurs every 48 hours in *P. falciparm*. In non immune individuals the process of destruction is magnified several fold.

While fever is a cardinal presentation other manifestations may vary such as headache, chills, diaphoresis, myalgia and vomiting in uncomplicated disease or seizures, altered sensorium, renal failure, hepatitis and ARDS in severe disease. Indicators of severe malaria and poor prognosis are listed. (Table 1) (27)

Severe disease which is often fatal results in 1.5 – 2.0 million deaths annually world wide. (28) In non endemic areas history of travel from an endemic region provides diagnostic clues to an underlying malarial infection.

Malaria is reliably diagnosed using thick and thin smears with a sensitivity of 90% and parasitic index expressed as a percentage of parasitized RBC s or parasites visualized in each microlitre of blood. Although one well examined negative smear is indicative of the absence of the disease repeat examinations are encouraged. Alternatively in areas where microscopy is not possible dipstick assays may be a good alternative, although the false negatives are reported. (29)

ARF occurs in 13-17.8% cases, particularly in those with heavy parasitemia and hemolysis, manifested by oliguria or anuria secondary to ischemic injury. Hemoglobinuria secondary to massive hemolysis may present with 'Blackwater Fever.' Acute tubular necrosis (ATN) is the most common biopsy picture. Metabolic acidosis and hyperkalemia are common complications. Patients with severe renal failure often require dialysis, for anuria, hyperkalemia and metabolic acidosis, till recovery of renal function. Ideally patients with severe disease should be managed in a high dependency unit as

mortality in this group of patients is as high as 29%.(29) In the Vellore data malaria related AKI was seen in 59.6% of those with *P.falciparum* and mixed malaria, requiring dialysis in 40.4% and death in 17.4% patients. In patients with *P. vivax* malaria no deaths were reported. (5)

Table 1. **Indicators of severe malaria and poor prognosis.** (27)

Manifestation	Features
Cerebral malaria	Unrousable coma not attributable to any other cause, with a Glasgow Coma Scale score ≤ 9. Coma should persist for at least 30 min after a generalized convulsion
Severe anemia	Hematocrit <15% or Hb < 50 g/l in the presence of parasite count >10 000/µl
Renal failure	Urine output <400 ml/24 hours in adults (<12 ml/kg/24 hours in children) and a serum creatinine>265 µmol/l (> 3.0 mg/dl) despite adequate volume repletion
Pulmonary edema and ARDS	The acute lung injury score is calculated on the basis of radiographic densities, severity of hypoxemia, and positive end-expiratory pressure
Hypoglycemia	Whole blood glucose concentration <2.2 mmol/l (<40 mg/dl)
Circulatory collapse (algid malaria)	Systolic blood pressure <70 mmHg in patients > 5 years of age (< 50 mmHg in children aged 1–5 years), with cold clammy skin or a core-skin temperature difference >10°C
Abnormal bleeding and/or DIC	Spontaneous bleeding from gums, nose, gastrointestinal tract, or laboratory evidence of disseminated intravascular coagulation
Repeated convulsions	≥ 3 generalised convulsions observed within 24 hours
Acidemia/acidosis	Arterial pH <7.25 or acidosis (plasma bicarbonate <15 mmol/l)
Hemoglobinuria	Hemolysis not secondary to glucose-6-phosphate dehydrogenase deficiency
Impaired consciousness	Rousable mental condition
Prostration or weakness	
Hyperparasitemia	> 5% parasitized erythrocytes or > 250 000 parasites/µl (nonimmune individuals)
Hyperpyrexia	Core body temperature >40°C
Hyperbilirubinemia	Total bilirubin >43 µmol/l (> 2.5 mg/dl)

Dengue Fever, Dengue Hemorrhagic Fever and Dengue Shock Syndrome

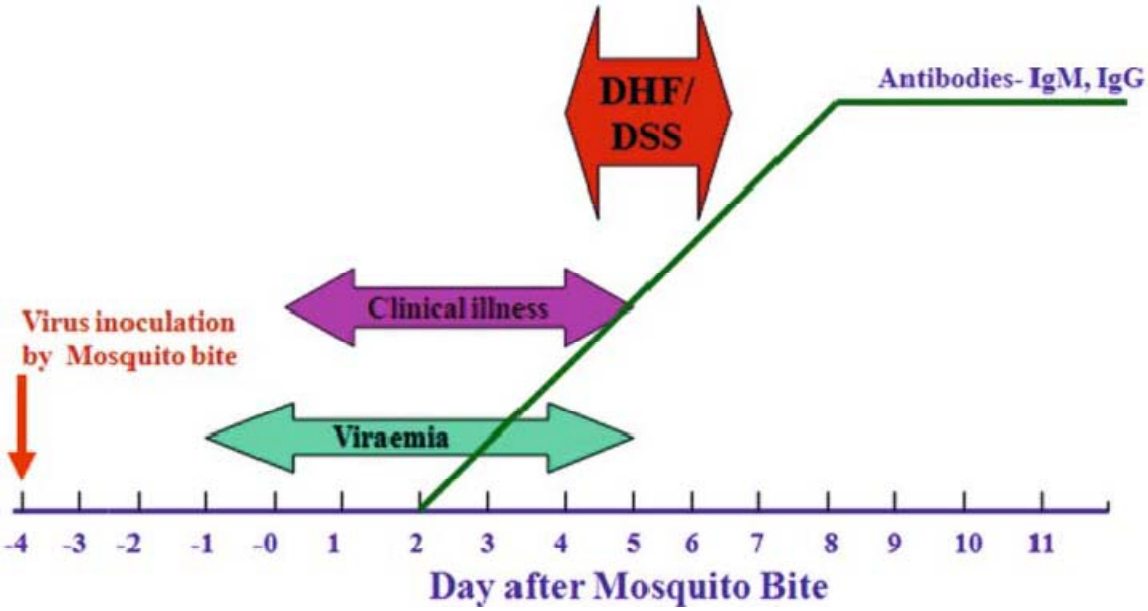
Dengue fever (DF) is a mosquito (*Aedes aegypti*) borne fever caused by RNA viruses DEN-1, DEN-2, DEN-3 and DEN-4 of the genus *Flavivirus*. It has epidemic transmission and the World Health Organization (WHO) estimates 2.5 billion people at risk for the infection with 20000-25000 deaths in about 50 million people affected by the disease annually.(30) It is hyperendemic in South East Asia and India, DEN-3 being the commonest form found in India.

Although DF started as an urban disease it has a presence in both rural and urban areas due to water stagnation, travel, migration, crowding and poor vector control. Mosquito control is the only effective preventive strategy. After infection by a blood meal antibodies are generated against non structural (NS) proteins of the virus causing endothelial injury, cytokine release and cell injury. A protein NS-3 stimulates CD4 and CD8 cells and high levels of interferon gamma, tumor necrosis factor alpha and beta lyse dengue virus (DV) infected cells. Endothelial dysfunction and a resultant capillary leak syndrome are compounded by impaired homeostasis, altered leucocyte function, coagulation defects, thrombocytopenia and hepatic dysfunction. (31) Once infected the incubation period ranges from 3-14 days and based on the severity of disease presentation it has been termed as Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).

It presents with a clinical syndrome characterized by saddleback pattern of fever, headache, myalgia, arthralgia and rash in DF and in addition hemorrhagic manifestations of varying severity in DHF.(32) Hemoconcentration, lymphocytosis and thrombocytopenia with transaminitis in DF and in addition prolonged partial

thromboplastin time, low fibrinogen level and increased fibrinogen degradation products in DHF and DSS is observed. Diagnosis is confirmed by isolation of the virus, detection of the viral antigen or viral RNA in serum / tissues or viral specific antibodies in serum. Antibody testing is routinely used in clinical scenarios for diagnosis and reaches a peak level for detection about 7-14 days after the bite. (Figure1)(31)

Figure 1. **Antibody detection in dengue fever.** (31)



ARF in DF was previously thought to be rare and explained by ATN secondary to hypotension.(33) However studies have documented an increasing trend of ARF from 0.3% in 2005 in Thailand, (34) to 3.3% in 2009 in Taiwan.(35) Case reports have documented renal failure with Hemolytic Uremic Syndrome (HUS), (36) myositis (37) and rhabdomyolysis.(38) Immune complex disease is considered less likely although DV particles have been isolated in the kidney, as the complexes are small enough to be filtered and are considered likely only in kidneys having suffered glomerular injury

previously. However glomerular involvement is documented in an older series showing mesangial and endothelial hyperplasia with IgG, IgM and C3 deposition in capillary walls.(39) Mice after innnoculation of DEN-2 have shown proliferative glomerular injury on biopsy in one study and increased endocapillary and mesangial hypercellularity in another. (40)(41)

DSS is an independent factor for AKI in DF. (42) Data from Vellore, has documented an incidence of 35.7% AKI in patients with DF. RIFLE grades R in 14.3%, I in 3.6% and F in 17.9% with hemodialysis requirement in 7.1% and death in 25 % are observed.(5) In patients with severe renal failure and having indications for dialysis Continuous Renal Replacement Therapy (CRRT) has been suggested as an alternate to conventional hemodialysis. (43)

Leptospirosis

Leptospirosis is a biphasic illness caused by the spirochete *Leptospira interrogans*. It has a presence across all inhabited continents, with a prevalence of 10-100 per 100000 in tropical areas. (44)

Leptospira are spread to man by shedding in the infected urine of a reservoir of animals, usually rats, and transmitted through cuts, bruises, conjunctiva or oral ingestion while working in fields, barns, water logged areas and sewers.

Pathophysiology of renal involvement in Leptospirosis is explained by an immune / allergenic response to leptospiral endotoxins inhibiting the Na-K ATPase in renal tubules and a generalized vasoconstriction and hypovolemia as a result of the endotoxemia.

Leptospirosis presents as an innocuous self limiting anicteric disease in 85-90%, but in the remaining who suffer the icteric form the presentation is with jaundice, sub-

conjunctival hemorrhage and systemic manifestations. Renal manifestations include azotemia, oliguria and anuria, usually appearing in the second week of the illness. Urinalysis shows hematuria, casts and pyuria.

Although renal involvement is documented in both forms it is symptomatic and severe in the icteric form, often with severe oliguric renal failure and poor prognosis. ARF presents with ATN and acute interstitial nephritis (AIN) in 16-40% of patients with severe infection.(45) *Leptospira* induced ARF in tropical areas may occur in 44-67%.(46) In a study from Romania, ARF presented predominantly as multiorgan failure leading to death in 26% and mild persistent renal failure in 10% of the survivors. Post mortem renal biopsy available in 15 patients showed AIN and ATN in the majority (14 and 13 patients respectively) with features of acute vasculitis in four patients. (47)

Renal failure has also been associated with rhabdomyolysis and thrombocytopenia. (48) Proximal tubular dysfunction is common with high distal sodium delivery and potassium loss in the normal distal tubule and resultant hypokalemia. High fractional excretion of sodium with potassium loss in excess of 1000 mEq/day has been reported even in volume depletion. (47)

Although renal complications occur in the second or third week of illness, they may occur as early as the first week. Onset of diuresis in anuric patients is a sign of renal recovery. Other involvement in severe disease includes hepatic, pulmonary and neural involvement. The average mortality rate is 10% in confirmed cases worldwide.

Post Graduate Institute of Medical Education and Research in Chandigarh have reported a rising incidence of leptospirosis from 11.7% in 2004 to 20.5% in 2008, with peak numbers during the rainy season. Renal failure was observed in 60.5% and was the

commonest complication as compared to respiratory failure in 20.9%, neuroleptospirosis in 11.6% and disseminated intravascular coagulation (DIC) in 11.6%. The case fatality rate was 5.9%.(49) Another study has shown a case fatality of 7.7% (50)

Data from Chennai shows a decline of ARF in leptospirosis from 31% to 7.5% over a period from 1987 to 2004. (12) This decline has been attributed to improved awareness, better diagnostics, reduced seroprevalence of virulent *Leptospira autumnalis* and early empirical treatment with doxicycline. (51) In data from Vellore AKI was present in 50.0% of whom 25.0% presented in RIFLE R and 8.3% and 16.7% in I and F respectively with no patients requiring hemodialysis or any deaths.(5) ARF in leptospirosis has a significant mortality especially due to delay in diagnosis and late institution of treatment with penicillin.(52)

Typhoid Fever

Typhoid is a systemic infection caused by *Salmonella typhoid* and has a rising global presence with about 260000-600000 deaths annually worldwide and a crude incidence across Asia of 274/100000 population. (53) These range from 15.3 per 100000 in China to 451.7 per 100000 in Pakistan and is endemic in most developing countries including India. Incidence in India has been reported from 136.7/100000 population (54) - 980/100000 (55) and mortality of 10 - 15 % as a result of disease related complications.(56)

Typhoid presents with fever and abdominal symptoms, which if untreated progress to severe disease manifested by altered sensorium, shock and multi organ dysfunction syndrome (MODS). Blood culture continues to be the gold standard for diagnosis detecting about 70% of patients with suspected typhoid fever. Serological tests like the

Widal test continue to be used in endemic areas with a high sensitivity in detecting typhoid. It is however hampered by differing rates of sensitivity and specificity across populations. Other tissues like bone marrow and stool cultures can detect *Salmonella* in 85-95% and 45-65% respectively.(57)

Renal involvement in typhoid occurs in 0-6% of typhoid with glomerular as well as tubular injury manifested by renal failure, microscopic hematuria and proteinuria. Dehydration and rhabdomyolysis are incriminated in ARF, as is reversible endothelial dysfunction secondary to the *Salmonella* toxin. It occurs in about 3.9% patients and is usually responsive to treatment and hydration.

ARF in typhoid fever has also been reported with intravascular hemolysis, rhabdomyolysis and severe jaundice.

Absence of renal histology in most cases makes it difficult to predict the exact nature of pathology with conviction. In addition, the bacillus has not been isolated in available renal tissue and toxin induced or immune mediated nephropathy is more likely. (55) The kidneys involved as a sequalae of immune complex glomerulitis are found to be self resolving on serial renal biopsies.(58) Isolation of salmonella Vi antigen in a case report from the glomerular capillaries may not entirely rule out the possibility of direct involvement. (58)

Data from Vellore has documented an incidence of 6.2 % renal failure in patients with typhoid with 3.1% each in the injury and failure groups.(5)

Undifferentiated Fever

Undifferentiated fever (UF) is defined as fever less than two weeks duration without any localized source of infection. A study from central India revealed a significant proportion

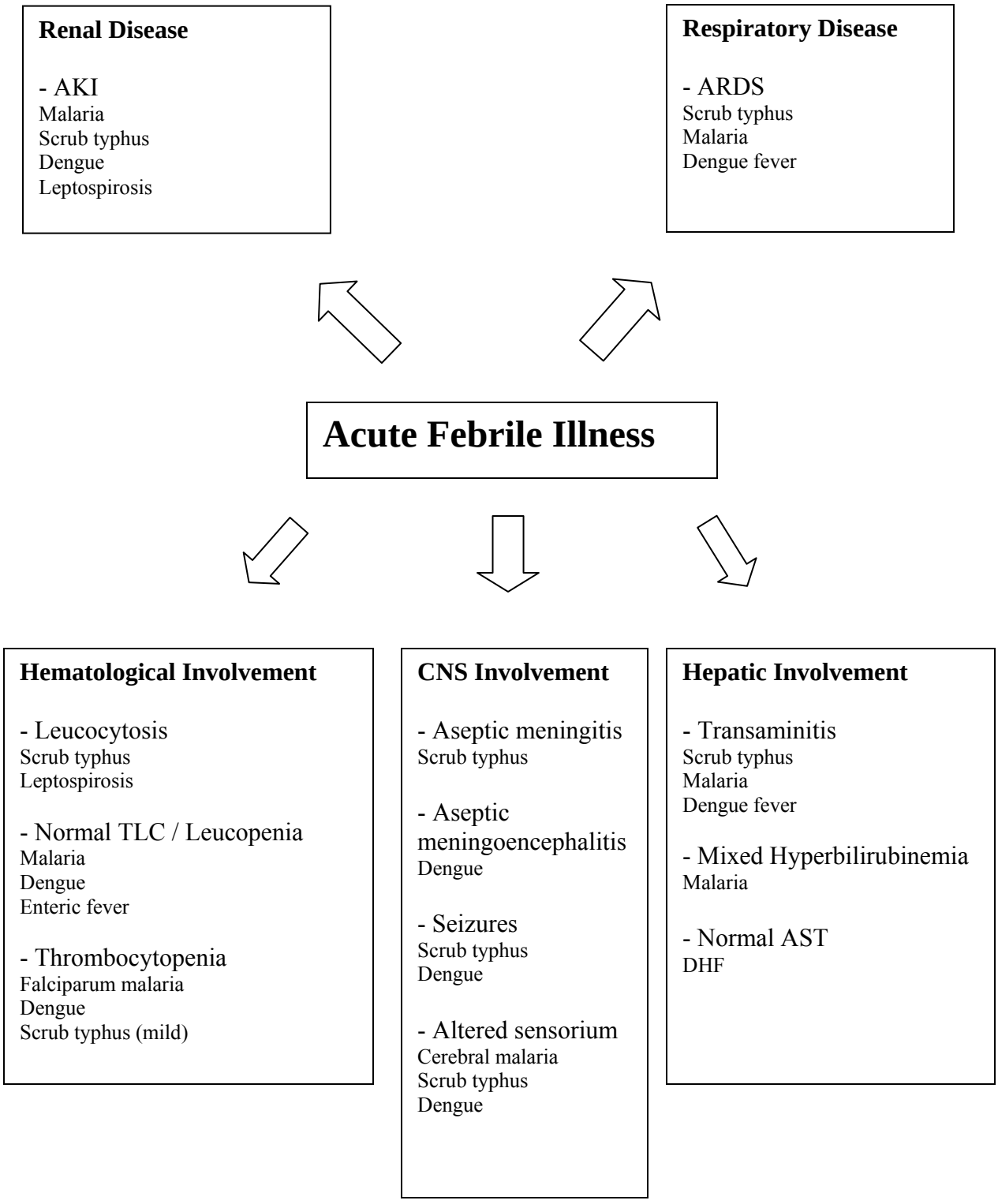
of fever to be non malarial acute undifferentiated fever, managed emperically with anti malarials despite laboratory evidence pointing to an alternate diagnosis (88% non malarial acute undifferentiated fever with 39.9 % of these patients treated with anti malarials). (59) In another study, from Mumbai studying the pattern of 160 deaths in patients with AFI in 2006, 53.75% were undifferentiated despite detailed evaluation including a post mortem. About 23% had ARDS with renal failure, 11% with hepatorenal failure and 11% had isolated renal failure. (60)

Data from the Vellore study showed undifferentiated fever in 8.4% with AKI in 35.5% of whom RIFLE R constituted 9.7%, I 19.4% and F 19.4%, with hemodialysis requirement in 6.5% and death in 19.4%. (5)

These fevers are often sub optimally evaluated owing to paucity of funds and diagnostic facilities and managed emperically with anti malarials (59) Awareness about the UF and the need to further delineate etiology in this group is the need for the hour, particularly because in the absence of targeted therapy morbidity and mortality continues to be high.

Identifying AFI etiology based on the above profile is challenging as red flags in identifying them are useful. (Figure 2)

Figure 2. Red Flags in Acute Febrile Illness - Adapted from Chrispal A, et al. (9)



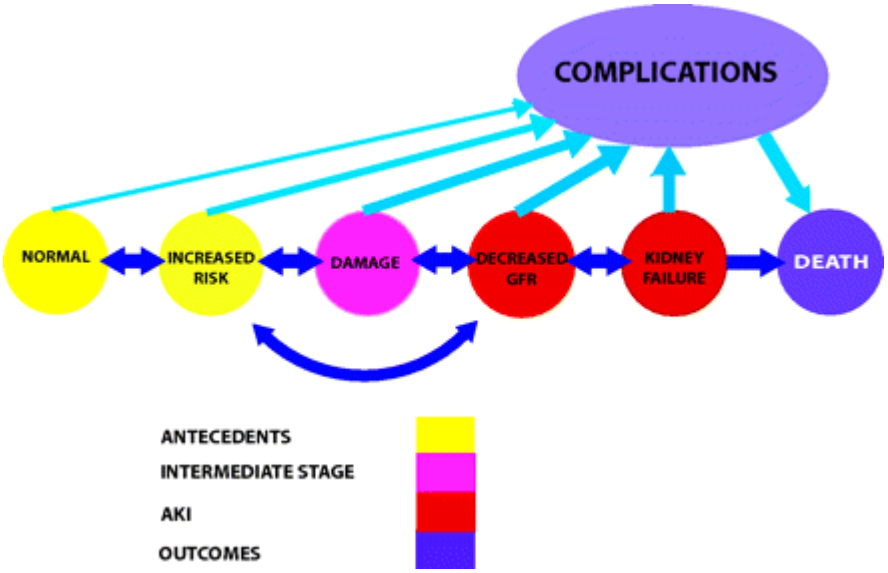
Acute Kidney Injury

Acute Kidney Injury (AKI) is defined by "an abrupt increase in serum creatinine over 48 hours resulting from an injury or insult that causes a functional or structural change in the kidney." It predisposes to chronic kidney disease and progresses thereafter to ESRD and death. (Figure 3) In critically ill patients severe renal failure requiring dialysis occurs in 4-5 % with a mortality rate of 60%. About 8-22% of these patients continue to require maintenance dialysis support thereafter. (61)

Pathophysiology of AKI

AKI has a common pathophysiological process despite its multifactorial etiology. (Figure 4) The commonest injury in hospital is ischemic or toxic, resulting in a downward spiral to AKI and ESRD if not evaluated or managed early. Once renal perfusion is reduced ischemic tubular dysfunction leads to loss of tubular cell polarity, followed by apoptosis and necrosis. Loss of ß-integrins and adhesion molecules cause sloughing of the tubular cells and the sloughed viable as well as necrotic cells lead to tubular obstruction and production of inflammatory mediators. These induce interstitial inflammation and vascular congestion. Once cells are sloughed, back-leak of filtrate occurs owing to increased intra-tubular pressure, worsening the inflammation cascade and ischemia as a result of vasoconstriction. The kidney may recover if the underlying insult is reversed early by a process of intact epithelial cells migrating over the denuded areas of the basement membrane, cell de-differentiation and proliferation to restore structural and functional integrity over a period of time. Time is of essence in this process of healing, with timely intervention resulting in regression of injury and recovery.(62)

Figure 3. **Progression of AKI and complications**. (63)



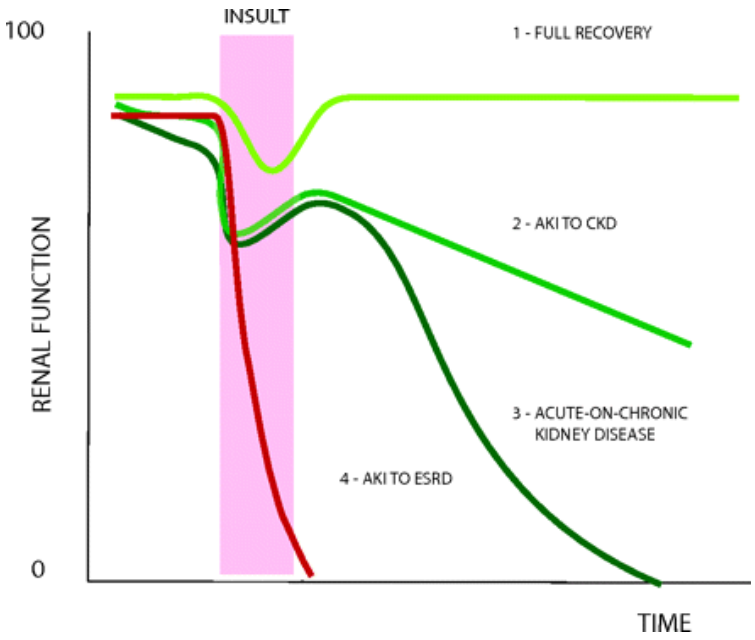
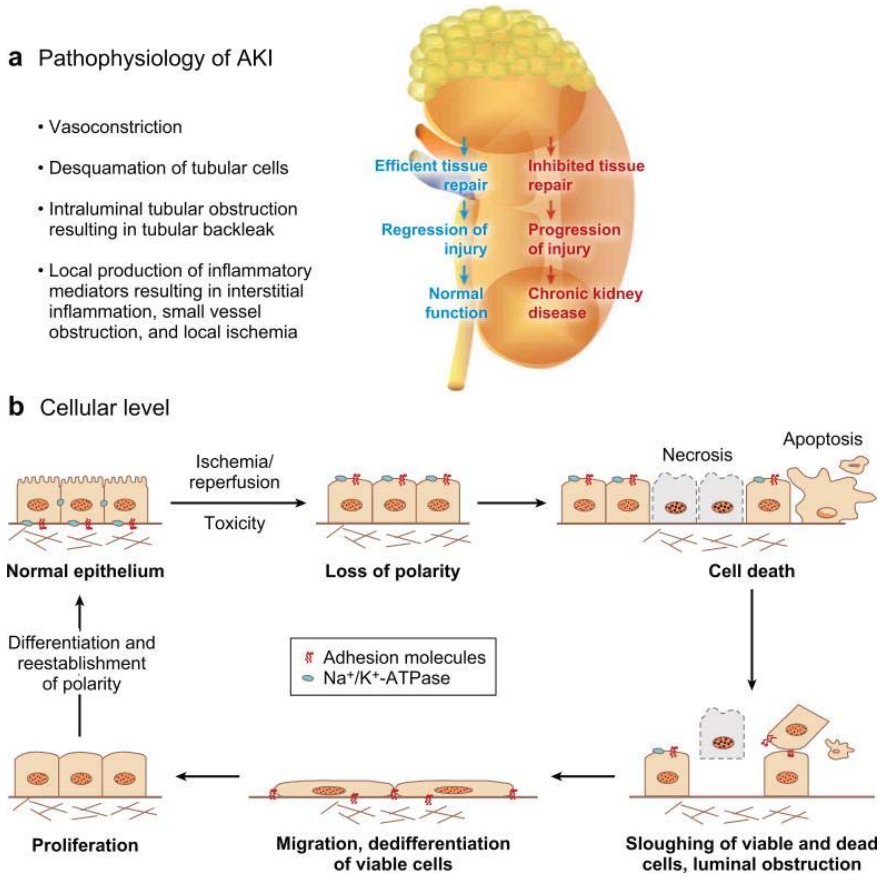


Figure 4. **Pathophysiology of AKI.** (62)



Acute Kidney Injury: The process of development.

"*The exact definition of a problem with a detailed description and accurate measurement of the factors involved provides already half the solution.*"—Anonymous.

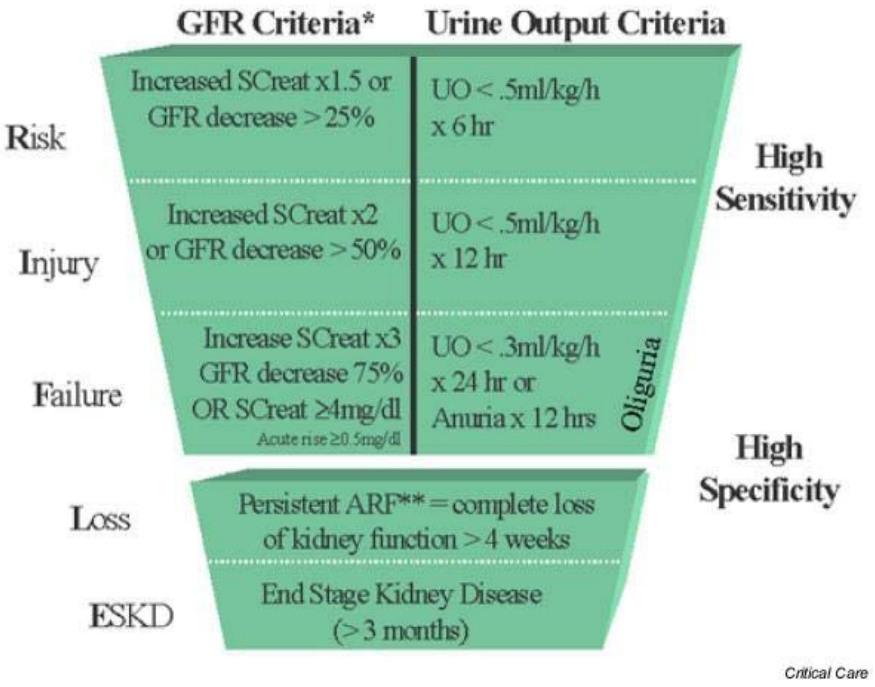
The problem with definitions like the above mentioned one is poor standardization both in terms of diagnosis and grading the severity of AKI. It was noticed that even modest increases in creatinine from the baseline translated to increased risk of mortality. A need to factor the risk associated with this rise in a manner that would sensitize treating

physicians to treat early as well as grade / prognosticate patients based on the severity of AKI was felt.

The Acute Dialysis Quality Initiative (ADQI) was born out of this long felt need to address AKI and related issues. The group comprised intensivists and nephrologists from the American Society of Nephrology (ASN), International Society of Nephrology (ISN), National Kidney Foundation (NKF) and the European Society of Intensive Care. They met in Vicenza, Italy, in September 2004 to generate protocols and guidelines aiming to standardize care and dialysis for the critically ill with AKI.

Their guidelines called the RIFLE criteria (Figure 5) graded AKI based on the rise in creatinine and decrease in urine output into Risk (R) where renal failure can be prevented, Injury (I) where damage is ongoing and Failure (F) where renal failure is established. Creatinine was used despite reservations regarding its applicability as it is widely available and affordable as a marker for tubular dysfunction. (64)

Figure 5. **RIFLE Criteria.** (64)



However with increasing applicability AKI using the RIFLE criteria, the need to establish a better, comprehensive and sensitive tool was felt along with a focused, multi disciplinary group to formulate these guidelines. Members of the ADQI collaborated with critical care societies to establish the Acute Kidney Injury Network (AKIN).

One of the fundamental tasks of this group was to improve outcomes for the risk grade as it was felt that they were most likely to benefit from early detection and intervention. They redefined AKI as "an abrupt (within 48 h) reduction in kidney function defined as an absolute increase in serum creatinine level of ≥26.4 μmol/l (0.3 mg/dl) OR a percentage increase in serum creatinine level of ≥50% (1.5-fold from baseline) OR a reduction in urine output (documented oliguria of <0.5 ml/kg/h for >6 h).These criteria are applied in the context of the clinical presentation and following adequate fluid resuscitation when applicable." The revised RIFLE criteria based on the above requirements was referred to as the AKIN classification. (Table 2) This was done in their first meeting in 2005 and published as the AKIN guidelines. It staged the patients as Stage I, II and III and removed the Loss (L) and E (ESRD) categories in RIFLE which were considered to be outcomes. (65)

Table 2. AKIN Classificaton of AKI. (65)

Stage	Serum creatinine criteria	Urine output criteria
1	Increase of ≥26.4 μmol/l (0.3 mg/dl) OR to 150–200% of baseline (1.5–2.0-fold)	<0.5 ml/kg/h for >6 h
2	Increase to >200–300% of baseline (>2–3-fold)	<0.5 ml/kg/h for >12 h
3[a]	Increase to >300% of baseline (>3-fold; or serum creatinine ≥354 μmol/l [4.0 mg/dl] with an acute rise of at least 44 μmol/l [0.5 mg/dl])	<0.3 ml/kg/h for 24 h OR anuria for 12 h

Only one criterion (creatinine or urine output) needs to be fulfilled to qualify for a stage. [a]Patients who receive renal replacement therapy are considered to have met the criteria for Stage 3, irrespective of the stage that they are in at the time of commencement of renal replacement therapy. Permission obtained from BioMed Central © Mehta RL *et al.* (2007) *Crit Care* **11:** R31.

RIFLE Classification

AKI has been a significant component of critical care scoring systems constituting 20% and 16.6% of the APACHE III (Acute Physiology and Chronic Health evaluation) (66) and SOFA (Sequential Organ Failure Assessment) scores. (67) ADQI formulated RIFLE grading AKI based on increasing severity (assessed by fall in urine output and rise in creatinine from baseline) as R (Risk), I (Injury) and F (Failure) and outcomes as L (Loss) and E (End Stage Renal Disease).(64) It has been validated in patients with renal failure in acute febrile illness (5) as well as critically ill hospitalized patients. (68) In patients presenting with AKI in AFI the incidence of AKI was 41.1% with 17.4%, 9.3% and 14.4% in the RIFLE R, I and F categories respectively. Mortality across the groups was 12.3 % with an incremental risk for requirement of hemodialysis and mortality from risk to failure. (5) In ICU s the incidence of AKI in patients in the R and I categories is 55% placing them at a higher risk of mortality.(69) In patients requiring renal replacement therapy (RRT) the overall in hospital mortality in two studies is 50.2% (70) and 76%. (61)

Limitations

Although the introduction of RIFLE provided insight into the high incidence of AKI and enabled early diagnosis and management, the criteria per se is not without limitations, in a practical scenario. Although urine output serves as a sensitive and specific parameter in the criteria, its accuracy in terms of measurement in a patient who is not on continuous bladder drainage or post diuretic use is questionable. Comparing these parameters has shown creatinine criteria to be a better marker for mortality, but in conjunction with urine output a stable result is likely.(71) The absence of a baseline creatinine in most patients

presenting with AKI does hamper accuracy of the criteria, although back calculation of baseline GFR using the MDRD equation has been advocated.(68)

RIFLE has also been validated successfully in non ICU based situations. In a retrospective study RIFLE; R, I and F were found in 9.1%, 5.2% and 3.7% respectively with overall mortality of 8.0%. An incremental mortality was observed from the non AKI patients across to those in failure (non AKI- 4.4%; R - 15.1%; I - 29.2%; and F - 41.1%). (72)

Acute Kidney Injury Network Criteria

AKIN is an international group of nephrologists including adult, pediatric and critical care specialists with a focused interest in AKI and development of evidenced based guidelines for improvement in care and outcomes of AKI.(65) They defined AKI as "an abrupt (within 48 hours) reduction in kidney function defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl (≥26.4 μmol/l), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (oliguria of less than 0.5 ml/kg per hour for more than six hours)."

Urine output is used as a diagnostic criterion as it often heralds renal dysfunction before a rise in serum creatinine. It needs to be assessed in the clinical scenario of reliable measurement, optimal hydration, absence of diuretic use and urinary obstruction with the recognition that it may not be specific for in AKI stage I.(65)

AKIN versus RIFLE Criteria

A recent analysis of the Australian New Zealand Intensive Care Society (ANZICS) database found agreement with both RIFLE and AKIN criteria. There was <1% difference in the overall number of identified AKI with AKIN, slightly increasing the

number of patients classified as Stage I injury as compared to category R in RIFLE (18.1 versus 16.2%) but reducing those with Stage II injury as compared to category I in RIFLE (10.1% versus 13.6%). ROC curves for hospital mortality were similar (0.67 for AKIN and 0.66 for RIFLE. (73) This similarity has been demonstrated in other studies with a similar design.(74)

As there seem to be no additional benefits to the AKIN criteria at this point, future efforts aim to focus on successful application and extended use of either of these criteria, particularly RIFLE, as a surrogate marker for outcomes in trials to prevent and alleviate AKI.(73)

The Liano Scoring System for ARF

Liaño F and Pascual J conducted the first community based prospective study on ARF in 1996 generating data on epidemiology, etiology, clinical features and outcomes with an aim to initiate preventive strategies for ARF in Spain. Mortality of 45% with corrected mortality for ARF of 16.7% was observed. Patients requiring dialysis had a higher mortality of 65.9% and coma, assisted respiration, hypotension, jaundice and oliguria were found to be poor prognostic indicators. Based on the severity of ARF an expected outcome was calculated using the severity index which co related well with the observed clinical outcomes.

Severity of illness is scored using the Liano scoring measured by the formula

(0.032 * age in decades - 0.086 * male gender - 0.109 * nephrotoxic + 0.109 * oliguria + 0.116 * hypotension + 0.122 * jaundice + 0.150 * coma - 0.154 * consciousness + 0.182 * assisted respiration + 0.210) (75)

The Madrid study co relates well with others studies on ARF and related outcomes. (76) It has been validated recently in the Indian population with a sensitivity of 60.7% and specificity of 100%.(77)

The Vellore Model

Recognizing the need to develop an effective renal sensitive marker for ARF the Vellore model was developed in 2005. It compares favorably to generic predictive models like APACHE III, SAPS2 and Laino score. This model factored in parameters indicative of poor outcome like age, sex, oliguria, hypotension, jaundice, coma, assisted ventilation, hypoalbuminemia, sepsis and hospital acquired ARF to arrive at probability of death using the equation: $e^y/1+e^y$

y = (0.0196 * Age) – (0.5855 * male gender) + (1.5887 * oliguria) + (1.1427 * hypotension) + (1.3068 * jaundice) + (2.3466 * coma) + (0.8612 * assisted ventilation) + (0.5423 * hypoalbuminemia) + (0:7960 * sepsis) + (0.8389 * hospital acquired ARF) – 3.4741.

It is validated and found to be a useful predictive tool for ARF with good calibration. Sepsis and hospital acquired ARF herald poor outcomes using a discriminant score of 0.5 as cut off. Positive predictive value of 90% with 70% sensitivity was achieved for a population with tropical ARF.(78)

Biomarkers

Renal function is estimated by glomerular filtration rate. The gold standard for measurement is by inulin clearance or radio isotope measures, which are impractical in acute critical care settings. In this scenarion creatinine is used as a poor but easily available substitute.

It is widely recognised that the Achilles heel of AKI management continues to be late diagnosis, not withstanding advances and improvement based on RIFLE and AKIN. This is owing to reliance on creatinine as marker which lags in detecting injury as well as recovery (79) and whose levels are modified in critical illness. (80) In addition, it is unable to convey any information regarding the site of renal injury (proximal or distal tubular, interstitial or vascular), duration of injury (pre renal, renal or post renal), etiology (ischemic, toxin or sepsis mediated), stratify risk or prognosticate the renal injury.(81)

A good biomarker aims to fulfil these properties and opposed to creatinine aims to detect tubular injury prior to decrease in filtration.

An abundance of research in biomarkers for AKI has identified cystatin C (CC), kidney injury molecule 1(KIM 1), neutrophil gelatinase–associated lipocalin (NGAL), interleukin 18 (IL-18), sodium/hydrogen exchanger isoform 3 (NHE 3), N-acetyl-β-d-glucosaminidase (NAG), and matrix metalloproteinase 9 (MMP 9) as markers of promise.

Cystatin C is considered an alternative to creatinine which is unmodified by age, weight and gender and is sensitive to incepient renal injury, being able to antedate renal injury as compared to creatinine.(82)

NGAL and KIM 3 are increased in urine as early as two hours after injury and IL-18 at 12 h which may serve as early detection biomarkers. These however await validation and standardization prior to widespread use and acceptability.(83) Promising biomarkers (Figure 6) and their utility in identifying AKI (Figure 7) is undergoing intense scrutiny.

Figure 6. **Promising AKI biomarkers and related pathophysiology.** (62)

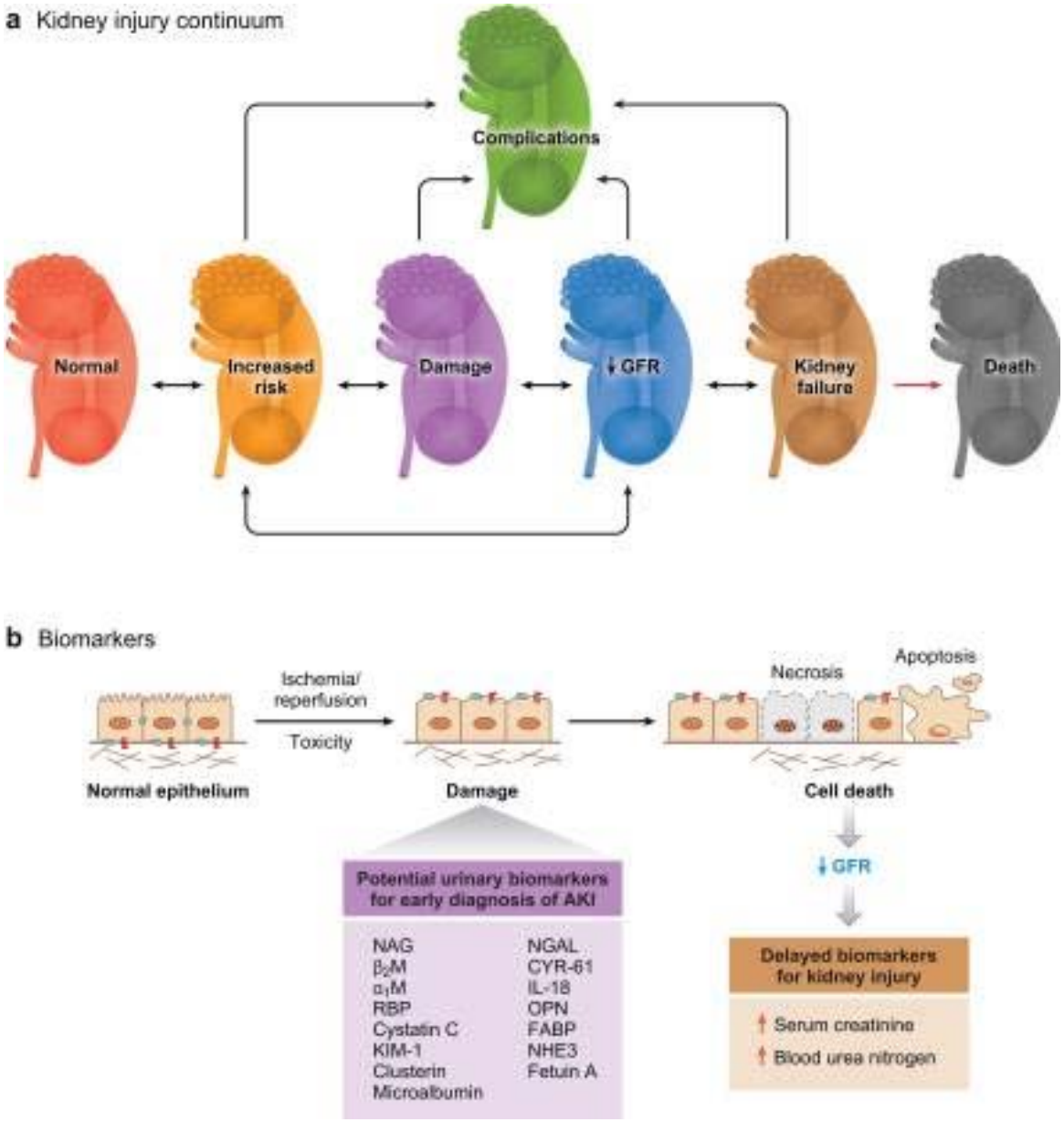
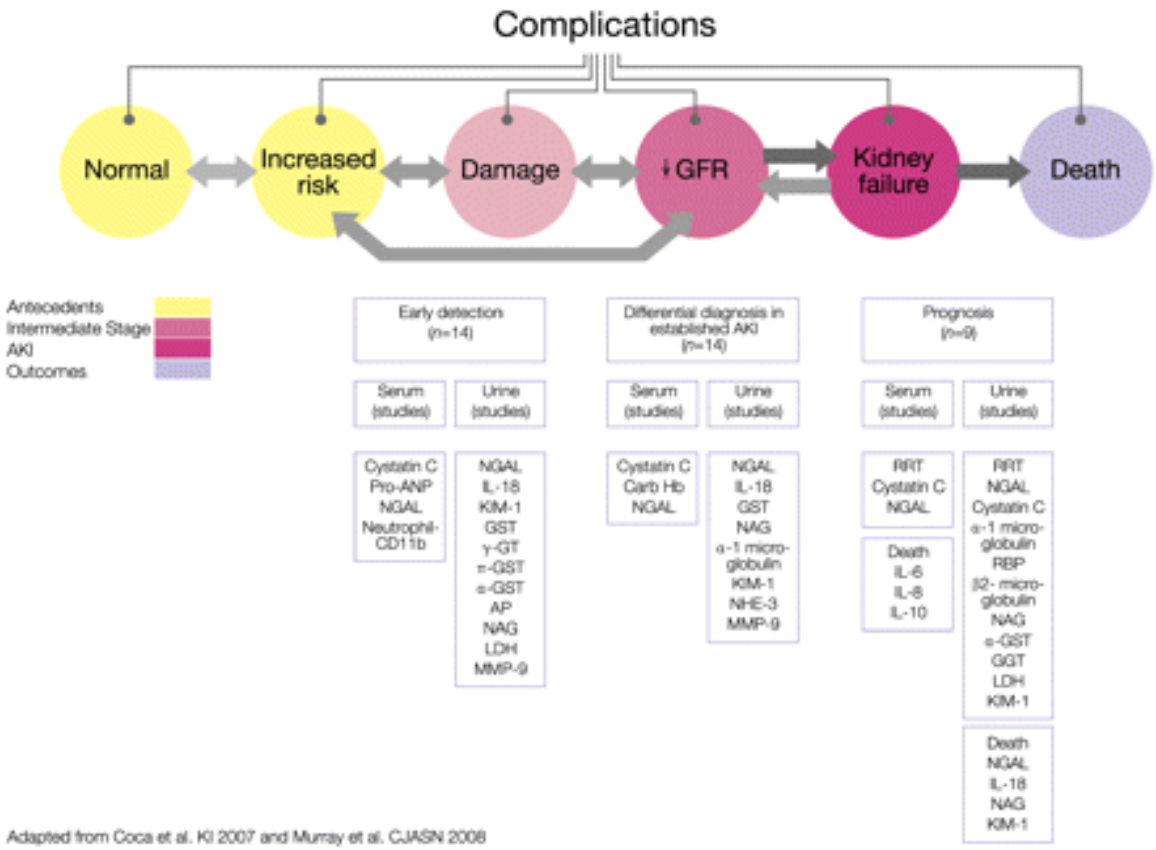


Figure 7. AKI indentification using biomarkers.



Renal Replacement Therapy in AKI

Nephrologists have always been challenged by the need to generate evidence based guidelines on indications for dialysis in AKI. When to initiate and withhold dialysis currently depends to a large extent on personal opinion.

Dialysis in AKI has been based metabolic parameters, attending renal physician's preferences for early or late initiation, availability of resources or empiricism. Standard indications for dialysis include absolute indications like blood urea nitrogen more than 100 mg/dL, hyperkalemia (potassium more than 6 meq/dL) with ECG abnormalities,

severe metabolic acidosis (pH less than 7.15), hypermagnesemia (Mg more than 8 meq/dL) with anuria and absent deep tendon reflexes and diuretic resistant fluid overload. Relative indications include blood urea nitrogen greater than 76 mg/dL, dysnatremia, hypermagnesemia (Mg more than 8 meq/dL), metabolic acidosis (pH more than 7.15), oliguria / anuria or diuretic sensitive fluid overload.

AKIN attempted to provide evidence based guidelines for initiation and discontinuation of dialysis but available evidence in literature is not adequately powered to provide the answers at present. It hopes to answer the question with a prospective study of AKI adults in ICU settings with standardized urea clearance and targets for initiation and discontinuation (GFR 20 ml/min based on the physicians discretion) and follow up for a year after discharge.(84)

Objectives

1. This study was undertaken to evaluate the clinical features, prognosis and outcomes of acute kidney injury (AKI) in patients presenting with tropical acute febrile illnesses (AFI) such as scrub typhus, malaria, dengue fever, typhoid, leptospirosis and undifferentiated fever.

2. Identify patients at high risk of developing AKI and mortality related to AFI.

3. Identify mechanisms for effective management and utility of RIFLE criteria for AKI in AFI.

4. Evaluate Cystatin C as a biomarker for diagnosis of AKI.

5. Indications and outcomes of hemodialysis in AFI related AKI.

Patients and Methods

The research proposal was submitted to and discussed at the Institutional Review Board (IRB) and Ethics Committee (EC). IRB and EC consent were obtained prior to proceeding with the study. Patients admitted to the Internal Medicine general wards, high dependency and intensive care unit with AFI and AKI during the period of 1st January 2010 to 30th September 2010 were invited to participate in the study. Once identified from the hospital database, these patients were screened by the primary investigator with a clinical history and examination to exclude fever as a result of localized infection or other systemic non infectious causes. They were invited to participate in the study and if willing to do so, an informed consent was obtained and recruited into the study. (Annexure1)

All patients were evaluated with a hemogram, creatinine, electrolytes, thin smears for malaria, blood culture and chest X-ray (CXR). Urine or other fluid cultures were done whenever indicated. A blood and urine sample was collected at recruitment and suitably stored.

The patients were screened for the presence of dengue fever, leptospirosis, typhoid, spotted fever and scrub typhus with case definitions for the diseases. (Table 3) This febrile work up was initiated in the ER or on admission to the ward and for those without a clear diagnosis at discharge the stored sera was used to complete evaluation with serology for scrub typhus, typhoid, leptospirosis and dengue fever.

These patients were followed up during hospital stay and accrued data reviewed after discharge to establish an etiology and analyze their presentation, management as well as complications, intervention with hemodialysis and outcome at discharge.

Table 3 Diagnostic criteria for Acute Febrile Illness. (9)

MALARIA

	CASE DEFINITION
DEFINITE CASE	Falciparum Malaria – AFI + Plasmodium falciparum visualised on thin blood smear
	Vivax Malaria – AFI + Plasmodium Vivax visualised on thin blood smear
	Mixed Malaria – AFI + Plasmodium falciparum and Plasmodium Vivax visualised on thin blood smear

SCRUB TYPHUS

	CASE DEFINITION
DEFINITE CASE	Acute Febrile illness + Definite Eschar
	Acute Febrile Illness + Scrub Typhus Elisa Positive + Febrile Response to Doxycycline < 48 hrs
	Acute Febrile Illness + Scrub Typhus ELISA sero-conversion in convalescent sera
PROBABLE CASE	Acute Febrile Illness + Scrub Typhus Elisa Positive + Other serology negative (BUT defervesence data not available)
	Acute Febrile Illness + Multisystem involvement + Scrub Elisa Positive + Other serology are negative (BUT defervesence occurs upto 96hrs)
	Acute Febrile Illness + Multisystem involvement + Febrile response to Doxycycline <48hrs + Other serology are negative (BUT Scrub Typhus serology negative)

ENTERIC FEVER – SALMONELLA PARATYPHI OR TYPHI

	CASE DEFINITION
DEFINITE	AFI + Blood culture positive for S.Typhi or S.Paratyphi
	AFI + Typhidot (IgM) positive + other serologies negative
	AFI + Fourfold rise in titre on the WIDAL

SPOTTED FEVER

	CASE DEFINITION
DEFINITE	AFI + Rash+ Spotted Fever IgM ELISA positive + other serologies negative
-OTHER RICKETSIOSIS	AFI + Rash+ OXK19 positive + skin biopsy suggestive of Rickettsial vasculitis

LEPTOSPIROSIS

	CASE DEFINITION
DEFINITE	AFI + 1st Leptospira IgM ELISA negative followed by a positive test on convalescent sera
PROBABLE	AFI + Leptospira IgM positive + all other serologies negative

DENGUE FEVER/ HEMORRHAGIC FEVER/ SHOCK SYNDROME/

	CASE DEFINITION	
DEFINITE	AFI + Dengue IgM positive + other serologies negative	
	AFI + Dengue IgM negative + Dengue IgM or IgG positive on convalescent sera	
A case was diagnosed as Hemorrhagic Fever if there was presence of thrombocytopenia + coagulopathy + features of hemorrhage **A case was diagnosed as Shock Syndrome if there was presence of Shock (BP < 90mmHg) + other features of DHF**		
PROBABLE	AFI + All serologies positive + Clinical features compatible with a diagnosis of Dengue Hemorrhagic Fever Thrombocytopenia (100 000 cells or less per mm^3) **And** evidence of plasma leakage due to increased vascular permeability, manifested by one or more of the following: • ≥20% rise in average hematocrit for age and sex + hypoalbuminemia + effusions Plus - Positive tourniquet test - **OR** - Bleeding: mucosa, gastrointestinal tract, injection sites or other hematemesis or melena	

Acute undifferentiated febrile illness was defined as an undefined case of fever after the above work was negative.

*Febrile serology: scrub typhus IgM ELISA (Scrub Typhus Detect™, Inbios International Inc, Seattle, USA); Qualitative assays: Leptospira IgM ELISA (SD Leptospira IgM, Standard Diagnostics Inc, Kyonggi-do, Korea), Typhidot [IgM and IgG]

(Test-it^{TM} , Life Assay Diagnostics Ltd, Cape Town, South Africa); Rapid assay: Dengue IgM-IgG ELISA (Dengue Duo Cassette, PanBio Ltd). Spotted fever IgM ELISA (PanBio Ltd) was done for patients with rash when indicated.

Acute Kidney Injury

AKI was defined by RIFLE criteria using the definitions summarized in Figure 3 and Table 2 respectively. Urine output was not used in the study design owing to inability to monitor and measure of hourly urine output or factor unanticipated diuretic use. (64)(65)Whenever a baseline creatinine was not available it was derived using the abbreviated MDRD equation assuming a baseline GFR of 90 ml/min/1,73 sq m. A similar approach was used to calculate RIFLE based on Cystatin C GFR using the Grubb equation and deriving a baseline Cystatin C.

Serum creatinine was measured using the modified Jaffe's kinetic alkaline picrate method using an automated analyzer Olympus AU 2700 (Japan)

Cystatin C was measured by particle enhanced immunoturbidimetry.

Liano score

Severity of illness at admission was standardized using the Liano score, measured by the formula (0.032 * age in decades - 0.086 * male gender - 0.109 * nephrotoxic medications + 0.109 * oliguria + 0.116 * hypotension + 0.122 * jaundice + 0.150 * coma - 0.154 * consciousness + 0.182 * assisted respiration + 0.210). Oliguria was defined as urine output less than 400 ml /day, hypotension as systolic blood pressure less than 100 mm for 8 hours with or without ionotropes, jaundice as total bilirubin more than 2 mg % and GCS equal to or less than equal to 5.

Systemic Inflammatory Response Syndrome (SIRS)

SIRS was defined as presence of two or more of temperature more than 38 or less than 36 °C, heart rate more than 90 / min, respiratory rate more than 20/min and leucocyte count more than 12000/ cu mm or less than 4000/ cu mm or 10% band forms.(85)

FENa Interpretation

Fractional excretion of sodium (FENa) was calculated using simultaneous urine and serum samples for sodium and creatinine at recruitment and applying the formula: (Urine Na * Serum Creatinine) / (Urine creatinine * Serum Na)

ATN was interpreted as FENa > 2 and pre renal AKI as FENa < 1. (86)

Renal Failure Index

Renal failure index (RFI) was calculated using the formula: Urine sodium * (Plasma creatinine / Urine creatinine) and was interpreted as ATN if RFI > 2 and pre renal AKI if RFI < 1.

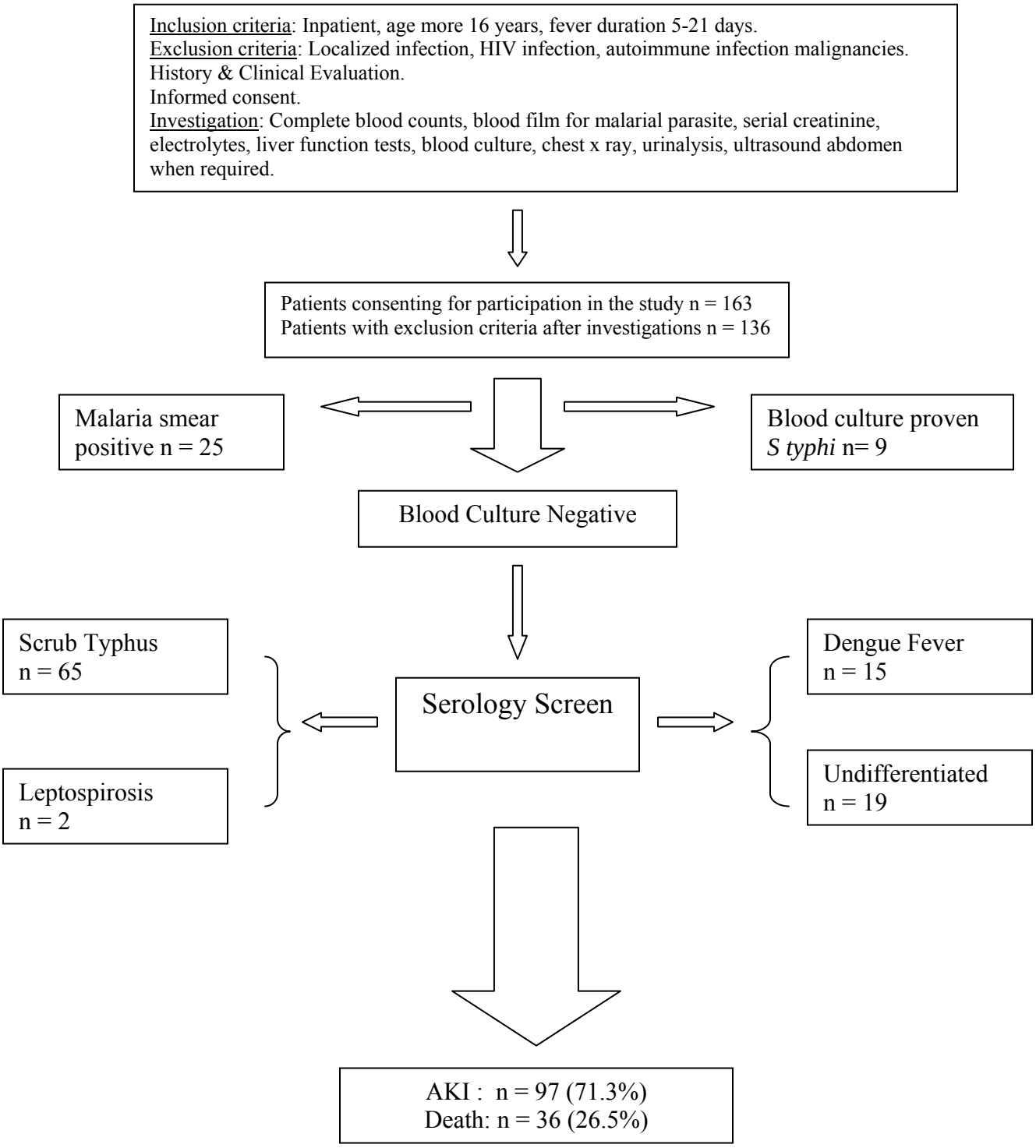
End Points

The primary end points were death during in hospital stay or recovery of renal function at discharge.

Patient data was collected by the primary investigator from the patient and from hospital records. Demographic data was obtained from hospital records and laboratory data from the hospital electronic laboratory database.

Results

Recruitment and categorization of patients according to disease etiology is summarized.



Baseline Characteristics

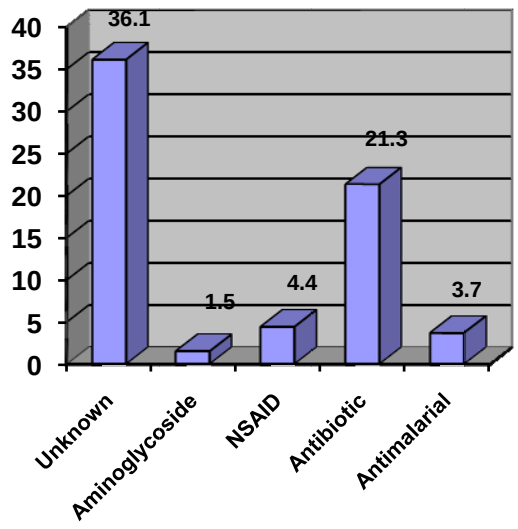
Demographics

163 patients were enrolled in the study for evaluation after admission. Of these patients 27 patients were excluded as they were subsequently diagnosed to have localized infections including microfilarial infection, tuberculosis, viral meningoencephalitis, vasculitis, pneumonia, HIV infection, urosepsis, thrombotic thrombocytopenic purpura, H1N1 infection, post partum sepsis or bacteremia and heatstroke. 136 patients were included for final analysis in the study. The mean age was 40.9 ± 15.6 (16 to 77 years) with a sex ratio 2:1 (male 91: female 45). The patients predominantly belonged to the states of Tamil Nadu and Andhra Pradesh, with a mean distance from the hospital of 76.7 km (5 to 557 km). 95.6% patients were admitted from the emergency room (ER).

Clinical Presentation

Prior to admission at our institution 78 (57.4%) patients visited a local physician and received treatment; however the nature of treatment and medications received were often not known. 52.2% of the patients received medications prior to admission, of whom the use of antibiotic could be confirmed in 29 (21.3%), aminoglycosides in 2 (1.5%), NSAIDS in 6 (4.4%) and anti malarials in 5 patients (3.7%). Medications taken by the 48 (35.3%) patients could not be identified. (Figure 8)

Figure 8: Medication use prior to admission.



Diabetes mellitus type 2 was diagnosed prior to admission in 20 patients (15%) and hypertension in 9 patients (6.8%).

Fever

The mean duration of fever was 7.3 ± 5.1 days. The predominant pattern of fever was high grade with chills and rigors in 74.3 %. Cough (37.5%), dyspnea (58.1%), abdominal pain (33.1%), jaundice (19.9%), diarrhea 16.2%, myalgia (30.9%), oliguria (25%) and anuria (2.2%) were the common associated complaints at admission.

Vital Signs

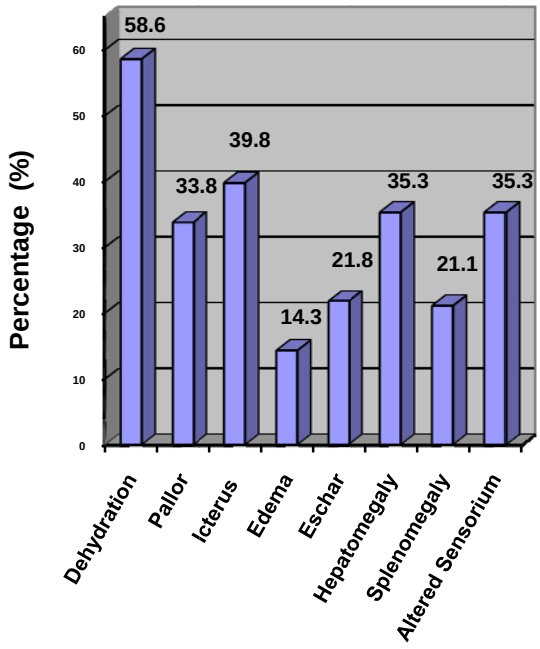
Mean pulse was 110.6 ± 21.7 / min, respiratory rate 30.6 ± 8.8 / min and temperature 99.8 ± 10.4 ° F. The mean arterial blood pressure was 77.2 ± 21.3 mm Hg.

84.6% patients presented in SIRS.

General Physical Examination

General examination findings are shown in Figure 9. Systemic examination showed hepatomegaly in 34.6% patients, splenomegaly in 20.6%, altered sensorium in 31.2% (drowsy 25%, stuporose 3.8%, delirious 1.7% and comatose 0.7%) and positive respiratory findings on examination in 48.1%.

Figure 9: General physical examination: Signs.



Baseline Investigations

Baseline investigations (Table 5) and arterial blood gas values (Table 6) are depicted.

Table 5. Baseline Investigations.

Mean hemoglobin (Hb)	11.9 ± 2.6 gm/dL
Total leucocyte count (TLC)	12211 ± 8682.7 /cu mm
Platelet (plt) count	99 ± 180 x 10^9 /L
Prothrombin Time (PT)	14.7 ± 4.8 secs
Serum creatinine (creat)	2.5 ± 2.4 mg/dL
Serum sodium (Na^+)	132 ± 6 mEq/L
Serum potassium (K^+)	4.2 ± 0.8 mEq/L
Serum bicarbonate (HCO_3^-)	16.6 ± 6.5 mEq/L
Total bilirubin (TB)	3.8 ± 6.2 mg/dL
Direct bilirubin (DB)	2.7 ± 5.4 mg/dL
Serum albumin (alb)	2.9 ± 1.7 gm/dL
Aspartate aminotransferase (AST)	234 ± 758 U/L
Alanine amintransferase (ALT)	107 ± 246 U/L.

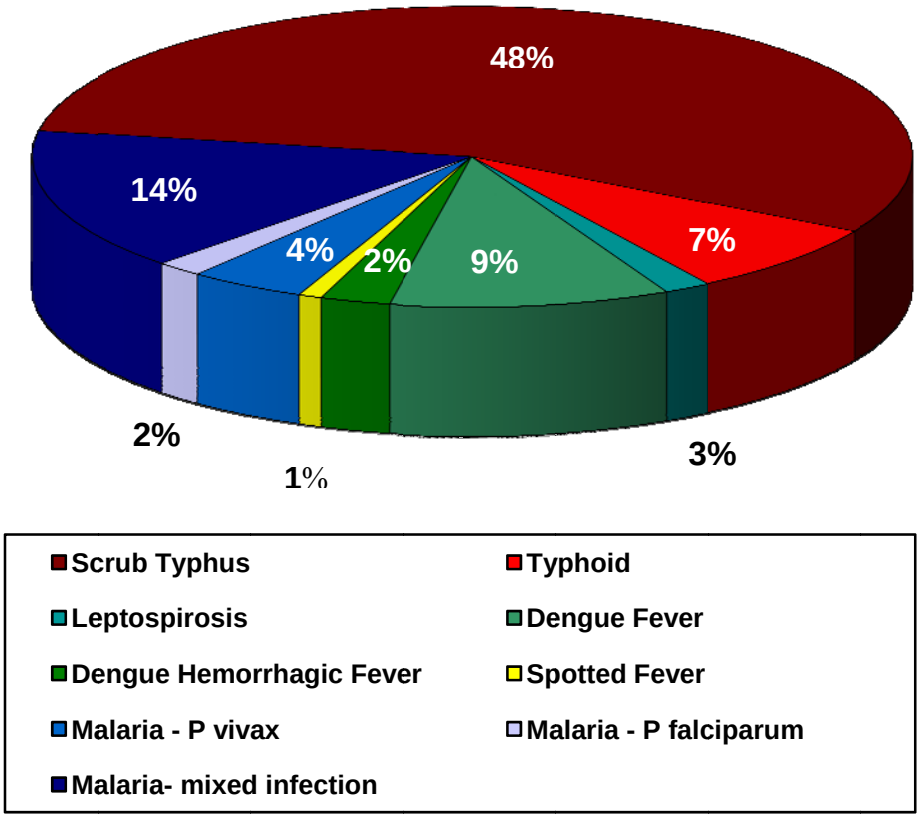
Table 6. Baseline Arterial Blood Gas Values.

pH	7.32 ± 0.1,
pCO_2	29.1 ± 6.9 mm Hg
pO_2	114 ± 66.9 mm Hg
HCO_3	19.1 ± 19.2 mEq/L
Base excess (ABE)	- 9.6 ± 6.2 mmol/L
Lactate (lac)	4.7 ± 4.2 mmol/L

Etiology of AFI.

The etiology after a detailed clinical and serological evaluation of AFI showed scrub typhus in 65 (47.8%), typhoid in 9 (6.6%), leptospirosis in 2 (1.5%), dengue fever in 12 (8.8%), dengue hemorrhagic fever in 3 (2.2%) and spotted fever in 1 (0.7) and malaria in 25 (18.4%) – *P. vivax* in 5 (3.7%), *P. falciparum* in 2 (1.5%) and mixed malarial infection in 18 (13.2%). (Figure 10)

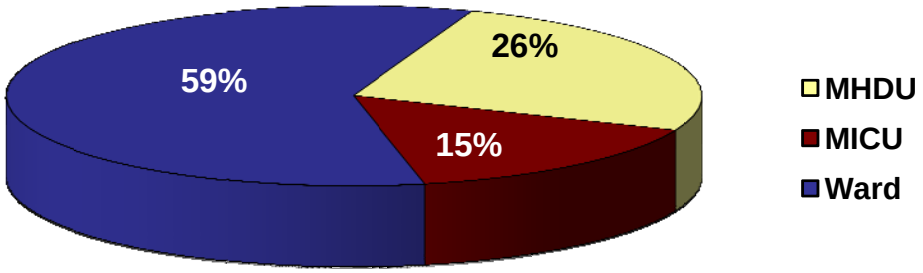
Figure 10. Etiology of AFI.



Site of admission.

Admissions were made to medical general wards (58.8%), high dependency unit (15.4%) and intensive care unit (25.7%). (Figure 11)

Figure 11: Site of admission.



Acute Kidney Injury in AFI

Overall AKI as defined by RIFLE criteria was seen in 71.3% (n = 97/136) of the study population. The baseline creatinine and GFR was 2.5 ± 2.4 and 52.3 ± 35 ml/min/1.73 sq m respectively.

Using the highest creatinine and lowest estimated GFR (e GFR) calculated by the abbreviated MDRD equation the worse criteria was used as determinant for RIFLE grading. (Table 7)

Table 7. **RIFLE Staging.**

RIFLE GRADE	No AKI	Risk	Injury	Failure
RIFLE $_{Creat}$	54 (39.7%)	14(10.3%)	19 (14%)	49 (36%)
RIFLE $_{GFR}$	39 (28.7%)	27 (19.9)	25 (18.4%)	45 (33.1%)
RIFLE $_{Final}$	39 (28.7%)	27(19.9%)	21(15.4%)	49(36%)

AKI vs non AKI.

Comparison of the groups by RIFLE categorization is depicted in table (Table 8)

Table 8. **Non AKI vs AKI patients comparison.**

	No AKI	Risk	Injury	Failure	p
Distance from Vellore (Km)	97.2±94.5	77.5±116	57.9±70.1	117±27.7	0.607
Duration fever (days)	8.1±2.9	8.4±3.8	7.2±2.9	8±4.1	0.712
Hospital Stay (days)	6.1±3.2	7.1±5.5	6.2±3.2	8.9±6.3	0.049
Ionotropes requirement (n,%)	5 (12.8%)	7 (25.9%)	5 (23.8%)	29(59.2%)	< 0.001
Ventilation requirement (n,%)	8(20.5%)	7 (25.9%)	8 (38.1%)	25 (51%)	0.043
Transfusion requirement (n, %)	6 (15.4%)	2 (7.4%)	4 (19%)	19(38.8%)	0.007
Dialysis requirement (n, %)	-	-	1 (4.8%)	24 (49%)	< 0.001
Survivors:Dialysis (n,%)	-	-	-	9 (7.5%)	0.444
Death (n,%)	4 (10.3%)	2 (7.4%)	6 (28.6%)	24 (49%)	< 0.001

The mean age of patients with AKI was higher (44.5 ± 15.2 vs 32.1 ± 13 yrs, p < 0.001) as were the admission severity scores using the Liano score (0.4 ± 0.2 vs 0.3 ± 0.2, p = 0.002). Patients in the R, I and F had prolonged hospital stay and progressively worse outcomes and organ support progressing from R to F. Similarly mortality and dialysis requirement had an incremental trend with increased requirement and mortality in the intensive care unit (ICU) and high dependency unit (HDU).

AKI in Elderly with AFI.

14 elderly patients were studied for outcomes. (Table 9)

Table 9. **AKI in elderly.**

	Age < 65 yrs	Age ≥ 65 yrs	p
No AKI (n,%)	39 (32%)	-	-
Risk (n,%)	27 (22.1%)	-	-
Injury (n,%)	16 (13.1%)	5 (35.7%)	0.002
Failure (n,%)	40 (32.8%)	9 (64.3)	0.002
Dialysis (n,%)	22 (18%)	3 (21.4%)	< 0.001
Death (n,%)	29 (23.8%)	7 (50%)	< 0.001

All the elderly patients ie age ≥ 65 years (n=14/136) had AKI with I in 35.7% and F in 64.3% respectively (p=0.002).Dialysis requirement (3/14, 21.4%, p < 0.001) as well as death (7/14, 50%, p < 0.001) was high in this group.

RIFLE criteria and AKI in AFI.

AKI at admission was established in 87 patients (R-26, I-21 and F-40) with subsequent worsening noticed from R to I in 3 and I to F in 6 patients (shaded area) . Of the 48 (35.6%) patients without AKI at admission 4 progressed to R, 3 to I and 3 to F during the hospital stay and these 10 patients (red box) could be referred to having hospital associated AKI ($p < 0.001$). (Table 8)

Table 10. Shift of RIFLE class post admission.

RIFLE category based on admission creatinine	RIFLE category based on highest creatinine during admission					
	N (%)	No AKI	Risk	Injury	Failure	Total
	No AKI	38 (100)	4 (14.8)	3 (14.3)	3 (6.1)	48 (35.6)
	Risk	-	23 (85.2)	3 (14.3)	-	26 (19.3)
	Injury	-	-	15 (71.4)	6 (12.2)	21 (15.6)
	Failure	-	-	-	40 (81.6)	40 (29.6)
	Total	38 (28.1)	27 (20)	21 (15.6)	49 (36.3)	135 (100)

An improvement in the RIFLE grading from F to I in 6, F to R in 7, F to no AKI in 9, I to R in 4, I to no AKI in 9 and from R to normal renal function in 20 patients (shaded area) was noted. (Table 9)

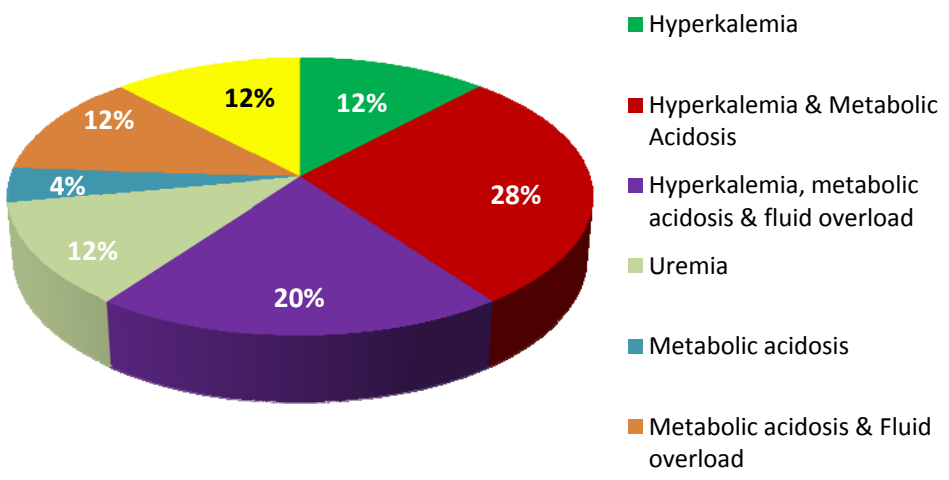
Table 11: **Shift of RIFLE class at discharge.**

RIFLE category based on highest creatinine	RIFLE category based on discharge creatinine during admission					
	N (%)	No AKI	Risk	Injury	Failure	Total
	No AKI	39 (50.6)	-	-	-	39 (29.1)
	Risk	20 (26)	5 (31.3)	-	-	25 (18.7)
	Injury	9 (11.7)	4 (25)	8 (57.1)	-	21 (15.7)
	Failure	9 (11.7)	7 (43.8)	6 (42.9)	27(100)	49 (36.6)
	Total	77 (57.5)	16 (11.9)	14 (10.4)	27 (20.1)	134 (100)

Dialysis

Hemodialysis was required in 25 (17.6%) patients of whom 24 patients were in F and one patient in I. The indications for dialysis were hyperkalemia (12%), metabolic acidosis (4%), metabolic acidosis with fluid overload (12%), hyperkalemia and metabolic acidosis (28%), hyperkalemia with metabolic acidosis and fluid overload in 20%, uremia (12%) and anuria (12%). (Figure 12)

Figure 12. **Indications for dialysis.**



Heparin free dialysis was done for 72% patients predominantly in the ICU. Slow Low Efficiency Dialysis (SLED) was done in 48 % patients, who were hemodynamically unstable and mortality of those who underwent SLED was 100%. Patients who were hypotensive at admission and required ionotropic or ventilatory support also had poor outcomes. 18 (72%) patients who underwent dialysis were admitted to the ICU or HDU of whom 4 (16%) survived, while in the ward 5 out of 7 (71.4%) survived (Table 12).

Table 12. **Dialysis non survivors vs survivors.**

	Non Survivors n=16	**Survivors n=9**	**p**
Males (n,%)	11 (44%)	9 (36%)	0.061
Mean Age (in years)	46.8 ± 14.8	30.9 ± 10.9	0.010
Oliguria (n,%)	12 (48%)	7 (28%)	0.396
Mean MAP (mm Hg)	74 ± 25.9	90.4 ± 17.8	0.109
Mean Creatinine (mg/dL)	4 ± 2.1	7.5 ± 3.8	0.006
SIRS (n,%)	15 (93.8%)	8 (88.9%)	0.667
Altered Sensorium (n,%)	11 (44%)	2 (8%)	0.004
Ventilation (n,%)	13 (52%)	2 (8%)	0.004
Ionotropes (n,%)	14 (56%)	2 (8%)	0.001
SLED (n,%)	12 (48%)	-	< 0.001
Heparin Free (n,%)	12 (48%)	4 (16%)	0.192
Admission: Ward (n,%)	2 (8%)	5 (20%)	0.049
HDU / ICU (n,%)	14 (56%)	4(16%)	0.049

A mean of 2.9 ± 2 sessions (1 to 8 sessions) for 2.9 days (0 to 12 days) was done with no significant difference in duration between survivors and non survivors while on dialysis (2.8 vs 3.1 days). The nine patients who survived after dialysis to discharge, with improvement of renal function, had a mean discharge creatinine of 2.6 ± 1.5 mg/dL (creatinine values: 1.2, 1.2, 1.2, 1.7, 1.9, 2.8, 4, 4.5 and 4.9 mg/dL). None of them underwent dialysis after discharge. The mean age of this survival group (30.9 ± 10.9 vs 46.8 ± 14.8 yrs, p = 0.01) compared favorably to those who died. Other baseline parameters were not significantly different across both groups of patients. Of note was the fact that patients who survived had a higher mean creatinine at admission (7.5 ± 3.8 vs 4 + 2.1 mg/dL, p = 0.006) and comparatively less multi organ dysfunction.

Disease Etiology

Scrub Typhus

Scrub typhus was the most common diagnosis in 47.8% patients. 95.4% presented with tachycardia (pulse rate 90/min) and mean pulse rate was 106.4 ± 24.7 /min. 98.4% had tachypnea (respiratory rate 20 /min) and mean respiratory rate was 29 ± 9.2 /min. Oliguria was observed in 30.8% patients.

When patients with scrub typhus were compared to those with other etiologies ie malaria, dengue fever, typhoid, spotted fever and undifferentiated fever, the former had less coagulopathy (PT 13.4 ± 3.6 vs 15.7 ± 5.5 secs, p = 0.030) and milder hyperbilirubinemia (2.3± 2.6 vs 5.2 ± 8mg/dL, p = 0.007). Lower FENa (2.3 ± 2.7 vs 6.4 ± 10, p = 0.005) as well as RFI (3 ± 3.2 vs 8.2 ± 13.5, p = 0.006) was noted.

Incidence of AKI was comparable across both groups (69.2 vs 53.6%, p = 0.4) with R (20 vs 19.7%), I (16.9 vs 14.1%) and F (32.3 vs 39.4%) as were the dialysis requirement (32 vs 68%, p = 0.080) and mortality (21.5 vs 31%, p = 0.212).

Malaria

Malaria was the diagnosed in 18.4% patients constituted by mixed malarial infection in 13.2%, *P. vivax* in 3.7% and *P. falciparum* in 1.5%. Tachycardia was observed in 80% with mean pulse rate 104.4 ± 15.7 /min. Oliguria was observed in 32% patients. Splenomegaly (48 vs 14.8%, p 0.001) was commonly observed when compared to non malarial patients.

When baseline investigations of malarial and non malarial patients were compared they had worse anemia (10.6 ± 2.9 vs 12.2 ± 2.5 gm/dL, p = 0.005) and hypoalbuminemia (2.6 ± 0.5 vs 3 ± 0.7gm/dL, p = 0.023) and hyperbilirubinemia (10.5 ± 10.5 vs 2.3 ± 3.2 mg/dL, p < 0.001). Incidence of AKI was not different across the groups (64 vs 73%, p=0.4) with R (16 vs 20.7%), I (8 vs 17.1 %) and F (40 % vs 35.1%).

Their mean hospital stay, dialysis requirement as well as mortality were not significantly different. However, among patients who required dialysis the mortality was higher (80 vs 10%, p < 0.001) in the malaria group.

Dengue Fever.

Dengue including hemorrhagic fever was diagnosed in 11% patients. At clinical presentation tachycardia was observed in 61.5% with mean pulse rate 102.5 ± 21.3 / min. Oliguria was observed in 21.4 %.

When baseline investigations of patients with dengue were compared with fever of other etiologies transaminitis (AST 942.9 ± 2192 vs 145.7 ± 141 U/L, $p < 0.001$; ALT 346.9 ± 682 vs 76.9 ± 69.5 U/L, $p < 0.001$), higher FENa (8.4 ± 17.2 vs 3.7 ± 5.3, $p = 0.051$) as well as RFI (11.6 ± 23.8 vs 4.8 ± 7.1, $p = 0.036$) was observed. AKI was seen in 60% with R (13.3 vs 20.7%), I (20 vs 14.9 %) and F (26.7 % vs 37.2%) compared to the non dengue group.

The mean hospital stay (7.3 ± 5 vs 7.3 ± 5.1 days, $p = 0.900$), blood and related products transfusions (40 vs 20.7%, $p = 0.092$), dialysis requirement (26.7 vs 17.4 %, $p = 0.400$) and mortality (33.3 vs 25.6%, $p = 0.500$) was comparable. However in those requiring dialysis the mortality was higher (80 vs 10%, $p < 0.001$).

Typhoid Fever

Typhoid was diagnosed in 6.6% patients. When compared to patients with other etiologies they presented with diarrhea (55.6% vs 13.7, $p= 0.001$) and dehydration (88.9 vs 56.5%, $p = 0.056$). Overall they compared to non typhoid patients in the study except more severe hypoalbuminemia (2.9 ± 0.7 vs 3.3 ± 0.8, $p = 0.051$). Admission creatinine (2.2 ± 1.9 vs 2.6 ± 2.5 mg/dL), FENa (1.36 ± 1.5 vs 4.37 ± 1.4, $p = 0.3$) and RFI (1.7 ± 1.8 vs 5.7 ± 10.1, $p = 0.3$) were comparable.

AKI was seen in 66.7% patients of whom R was present in 44.4% and F in 22.2%. Ionotropic support was required in one patient and hemodialysis in two patients, both of whom succumbed to their illness.

Leptospirosis

Leptospirosis was seen in two patients both of whom had AKI, one each in the R and F categories. The creatinine at admission was 3.8 ± 3.5 mg/dL with GFR 28.3 ± 26.8 ml/min. They did not differ significantly when compared with patients who did not have leptospirosis.. Both patients improved at discharge without requirement of dialysis.

Undifferentiated Fever

When undifferentiated fevers were segregated from the group of confirmed fevers and compared, they presented with increased incidence of systemic features like tachypnea (82.4 vs 56.5%, p = 0.040), hypotension (25 vs 18.4%, p =0.5) and oliguria (52.9 vs 29.3%, p = 0.8). Few diagnostic clues were seen on clinical examination.

Baseline investigations showed normal platelets (3.68 vs 0.78 lacs/cu mm, $p < 0.001$), coagulopathy (PT 19.6 ± 6.6 vs 13.6 ± 3.7 secs, $p < 0.001$), hypoalbuminemia (3.3 ± 0.6 vs 2.9 ± 0.7 mg/dL, p = 0.006), increased proteinuria (UP/UC 2.6 ± 3.5 vs 1.1 ± 1.2, p = 0.002), higher FENa (9.3.± 8.8, 3.6 ± 6.9, p = 0.012) and RFI (13.2 ± 12.6 vs 4.6 ± 9.2, p = 0.005).

AKI was commonly observed (94.7% vs 67.5, p = 0.010) with significantly more patients in the in I and F grades. AKI split as R (10.5 vs 21.4%), I (26.3 vs 13.7%) and F (57.9 vs 32.1%) was significantly more in the undifferentiated group (p = 0.020).

The mean hospital stay was comparable (6.6 ± 5.5 vs 7.4 ± 5.1 days, p = 0. 508) but this was influenced by early deaths during hospital stay. They had higher ionotropic support requirement (63.2 vs 29.1%, p = 0.004) and admission to the ICU or HDU (78.4 vs 36.8%, p = 0.023).Mortality was higher in this group (56.2 vs 22.2%, p = 0.010). For the patients with available data the CPK, LDH, amylase, lipase and procalcitonin levels were not significantly different across the groups.

Summary AFI in AKI

Falciparum malaria had the highest incidence of AKI (100%). Undifferentiated fevers had the highest dialysis requirement (26.3%) and mortality (52.6%). In the differentiated fevers dialysis requirement was highest in the mixed malarial infection (27.8%) and mortality in dengue fever (42.7%). (Table 13) In the patients who died multi organ dysfunction with higher baseline Liano scores was noticed. Requirement of organ support in terms of dialysis, ventilatory and ionotropic support predicted poor outcomes.

Table 13. AFI etiology and AKI.

AFI etiology (n,%)	No AKI	Risk	Injury	Failure	AKI (%)
Scrub typhus	20 (30.8)	13 (20)	11 (16.9)	21 (32.3)	69.2%
Malaria: Mixed	20 (33.3)	13 (11.1)	11 (11.1)	21 (44.4)	66.7%
Malaria : Falciparum	-	1 (50)	-	1 (50)	100%
Malaria: Vivax	3 (60)	1 (20)	-	1 (20)	40%
Dengue fever	5 (41.7)	1 (8.3)	2 (25)	3 (25)	58.3%
Dengue: Hemorrhagic	1 (33.3)	1 (33.3)	-	1 (33.3)	66.7%
Typhoid	3 (33.3)	4 (44.4)	-	2 (22.2)	66.7%
Leptospirosis	-	1 (50)	-	1 (50)	100%
Undifferentiated	1 (5.3)	2 (10.5)	5 (26.3)	11 (57.9)	94.7%

Urinary Indices in AKI

The mean specific gravity was 1.019 ± 0.006, pH 6.07 ± 0.62, RBCs 13.3 ± 22.0 /HPF and WBCs 7.9 ± 16.4 /HPF. The urine spot sodium was 88.8 ± 51.4 with FeNa 4.2 ± 7.2 meq/dL and UP/UC 1.28 ± 1.8. Mean urine spot potassium was 23 ± 14.6 mEq/dL and no evidence of wasting. The urinary indices are compiled in Table 14.

Table 14. **Urinary Indices in AFI based on etiology.**

Urinary Indices	Sp Gravity	pH	RBCs	FeNa	UP/UC
Scrub Typhus	1.012±0.007	5.89±0.52	11.4±19.6	2.3±2.7	1.04±1.1
Vivax Malaria	1.013±0.003	6	9.3±8.5	4.4±6.9	0.3±0.3
Falciparum Malaria	1.01 ± 0.000	6	10	14.4	1.7±2.4
Mixed Malarial Infection	1.008±0.007	6.5	12.7±24.9	5.5±6.7	1.2±1.1
Dengue Fever	1.007±0.003	6.33±0.52	20.1±30.1	9±18.2	1.4±2.1
DHF	1.01±0.000	6	13.3±11.5	3	2.3±3.1
Typhoid	1.010	6	15.1±34.1	1.4±1.5	0.9±1
Leptospirosis	1.005	6	13 ± 9.9	-	1.1±0.2
Undifferentiated	1.013±0.008	6.1±0.32	11.7± 9.9	9.3±8.8	2.6±3.5
Spotted Fever	1.010	7	numerous	0.06	-

Urinary indices in AKI

Comparing the urinary indices in the non AKI vs AKI group RBCs (5.8 ± 7.8 vs 16.3 ± 24.9, p = 0.020) and FENa (1.5 ± 1.4 vs 5.4 ± 8.5, p = 0.010) were found to be high comparatively in the AKI group. In patients who died the FENa was significantly higher (7.5 ± 8.2 vs 3.2 ± 6.8, p = 0.013).

A comparison of the urinary indices in the AKI and non AKI group is shown in Table 15.

Table 15. **Urinary indices in AKI.**

Urinary Indices	Sp Gravity	pH	RBCs	FeNa	UP/UC
Non AKI	1.011±0.007	6.5±0.97	5.8±7.8	1.5±1.4	0.9±1.37
AKI	1.011±0.006	5.97±0.49	24.9±13.3	5.4±8.5	1.4±1.9
p	0.946	0.015	0.020	0.011	0.121

Comparing the urinary indices from R across to F in the RIFLE grades FENa (1.39 ± 0.9 vs 9.1 ± 10.6, $p < 0.001$) as well as proteinuria (0.6 ± 0.4 and 2.14 ± 2.4, $p < 0.001$ respectively) were found to increase. ATN interpreted by FENa > 2 was found in 46.6% and pre renal AKI interpreted as FENa < 1 in 29.1%. 23.9% patients in the AKI group had pre renal AKI of whom 13 (40.6%) in R, 9 (40.9%) in I and 3 (8.3%) in F were observed. ($p = 0.009$) ATN was observed in 56.3% in the AKI group with 6 (27.3%) in R, 5 (38.5%) in I and 29 (80.6%) in F grades ($p = 0.009$).

Cystatin C

Recruitment mean cystatin C was found to significantly differ in the non AKI and AKI groups (1.43 ± 0.41 vs 3.17 ± 2.44, $p < 0.001$) as well as increase across the RIFLE grades from R to F (R 1.6 ± 0.30 , I 2.15 ± 0.63 , F 4.45 ± 2.84 , $p < 0.001$) .The eGFR measured by the Grubb equation using Cystatin C and abbreviated MDRD equation using creatinine in the sample collected at recruitment differed significantly both in patients with AKI (26.1 ± 21.8 vs 47.9 ± 46.6 ml/min/1.73 sq m, $p < 0.001$) and non AKI groups (55 ± 24.8 vs 100.1 ± 21.4 ml/min/1.73 sq m, $p < 0.001$), when the groups were categorized on the basis on creatinine

When the RIFLE categorization done using Cystatin C was compared with that using creatinine, the grades based on Cystatin C were found to differ ($p < 0.001$). (Table 16)

Table 16. **RIFLE comparing creatinine and cystatin C based eGFR.**

	No AKI	R	I	F
$RIFLE_{creat}$	39 (28.7%)	27 (19.9%)	21 (15.4%)	49 (36%)
*$RIFLE_{cystatin\ c}$	17 (12.5%)	22 (16.2%)	39 (28.7%)	47 (34.6%)

* Data from 125 (92%) patients

The 39 patients in the no AKI group were redistributed as 12 in non AKI, 14 in R, 12 in I and 1 in F. Similarly in 25 patients in R based on creatinine 4 were reclassified as no AKI, 14 as I and 2 as F. Of the 17 patients in I, 1 was reclassified as R and 7 as F. Of the 44 patients in F by creatinine 1 was reclassified to no AKI, 2 as R and 4 as I respectively. ($p < 0.001$) (Table 17)

Table 17. **RIFLE class shifts using creatinine and Cystatin C based eGFR.**

	RIFLE grades using Cystatin C					
	Patient No	No AKI	Risk	Injury	Failure	Total
RIFLE grades using Creatinine	No AKI	12 (30.8)	14 (35.9)	12 (30.8)	1 (2.6)	39 (31.2)
	Risk	4 (16)	5 (20)	14 (56)	2 (8)	25 (20)
	Injury	-	1 (5.9)	9 (52.9)	7 (41.2)	17 (13.6)
	Failure	1 (2.3)	2 (4.5)	4 (9.1)	37 (84.1)	44 (35.2)
	Total	17 (13.6)	22 (17.6)	39 (31.2)	47 (37.6)	125 (100)

* Data from 125 (92%) patients

Blood Urea: Creatinine Ratio

The blood urea : creatinine ratio was not predictive of AKI and no co relation was observed with RIFLE scoring. Similarly no information could be derived from its analysis for patients who had dialysis or survived to discharge.

Renal Failure Index

RFI significantly differed in the AKI vs non AKI groups and was found to increase from R to F (R 1.8 ± 1.3, I 2.6 ± 2.7, F 12.1 ± 14.6, $p < 0.001$). It was significantly higher in the patients who died (10.5 ± 11.6 vs 4.1 ± 8.9, $p = 0.005$) and those who required dialysis (14.7 ± 18.1 vs 3.7 ± 6.1, $p < 0.001$).

Scoring Systems

Both the Liano score as well as the Vellore score to predict mortality at admission were high at 0.40 ± 0.2 and Vellore score 0.97 ± 0.1. Liano scores in patients who developed AKI (0.43 ± 0.2 vs 0.33 ± 0.2, $p < 0.001$) as well as those who died (0.51 ± 0.2 vs 0.36 ± 0.2, $p < 0.001$) were higher. The Vellore score did not significantly differentiate between these groups.

Management

Treatment with doxycycline in 86.1% patients, often empirically at admission while awaiting the febrile illness work up, was observed and addition of antibiotics based on the suspected underlying etiology. Organ support was required in the form of invasive ventilation in 35.3%, ionotropes in 33.8% and hemodialysis in 18.4%. Diuretics were

used in 13.2%. Blood and product transfusion was required in 22.8% patients. Patients requiring ionotropes, blood or product transfusion, ventilation and dialysis were at high risk for mortality ($p < 0.001$)

Discussion

Baseline Characteristics

Epidemiologically AKI is commoner in males, 67% in our study compared to 64% in a multinational study.(87) Increasing age, severity of illness and greater distance from centers of care are associated with higher mortality in AKI and a similar association was seen for age and severity of illness in our study. (88)

AFI and AKI

AKI was found in 71.3% of our patients with R, I and F as 19.9%, 15.4% and 36% respectively and mortality of 30.9%. Using FENa as a marker for pre renal AKI, FENa < 1 was observed in 30%, 16.7% and 10% in R, I and F respectively suggesting a possibility of recovery with early management which decreases with progression from R to F. In most cases the group in R represents volume responsive hypovolemia and is managed effectively with fluids and ionotropes. However this benefit is not extended to late initiation of volume replacement and restoration of renal perfusion.(89)

Early AKI diagnosis has better outcomes as compared to late AKI.(69) Mortality in R (0%), I (0%) and F (12.5%) for admission to wards compared favorably to R (50%), I (100%) and F (84%) in the MHDU/ICU patients, who predominantly presented with established multi organ dysfunction. A multi center study in Brazil on AKI in ICU, with sepsis as the main etiology, showed 71% mortality with distribution in RIFLE grading R (28%), I (24%) and F (48%) indicating high incidence of AKI and death in ICU care.(90)

Distance of travel for treatment did not affect outcomes probably related to a referral bias, whereby sick patients at high risk for mortality were referred for admission irrespective of distances. Although their duration of fever was comparable, patients in

RIFLE – F traveled further distances for care reducing the period for early intervention. They also had longer duration of hospital stay with high dependency care and organ support including ionotropes, invasive ventilation and dialysis. It is noteworthy that despite a lower mean age 40.9 ± 15.6 yrs and relatively low co-morbid conditions prior to admission the incidence of AKI and death was high.

Mortality in AFI related AKI

Patients in ICU as well as those transferred to the wards after ICU care were at higher risk for death.(91) Death was common in ICU in the non AKI group in high dependency care as well indicating multi organ dysfunction as a poor prognostic indicator for survival in AFI. A recent study supports the theory that the severity of illness confers an increased risk, putting those who develop AKI or at risk of AKI as a result of their illness at risk for death.(92) In our study patients who presented in SIRS were at higher risk of death in the presence of AKI as compared to those without AKI (32.5 vs 11.4%, p = 0.013).

A rise of serum creatinine by as much as 0.3 mg/dL increases the risk of death (93), evidenced by high death rates across from R to F. This has been recognized by AKIN in an attempt to improve the RIFLE criteria by using this 0.3 mg/dL rise to label Stage I AKI. Comparison of AKIN and RIFLE staging and outcomes were not assessed in this study but based on available evidence results are comparable for both.(74)

Dialysis uniformly had poor outcomes with SLED being the predominant modality of renal replacement in ICU patients owing to hemodynamic instability. When to initiate dialysis and how much continues to be debated. Early and more dialysis in terms of frequency (94) and intensity (95) as proposed earlier has been recently addressed with no

beneficial effects observed when compared to thrice a week intermittent hemodialysis or CRRT at 20 ml/hour. (96) Our policy is to offer hemodialysis based on standard indications for dialysis.

Death in AFI related AKI

Our incidence of AKI and death in AFI is high owing to a referral bias and triage in the emergency room (ER) by a specialized medical team. This team ensured early management and stabilization, often with short ER stay less than 24 hours in the ER of many patients, thus selecting a higher number of patients with SIRS and MODS for admission. This may explain the difference compared to an earlier study showing AKI to be 42.1 %.(5) 31.1% of our study population was managed in the HDU and ICU during hospitalization with 51.5 % patients in these areas having AKI, dialysis requirement in 72% and 78 % mortality.

Outcomes of dialysis in AFI related AKI

Dialysis was necessitated for care of AKI in 18.4% in our study. Dialysis requirement in AFI has poor outcomes with and overall mortality of 64% in our study. ICU mortality in patients undergoing dialysis was 77.8%. Recent literature (21) demonstrates a major epidemiological shift in management of AKI from the wards to ICUs. It has major ramifications on health care allocation and cost of ICU care which is beyond the reach of most patients in India. The period of hemodialysis is prone to infection, 90% in an ICU study from Belgium, which however does not contribute to mortality. (97)

It is interesting to note that 36% patients who survived to discharge after hemodialysis did not touch baseline in most cases at the time of discharge. In the absence of follow up, progression to CKD could not be estimated. There is immense concern on a nexus between AKI, CKD and dialysis dependence. Progression to CKD post AKI is characterized by hyperfiltration, microalbuminuria and hypertension. (98) 6% of these patients are known to progress to ESRD within two years. (99) About 25% of the increase in incidence of ESRD in the USRDS has been attributed to AKI (100) and considering high incidence of AFI in India, the incremental burden of CKD as a result of AKI in ARF in the years to come is likely to be very high.

Early intervention for AKI in AFI

Majority of our patients had contact with a physician at varying stages of their illness prior to admission at our center. Awareness amongst physicians, who first manage AFI at the community level of a possibility of AKI in AFI, thus avoiding nephrotoxic drugs and toxins, preventing dehydration and hypovolemic shock and initiation of appropriate empirical antibiotics may reduce the percentage of patients who have established AKI and tubular injury on first evaluation in tertiary care. Early and aggressive management in a tertiary care center with renal triage using RIFLE can direct these resuscitative efforts before establishment of renal injury and failure. Recognizing AKI as an expression of sepsis and managing sepsis effectively and early may reduce AKI incidence. Although our study excluded patients with CKD, factoring them for early triage and ensuring least insult to an already compromised kidney at high risk for irreversible damage and dialysis dependence is imperative.

AFI etiology and AKI

Scrub typhus had a high incidence of AKI (69.2%) and complete recovery in 50% of these. In an earlier study on scrub typhus shock, altered sensorium, ARDS and metabolic acidosis and AKI were poor prognostic markers. AKI defined as creatinine more than 1.4 has been observed in about 20% patients . (101) Use of RIFLE criteria as in our study could explain the higher incidence as well as earlier identification of AKI in patients with AFI. An early and dramatic response to doxicycline and IV fluid supplementation in the ER was found with a remarkable role in preventing organ dysfunction and death. Careful examination of an eschar observed in 44.6% compared to 45.5% in the earlier study, is a useful clinical clue to direct early management pending diagnostic serology.(101)

Prognosis using Liano score in AFI related AKI

Prediction of AKI and death at admission is important for responsible fiscal allocation of limited hospital and ICU care in India. The BEST (Beginning and Ending Supportive Therapy for the Kidney) study for Mortality Prediction Models (MPM) including the Mehta, Paganini, Chertow and Liano models showed ROCs ranging from 0.6 for Chertow to 0.7 for Liano scoring.(87) The mean Liano score was high in our study (0.4 ± 0.2). In patients who developed AKI or died the Liano score was significantly higher. It could be used as a tool to prioritize access to limited ICU care, but all MPM s studied till date have shown sub optimal discrimination as robust predictors of mortality.(90)

RIFLE criteria and prediction of mortality in AFI

RIFLE classification provides a clear trend in increasing mortality from R (7.4%), I (28.6%) and F (49%) in our study. This trend has been noticed with varying degrees in all studies most of which are done exclusively in critically ill patients admitted to ICU patients. (69) Class shifts from no AKI to AKI and across risk to injury to failure, at every level were found to have increasing dialysis requirement and mortality. (5) Hospital associated AKI was low in our study owing to established AKI at admission in most patients and effective interventions once admitted to the ER reducing progreson once admitted to the hospital.

In a study by Uchino S, et al of 20126 general admissions to hospitals with 14.7% ICU admissions, mortality was R (15.1%), I (29.2%) and F (41.1%). Multivariate analysis showed RIFLE to be a predictor for hospital mortality with linear increase in odds ratio from Risk to Failure.(72) Patients with delayed AKI presenting in sepsis and hypotension require mechanical ventilation and have a higher mortality. (102) AKI in AFI across the spectrum of RIFLE increases the risk of death. Late presentation with sepsis and AKI explain the high mortality in our study.

Primary involvement and secondary involvement of the kidney in multiorgan dysfunction continues to be studied. Early AKI and progression result in salt retention, fluid overload, hyperkalemia and metabolic acidosis and consequently hypotension, impaired organ perfusion, insulin resistance, protein catabolism, anemia and infection arising out of impaired innate immunity. This spectrum was commonly observed in our patients. The

kidney in animal models has shown to stimulate a systemic pro inflammatory response as a result of ischemia- reperfusion injury often manifesting as ARDS. (69)

Limitations of RIFLE classification: Early predictors of AKI in AFI

Despite its utility RIFLE does not provide functional information on the nature of AKI. In this context previous established but relatively less used indices like FENa are useful adjuncts to management. 13/32 (43.3%) patients had pre renal using FENa in the no AKI group and these could represent a population with ongoing renal damage undetected by RIFLE who could benefit from early intervention. This also may be a case for use of biomarkers to detect AKI earlier. Despite its limitations FENa continues to be a useful tool in identifying patients in early AKI and used in conjunction with RIFLE may be effective in reversing AKI and preventing progression after admission. As a cheap and easily available tool it could effectively reduce costs and promote management at local centers with volume repletion by the primary physician.

Cystatin C using the Grubb equation showed lower GFR compared to the creatinine based abbreviated MDRD equation. RIFLE grading using the Grubb GFR showed increased severity of AKI. This may be a case for using admission Cystatin C as a biomarker of AKI. Cystatin C predates detection of AKI by two days compared to creatinine with high diagnostic accuracy (103) and could differentiate presentations in pre renal azotemia and AKI. The future of AKI management could be revolutionized by availability of newer biomarkers for early diagnosis.

Limitations of study

This study was done in a tertiary referral center and the patients may not be representative of other centers where the case mix and referral patterns may be different. It used creatinine and GFR criteria for interpretation of RIFLE, excluding the urine output criteria. A true baseline as recommended by the ADQI was unknown for all patients and the calculated baseline from the MDRD equation using a baseline eGFR of 90 ml/min which may have led to a greater estimate of change and consequently higher estimation of AKI. Although the RIFLE using MDRD equation with a baseline of 90 ml/min/1.73 sq m is validated recently in this group of patients it remains a substitute for actual GFR. Using a lower cut off as per the ADQI recommended baseline of GFR of 75 ml/min, reduced the AKI in terms of numbers but the trends in classification and related morbidity and mortality held true.

Lastly there was limited follow-up after hospital discharge and no data to assess recovery and progression to CKD over a time frame.

The study also did not use novel biomarkers of kidney function to further delineate etiology and predict early renal dysfunction.

Summary

1. In this study of AKI in tropical AFI inpatients at a tertiary care hospital had a high incidence of AKI (71.3%) and death (26.5%).

2. Tertiary referral is often late and presentation with SIRS was observed in 84.6% at admission. High dependency care was required in 41.2% patients, often for initial stabilization and multi organ dysfunction.

3. AKI was observed at admission in 87 (64%) with 10 (7.4%) patients developing hospital associated AKI.

4. Undifferentiated fever had the highest incidence of AKI (94.7%) with dialysis requirement in 26.3% and death in 52.6%.

5. In differentiated fevers highest AKI was in falciparum malaria (100%) with highest dialysis requirement in mixed malarial infection (27.8%) and highest mortality in dengue fever (42.7%). Scrub typhus had a good response to treatment.

6. Promising diagnostic utility of Renal Failure Index, FENa and serum Cystatin C in early detection of AKI in AFI.

7. Grading AKI using RIFLE classification showed risk (R) in 19.9%, injury (I) in 15.4% and Failure (F) in 36%. RIFLE was identified as a sensitive tool for diagnosis of AKI in AFI and patients have a worse prognosis and outcomes from risk through injury and failure stages in terms of organ support, dialysis requirement and death.

8. RIFLE criteria using Cystatin C appears to be more sensitive in diagnosing AKI earlier and may be a useful adjunct in earlier management.

9. Liano scoring at admission identifies high risk patients and may be useful for triage to high dependency care.

10. Metabolic acidosis, hyperkalemia, fluid overload and uremia necessitated hemodialysis in 18.4% of whom 48% required SLED.

11. Death in patients initiated on hemodialysis for AKI was high (64%) with 100% mortality in those requiring SLED, in view of hemodynamic instability.

12. Early management of AFI with well directed empirical antibiotic treatment and AKI with hydration as well as avoiding nephrotoxic medications improves outcomes.

Conclusion

AKI in AFI is common often requiring multi multispeciality care with dialysis and hemodynamic as well as ventilatory support. Mortality is high with shifting trends in management from wards to ICUs.

Severity of AKI in AFI is based on etiology of fever, increasing age, late presentation, inappropriate medication use and delayed recognition.

RIFLE categorization has an incremental risk of adverse outcomes from Risk to Failure and helps to detect early AKI and predict unfavorable outcomes, especially in patients with multiorgan requirement requiring dialysis and ICU care.

Cystatin C is an early biomarker and its use improves early detection of AKI as compared to creatinine in the RIFLE criteria.

FENa is a useful, easily available test for early detection of AKI in AFI and its use should be encouraged at first contact with a physician to encourage early intervention even at a community level.

Emphasis on prevention and management at the earliest point of contact, particularly the community level by educating registered medical practitioners on AFI pattern recognition, renal function assessment and early hydration, appropriate antibiotic use, avoidance of nephrotoxic drugs, nutrition and early referral to nephrologists for patients in AKI will reduce the burden of disease and CKD in the long run.

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Annexure 1. Informed Consent

Informed consent

Study Information

You are being invited to take part in a study titled "Acute Renal Failure in Acute Febrile Illness: Incidence, Prognosis and Outcomes" This study is being done by the departments of Nephrology and Medicine at Christian Medical College, Vellore.

You will be examined by doctors in the Nephrology and Medicine department and will be asked to undergo pertinent tests which are done as part of routine protocol for any patient undergoing evaluation for fever and acute renal failure. No additional tests will be done.

Strict privacy will be maintained during the interview, clinical examination and information of laboratory results. Your name will not appear on the study records, but will be linked to them by a study number which will be kept confidential by the study investigator. This study will not require that you be regularly followed up or be involved in any way beyond the time you spend in the hospital for your presenting illness.

Although you are being asked to participate in this study, you are free to decline your consent to participate in this study at any time and you will continue to receive treatment at Christian Medical College for your illness.
Please feel free to ask any doubts regarding this study. After understanding all the aspects of the study, you may sign below as consent to participation in this study.

Consent

I have been clearly explained in my own language about the proposed study and the related investigations to be done thereof, with the understanding that no additional charges will be attributed to me in addition to my regular treatment requirement. I consent for my blood to be collected, stored and used for diagnostic and research purpose for this study or any related research in the future approved by the Institutional Review Board.

Subject name: Serial No:

Hospital number:

Signature (or thumb impression) of subject/legally acceptable representative:

Signatory's name:

Date: Serial No.

Signature (or thumb impression) of subject/legally acceptable witness

Witness' name:

Date:

Primary Investigator

Date:

Annexure 2. Study Proforma

Proforma

Ser No

Name **Age** **Sex**

Co morbid

Dehydration Diabetes Mellitus Hypertension Coronary Artery Disease

Nephrotoxic Drugs: Intake unknown NSAIDS Aminoglycosides Radiocontrast

Duration of fever

Less than 1 week 1-2 weeks more than 2 weeks

Type of Fever

Continuous Remittent Intermittent

Grade Low Intermediate High

Chills Rigors

Upper Respiratory

Rhinorrhoea Throat Pain Headache

Lower Respiratory

Dyspnoea Cough Expectoration Hemoptysis

Abdominal

Pain Vomiting Diarrhoea MelenaDistention

Urinary

Dysuria Oliguria Anuria Hematuria

Urine output

CNS

Altered Sensorium		Seizures		Focal Defecits
Musculoskeletal				
Muscular pain	Arthritis	Arthralgia	Myalgia	
Examination				
Pallor	Mild	Moderate	Severe	
Icterus	**Cyanosis**	**Edema**	**Asterexis**	
Skin	Rash	Eschar	Petechia	Purpura
Pulse Rate	80-100/min	100-120/min	greater than 120/min	
Respiratory Rate	less than 20/min		more than 20/min	
BP	MAP less than 70		MAP less than 70	
CVS	S1	S2	S3	Murmurs
Respiratory	Crepts		Ronchi	
GI	Hepatomegaly	Splenomegaly	Ascitis	
Nervous	Concious/Drowzy/Stuporose/Comatose		Focal Defecits	
Musculoskeletal	Tenderness	Joint swelling	Joint stiffness	
Investigations				
Hb	TLC	DLC	Plat	Film
PT	PTT	Fibrinogen	Procalcitonin	
BU	Creat	Potassium	HCO3	
TP	Alb	SGOT	SGPT	
Serology	Dengue	Leptospira	Typhiod	Scrub
Malarial parasite	Present /Absent			
USG Kidneys			CXR	

Urine C/S Blood C/S Sputum C/S

Stool C/S

Urine R/E Microscopy UP/UC

BBVS

Transfusions PC FFP PRC

RIFLE

Course in hospital

Day								
Creat								
eGFR								
Urine Output								

Days from onset of fever to renal failure

Indication for hemodialysis

Hyperkalemia Metabolic Acidosis Anuria Fluid Overload

Duration of hemodialysis

Number of sessions of hemodialysis

Schedule of hemodialysis Daily Intermittent

Nature of hemodialysis Regular SLED

Hemodialysis Access

Heparin Schedule: Saline Rigid bolus Rigid Heparin Systemic Heparin

Complications during dialysis

Follow up

Hb	TLC	DLC	Plat
PT	PTT	Fibrinogen	Procalcitonin
BU	Creat	Potassium	
HCO3	TP	Alb	SGOT
USG		CXR	

Time to Recovery

RIFLE

Outcome at Discharge: Recovered Improving Death

No	Hosp No	Dia	Age	Sex	Town	Dist	Adm	Dur	Disc	Dur	Typ	Gra	Puls	Res	SIR	MAP	Tem	DM	HT	DrU	AG	NSA
1	608559D	1	62	1	Kaveripa	63	0	4	1	5	1	2	92	26	1	.	100	0	0	0	0	0
2	613301D	1	42	1	Chitoor	34	2	9	0	14	1	2	86	36	1	117	99	1	0	1	0	0
4	613309D	1	38	1	Chitoor	34	0	7	0	10	1	3	106	32	1	87	98	0	0	0	0	0
5	613360D	1	40	1	Kadapa	248	2	7	0	5	1	1	120	32	1	90	98	0	0	0	0	0
6	613495D	1	65	1	Gudiyata	29	2	2	1	10	1	3	112	22	1	90	98	0	1	0	0	0
7	616102D	1	26	1	Chitoor	34	0	3	0	10	1	1	124	24	1	73	100	0	0	0	0	0
8	081136C	1	29	1	Polur	50	0	2	0	10	1	1	106	28	1	77	103	0	0	0	1	0
9	618110D	1	62	1	Chitoor	34	0	5	0	10	1	2	140	42	1	93	101	1	0	1	0	0
11	616372D	9	31	1	Bankura	1809	0	19	0	5	1	3	112	40	1	70	100	0	0	0	0	0
12	620012D	1	40	1	Tiruvana	77	2	6	0	10	1	1	130	40	1	50	99	0	0	1	0	0
14	620117D	6	46	2	Ranipet	141	1	8	0	15	1	1	98	.	3	93	.	0	0	0	0	0
15	620047D	1	68	2	Somalap	.	0	6	0	5	1	1	110	34	1	53	.	1	0	1	0	0
16	620107D	1	50	1	Chittor	34	0	3	0	5	1	1	108	28	1	83	100	1	0	0	0	0
17	616378D	1	51	1	Kadapa	248	0	7	0	15	1	3	84	40	1	100	99	0	0	1	0	0
18	620330D	1	18	2	Chitoor	34	1	14	0	9	1	1	112	44	1	63	.	0	0	0	1	0
19	620377D	6	35	2	Tirupatu	91	2	5	1	7	1	1	110	32	1	67	103	0	0	0	0	0
20	763636A	1	62	1	Vellore	5	2	11	0	10	1	1	114	.	1	83	.	0	1	0	0	0
22	620539D	6	34	1	Chitoor	34	2	3	1	7	1	1	104	44	1	73	100	0	0	0	0	0
23	620470D	1	55	2	Vellore	5	0	4	0	5	1	1	132	40	1	107	103	1	1	0	0	0
24	620462D	1	53	2	Kadapa	248	0	6	0	10	1	1	130	36	1	73	99	0	0	0	0	0
25	620556D	1	21	1	Tiruvana	77	2	9	0	10	1	1	92	28	1	103	102	0	0	0	0	0
28	625048D	3	43	1	Tiruvana	77	0	6	0	7	1	1	104	32	1	83	.	1	0	0	0	0
29	625243D	4	18	1	Tiruvana	77	0	6	0	7	1	1	130	20	1	93	101	0	0	0	0	0
30	625434D	6	23	1	Tiruvana	77	1	17	0	6	1	3	104	.	1	113	.	0	0	0	0	0
31	625413D	1	32	2	Kadapa	248	2	4	1	5	1	1	128	36	1	80	102	0	0	0	0	0
32	625516D	1	54	1	Madanu	35	0	5	0	10	1	1	110	40	1	83	101	0	0	0	0	0
33	625444D	1	20	2	Tiruvana	77	0	3	0	10	1	1	106	28	1	83	103	0	0	0	0	0
34	625692D	3	34	2	Gudiyata	29	2	8	1	10	1	1	128	40	1	80	101	0	0	0	0	0
35	625567D	1	30	1	Ranipet	141	0	6	0	7	1	1	110	44	1	83	104	0	0	0	0	0
36	625550D	1	68	2	Ranipet	141	2	3	1	6	1	1	128	30	1	57	101	0	0	1	0	0
37	630008D	1	25	1	Dharma	136	1	6	0	10	1	1	104	30	1	80	104	0	0	0	0	0
38	630131D	1	39	1	Sathur	80	2	5	0	7	1	1	120	44	1	57	103	0	0	0	0	0
39	630295D	4	21	1	Vellore	5	2	13	1	14	1	1	152	32	1	80	101	0	0	0	0	0
40	648234D	1	52	1	Walajah	25	0	3	0	5	1	1	98	24	1	73	99	1	0	0	0	0
42	819985C	1	48	2	Chitoor	34	0	5	0	7	1	1	104	24	1	97	101	1	0	0	0	0
43	644390D	6	18	2	Kadapa	248	0	5	0	6	1	1	118	40	1	80	103	0	0	0	0	0
44	651311D	1	55	2	Tiruvana	77	2	13	0	7	1	1	120	24	1	80	100	0	0	0	0	0
45	839020C	3	36	1	Vellore	5	0	3	0	7	1	1	84	18	0	83	.	0	0	0	0	1
46	651470D	1	71	1	Vellore	5	1	6	0	5	1	1	102	28	1	93	98	0	0	0	0	0
48	658142D	4	23	1	Vellore	5	0	7	0	8	1	1	112	28	1	73	102	0	0	0	0	0
49	658185D	6	48	1	Tiruvana	77	2	22	0	3	1	1	0	.	1	0	.	0	0	1	0	0
50	484055C	6	32	2	Chitoor	34	0	1	1	7	1	1	.	.	3	.	.	0	0	0	0	0
52	667250D	13	35	1	Vellore	5	0	10	0	7	1	1	84	24	3	93	.	0	0	1	0	0
53	669406D	1	21	2	Chitoor	34	0	8	0	5	1	1	160	22	1	73	.	0	0	0	0	0
54	669796D	12	34	2	Chitoor	34	0	27	0	5	1	1	130	44	1	73	101	0	0	1	0	0
56	674066D	6	73	1	Peyad	701	2	4	1	.	.	.	.	.	3	.	.	.	.	.	.	.
57	626844D	6	57	1	Vellore	5	2	11	1	15	1	1	106	24	1	103	104	0	1	1	0	0
59	686473D	6	18	1	Chitoor	34	1	8	0	5	1	1	130	40	1	47	1	0	0	1	0	0
63	711029D	4	17	1	Kadapa	248	0	5	0	14	2	1	90	24	1	93	102	0	0	1	0	0
64	714593D	6	39	1	Chitoor	34	1	3	1	4	1	1	132	28	1	90	102	0	0	1	0	0

65	712413D	1	71	2	Vellore	5	2	4	1	7	1	2	136	32	1	103	98	1	0	1	0	0
67	724159D	1	55	2	Vellore	5	2	20	1	5	1	1	116	26	1	77	98	0	0	0	0	0
68	808565C	3	22	1	Vellore	5	0	5	0	5	1	1	100	24	1	93	100	0	0	0	0	0
69	724143D	9	36	1	Chitoor	34	1	4	0	3	1	3	90	24	0	93	100	0	0	0	0	1
70	724402D	13	21	2	Kadapa	248	0	7	0	5	1	1	112	24	1	57	99	0	0	0	0	0
71	730099D	6	40	2	Vellore	5	1	11	0	5	1	3	130	40	1	23	.	0	0	0	0	0
72	265407D	4	54	1	Tirunelv	557	0	14	0	5	1	1	98	24	1	93	101	1	0	0	0	0
73	730129D	1	39	1	Tiruvana	77	0	5	0	10	2	1	120	30	1	83	.	0	0	0	0	0
74	732578D	13	29	1	Vellore	5	0	7	0	10	1	1	100	18	0	90	.	0	0	0	0	0
75	730341D	15	46	1	Tirupatu	91	0	6	0	10	2	1	96	22	0	80	98	0	0	0	0	0
76	730349D	3	22	2	Chitoor	34	0	4	0	5	1	1	82	16	1	83	100	0	0	0	0	1
77	730354D	1	77	1	Vellore	5	0	4	0	8	1	1	92	26	0	107	.	0	0	0	0	0
78	730358D	1	48	1	Gudiyata	29	0	5	0	20	1	1	142	28	1	80	101	0	0	0	0	1
79	724598D	1	52	2	Tirupatu	91	2	11	0	10	1	3	102	24	1	60	103	0	0	0	0	0
80	735043D	15	23	1	Vaniyam	67	0	11	0	6	1	1	98	24	1	83	99	0	0	0	0	0
81	724594D	15	49	1	Chitoor	34	0	8	0	8	1	1	72	20	0	73	.	0	0	0	0	0
82	732388D	14	20	1	Kadapa	248	1	8	0	7	1	1	80	26	1	53	100	0	0	1	0	0
83	736797D	15	18	1	Kadapa	248	0	2	0	7	1	1	92	24	1	93	101	0	0	0	0	0
84	735224D	15	24	1	Vellore	5	0	5	0	7	1	1	112	24	1	70	102	0	0	0	0	0
85	735219D	15	22	1	Kadapa	248	0	6	0	5	1	1	112	24	1	60	.	0	0	0	0	0
87	739140D	15	60	1	Kadapa	248	0	5	0	5	1	1	120	22	1	73	99	0	0	0	0	0
88	739133D	15	35	1	Ambur	47	1	15	1	5	2	1	110	20	1	70	99	0	0	0	0	0
89	740478D	5	44	2	Tiruvallu	91	0	6	0	5	1	3	200	18	1	87	.	0	0	0	0	0
90	192293B	1	58	1	Dharma	136	2	4	0	15	1	1	130	28	1	23	103	0	1	0	0	0
91	739182D	1	35	2	Chitoor	34	0	5	0	10	1	1	92	40	1	70	103	0	0	0	0	0
93	739233D	1	34	1	Kadapa	248	0	4	0	5	1	1	92	36	1	60	100	0	0	1	0	0
94	739134D	1	28	1	Chitoor	34	0	6	0	5	1	1	102	16	1	73	103	0	0	0	0	0
95	739290D	6	30	1	Vellore	5	0	7	0	5	1	3	86	26	3	107	.	0	0	0	0	0
96	739001D	4	17	2	Vellore	5	0	11	1	12	1	1	104	22	1	80	.	0	0	0	0	0
98	735373D	3	20	1	Krishnag	119	2	13	0	5	1	1	120	40	1	87	.	0	0	1	0	0
99	739351D	4	35	1	Vellore	5	0	8	0	10	1	1	80	18	0	93	.	0	0	0	0	0
100	742727D	4	28	1	Vellore	5	0	2	0	5	1	1	88	18	0	93	101	0	0	0	0	1
101	744100D	1	26	2	Krishnag	119	0	3	0	14	1	1	112	24	1	80	.	0	0	0	0	0
102	744307D	1	38	2	Vellore	5	1	3	1	4	2	1	130	40	1	90	99	0	0	0	0	0
103	744246D	1	37	1	Vellore	5	0	2	0	5	1	1	96	26	1	80	104	0	0	1	0	0
105	745413D	1	40	2	Vellore	5	1	7	0	10	1	1	132	44	1	23	102	0	0	1	0	0
106	744172D	15	19	1	Vellore	5	0	4	0	10	1	1	104	24	1	77	99	0	0	1	0	0
107	749618D	13	47	1	Ariur	233	0	4	0	10	1	1	88	.	0	27	100	0	0	1	0	0
109	744179D	1	42	1	Krishnag	119	0	11	0	10	1	1	102	40	1	60	100	0	0	1	0	0
110	750131D	1	33	1	Vellore	5	2	3	1	5	1	1	124	32	1	70	101	0	0	1	0	0
111	750272D	1	45	1	Tiruvaro	244	2	21	1	20	1	1	120	24	1	57	102	0	0	1	0	0
112	745436D	4	19	1	Vellore	5	0	21	0	14	1	1	104	24	1	73	.	0	0	1	0	0
114	753036D	15	50	1	Kadapa	248	2	0	1	5	1	1	112	34	1	90	101	0	0	1	0	0
115	750287D	1	37	1	Chitoor	34	0	8	0	5	1	1	148	45	1	77	.	0	0	0	0	0
116	615538D	1	49	2	Vellore	5	0	4	0	14	1	1	100	22	1	83	.	1	0	0	0	0
117	753023D	1	30	1	Chitoor	34	0	5	0	5	1	1	104	20	1	80	99	0	0	1	0	0
118	753031D	1	45	1	Chitoor	34	0	0	0	15	1	1	100	32	1	73	103	0	0	1	0	0
119	750359D	3	22	1	Chitoor	34	0	14	0	6	1	3	86	26	0	97	98	0	0	1	0	0
120	755440D	6	35	2	Tiruvana	77	0	4	0	15	1	1	112	24	1	83	.	0	0	1	0	0
121	636328D	13	46	1	Vellore	5	1	6	0	10	1	1	92	44	1	80	103	0	0	1	0	0
122	753355D	1	38	2	Vellore	5	2	1	1	7	1	1	120	38	1	60	.	0	0	1	0	0

123	753391D	6	51	2	Vellore	5	0	0	1	7	1	1	130	60	1	63	.	1	1	1	0	0
124	756421D	1	65	1	Gudiyata	29	0	12	0	10	1	1	100	24	1	80	.	1	0	1	0	0
125	757989D	1	72	2	Walajah	25	0	12	0	5	1	1	106	42	1	73	99	0	0	0	0	0
126	759213D	1	25	1	Walajah	25	2	13	1	6	1	1	132	28	1	110	100	0	0	1	0	0
127	765174D	15	28	1	Tiruvana	77	1	18	0	15	1	1	122	28	1	60	99	0	0	1	0	0
128	777169D	15	35	1	Chitoor	34	0	11	1	3	1	1	132	36	1	100	99	0	0	0	0	0
129	777179D	3	16	2	Chitoor	34	2	4	1	3	1	1	150	32	1	20	106	0	0	0	0	0
130	777181D	1	26	1	Vellore	5	1	3	0	5	1	1	110	30	1	70	104	0	0	0	0	0
131	770345D	1	37	2	Tirupattu	91	1	8	0	8	1	1	96	46	1	97	103	0	0	1	0	0
132	774683D	14	45	1	Tiruvana	77	2	8	1	7	1	1	110	48	1	67	.	1	0	0	0	0
134	778200D	1	57	1	Tirupatu	91	1	21	1	3	1	1	160	46	1	.	106	0	0	1	0	0
136	777363D	6	62	1	Ambur	47	1	4	1	5	1	1	124	36	3	63	100	0	0	0	0	0
137	780326D	15	51	1	Chitoor	34	0	5	0	14	1	3	80	24	0	97	99	0	0	1	0	0
138	780145D	1	52	1	Tirupatu	91	0	7	0	6	1	2	140	36	1	93	.	0	0	1	0	0
139	780269D	1	48	1	Chitoor	34	0	8	0	10	1	1	124	28	1	97	101	1	0	1	0	0
140	019439B	6	66	2	Vellore	5	2	4	1	3	1	1	100	30	1	93	.	1	1	0	0	0
141	780029D	3	65	1	Vellore	5	2	11	1	.	.	.	.	.	3	.	.	.	.	.	.	.
142	780360D	3	51	2	Vellore	5	1	8	1	5	1	1	.	.	3	23	.	0	1	1	0	0
143	780106D	1	60	2	Chitoor	34	0	4	0	5	1	1	124	24	1	127	102	1	0	0	0	0
144	781260D	15	38	1	Chitoor	34	0	9	0	10	1	1	124	26	1	70	105	1	0	0	0	0
145	736718D	1	36	1	Chitoor	34	0	8	1	10	1	1	122	52	1	90	99	0	0	0	0	0
146	780220D	1	45	2	Vellore	5	0	2	0	10	1	1	84	26	1	70	102	0	0	1	0	0
147	780233D	5	71	1	Kadapa	248	0	12	0	10	1	1	110	24	1	110	104	0	0	1	0	0
148	777399D	1	65	2	Kadapa	248	0	7	0	10	1	1	124	28	1	93	100	0	1	0	0	0
149	780244D	3	27	1	Dharma	136	0	6	0	7	1	1	84	24	1	80	98	0	0	0	0	1
151	785014D	6	68	2	Nellore	236	2	2	1	.	.	.	.	.	3	.	.	.	.	.	.	.
152	784704D	3	40	2	Chitoor	34	2	1	1	6	1	1	112	24	1	53	100	0	0	0	0	0
153	782009D	15	50	1	Tiruvana	77	0	23	0	7	1	1	120	38	1	73	101	0	0	1	0	0
157	790004D	15	54	1	Krishnag	119	0	10	0	10	1	1	106	34	1	73	98	1	0	1	0	0
158	788255D	9	38	2	Gudiyata	29	0	3	0	5	1	1	80	22	0	23	.	0	0	0	0	0
159	788256D	1	42	1	Vellore	5	0	4	0	10	1	1	122	46	1	93	102	0	0	1	0	0
160	788090D	15	19	2	Kadapa	248	1	11	0	5	2	1	120	48	1	70	98	0	0	0	0	0
161	789204D	1	55	2	Chitoor	34	2	5	1	7	1	1	116	24	1	73	.	0	0	0	0	0
162	789232D	15	42	1	Tiruvallu	91	2	6	1	12	1	1	112	38	1	27	.	0	0	1	0	0
164	669789D	6	64	1	Tirupatu	91	0	6	0	5	1	1	100	22	1	100	101	1	0	0	0	0

AB	AM	PR	JA	DIA	UO	MY	DE	Pal	Ict	Esc	JVP	Cv	Res	Hep	Sp	Sei	Sen	GCS	Ven	pH	Bic	BE	Lac	Hb	TLC
0	0	0	1	0	0	1	0	1	1	0	1	0	1	0	0	0	1	15	1	.	.	.	.	11	12300
0	0	1	1	0	0	0	1	0	1	0	0	0	2	0	0	1	3	11	1	7.3	16	-10	2	11	5500
0	0	0	1	0	0	1	1	0	1	1	0	0	2	1	1	1	1	11	0	.	.	.	.	14	14100
0	0	0	1	0	1	0	0	0	1	1	0	0	1	1	1	0	0	15	0	7.4	17	-6	3	13	10200
0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1	8	1	7.2	7	-18	7	16	26800
0	0	0	0	1	0	1	1	0	0	0	0	0	1	0	0	0	1	15	0	.	.	.	.	13	11200
1	0	1	0	0	1	1	1	0	0	1	0	0	1	0	0	0	0	15	0	.	.	.	.	14	7900
0	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	3	15	0	.	.	.	.	13	10600
0	0	0	0	1	2	0	1	1	0	0	0	0	0	0	0	0	1	13	0	7.4	21	-5	2	4	61200
0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1	15	1	7.4	14	-10	3	12	11200
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	1	.	.	.	.	12	25000
0	0	1	0	0	1	0	1	1	1	1	0	0	2	0	0	0	1	11	0	7.3	16	-11	3	11	6100
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0	0	1	0	0	0	1	1	1	0	0	0	0	3	1	0	0	0	15	0	.	.	.	.	9	14700
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0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	4	1	.	.	.	.	9	28600
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1	0	1	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	15	0	.	.	.	.	9	7200
0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1	0	0	15	1	7.4	21	-5	2	10	8500
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0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	15	0	.	.	.	.	13	1800
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1	0	1	0	0	0	0	1	1	0	0	1	0	1	1	1	0	0	15	1	7.5	22	-1	3	8	12800
0	0	0	0	0	0	1	1	0	0	1	0	0	1	0	0	0	0	15	1	.	.	.	.	15	7600
0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	.	1	.	.	.	.	12	11200
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0	0	1	0	1	1	0	1	0	1	0	0	0	1	0	0	0	0	15	0	7	6	-24	8	14	13800
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0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	0	0	0	15	1	7.2	14	-14	6	12	7100
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0	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	15	1	7.2	12	-19	6	5	13600
0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	4	10	1	7.5	23	-3	2	14	16000
0	0	0	0	0	1	0	1	0	1	0	0	0	1	0	0	0	1	13	1	7.3	14	-15	7	12	9500
0	0	1	1	0	0	0	1	1	1	0	0	0	0	1	1	0	0	15	0	.	.	.	.	10	7800
0	0	1	0	0	0	0	1	0	0	1	0	0	1	0	0	0	0	15	0	7.3	##	-18	11	14	2300
0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	13	0	7.4	21	-5	4	13	11600
0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	15	0	7.2	17	-11	1	12	25500
.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	0	.	.	.	.	10	8100
0	0	1	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	15	1	7.2	15	-13	12	14	19800
0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	15	0	7.5	28	-4	1	12	3900
1	0	1	1	0	1	0	1	0	1	0	0	0	0	1	1	0	0	15	0	7.3	17	-11	3	13	7900
0	1	1	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	15	1	7.5	23	-4	3	12	14700
0	0	1	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	15	0	.	.	.	.	9	7100
0	0	1	1	0	0	1	1	0	1	0	0	0	1	0	0	0	1	13	0	7.3	14	-16	2	11	15600
0	0	0	0	0	2	0	1	0	0	0	0	0	2	0	0	0	0	15	0	.	.	.	.	13	16700
1	0	1	1	0	0	1	1	0	1	0	0	0	0	1	0	0	0	15	0	.	.	.	.	18	22600
.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	.	.	.	.	13	37700
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	1	6.8	.	.	20	12	42700
0	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0	0	1	13	0	7.3	6	-22	7	6	9700
0	0	1	1	0	1	0	0	0	1	0	0	0	1	0	0	0	0	15	0	7.4	19	-9	18	9	7100
0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	15	0	.	.	.	.	9	9200
0	0	1	1	0	1	0	0	0	1	0	0	0	0	1	0	0	0	15	0	7.4	17	-12	3	16	14100
0	0	0	1	0	1	0	1	1	1	0	0	0	0	1	1	0	0	15	1	7.4	19	-9	3	8	6800
1	0	1	1	0	1	0	0	1	1	1	0	0	1	1	0	0	4	6	1	7.2	14	-0	2	8	12300
0	0	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	15	1	7.2	11	-20	9	13	18500
1	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	1	9	0	.	.	.	.	13	8000

Neu	Plat	PT	Crea	Na	K	Bica	TB	DB	TP	Alb	AST	ALT	MF	PI	MF	MF	Wid	Wid	Wid	Wid	Sa	Da
82	64000	11	4.9	127	4.8	12	8.2	6.3	6.2	2.9	100	111	0	.	.	.	0	40	1280	40	1	0
74	70000	12	6.6	131	3.8	15	7.7	6.5	6.1	2.8	71	51	0	.	0	0	0	40	40	0	1	0
65	51000	11	1.1	122	3.9	20	12	9.2	6.7	2.7	172	188	0	.	0	0	0	20	20	40	1	0
72	30000	13	4.9	.	.	.	7.5	5.7	6.2	2.6	127	65	0	.	.	.	20	0	0	0	1	0
76	60000	16	4.6	137	4.7	10	3.7	2.8	6.9	2.8	100	111	0	.	0	.	0	40	0	0	1	1
85	88000	9	0.9	130	3.2	24	0.4	0.2	6.5	3	96	27	0	.	0	0	0	0	20	0	1	0
75	90000	.	1.4	129	3.8	20	0.6	0.3	6.2	3.5	96	154	0	.	0	0	0	0	0	0	1	0
77	60000	.	1.1	135	3.8	20	0.5	0.3	5.1	1.8	84	75	0	.	0	.	.	.	.	.	1	0
58	296000	17	4.4	131	5.9	60	1.5	1.2	4.2	2.4	8500	2600	0	.	0	0	0	20	0	0	0	1
85	60000	12	1.7	.	4.1	14	0.5	0.2	5.3	1.9	224	109	0	.	0	.	.	.	.	.	1	.
85	559000	16	2.3	137	5	16	0.4	0.2	7.6	3.4	48	38	0	.	0	.	0	0	0	0	0	0
72	58000	.	4.4	132	5.3	13	4	2.1	5.5	2.5	72	24	0	.	.	.	.	.	.	.	1	.
81	298000	11	1.1	133	4.4	22	0.4	0.2	8.8	4.4	34	27	0	.	0	.	.	.	.	.	1	.
83	90000	.	0.8	134	3.5	22	0.6	0.2	8.3	3.8	81	64	0	.	.	.	.	.	.	.	1	.
82	107000	13	0.7	139	3.5	19	0.7	0.2	5.9	2.9	95	53	0	.	.	.	.	.	.	.	1	.
79	35000	12	1.4	134	3.1	17	0.5	0.2	6.9	2.8	134	128	0	.	0	0	.	.	.	.	0	.
87	209000	16	2.4	126	4.4	11	0.5	0.2	5.2	2	142	29	0	.	0	.	0	20	0	0	1	1
71	249000	25	2	139	4.6	7	3	2	7.4	4.7	341	203	0	.	0	.	.	.	.	.	0	0
66	33000	.	1.8	132	3	18	0.6	0.3	7.8	3.1	149	77	0	.	0	.	.	.	.	.	1	0
93	16000	.	0.9	.	.	.	0.4	0.2	6.1	2.9	88	62	0	.	0	0	0	0	0	0	1	0
73	62000	15	1	135	3.9	16	1.4	0.7	5.3	2.4	236	101	0	.	.	.	.	.	.	.	1	.
72	12000	13	1.1	129	4	15	0.7	0.2	7.1	2.8	366	179	0	.	0	0	.	.	.	.	1	1
44	75000	.	1.4	125	4	21	0.5	0.3	5.9	3.3	224	61	0	.	0	0	80	1280	20	0	.	.
70	249000	20	5.6	154	2.9	17	0.8	0.2	6.4	3.6	84	37	0	.	.	.	.	.	.	.	0	.
75	28000	12	0.9	136	3.2	17	2.3	2	5.1	2.7	215	117	0	.	0	0	.	.	.	.	1	1
52	6000	13	1	123	6.2	19	6.8	5.7	7.1	2.8	133	277	0	.	0	0	.	.	.	.	1	.
72	180000	.	1	133	3.9	18	0.4	0.2	6.6	3.2	105	66	0	.	.	.	.	.	.	.	1	.
86	7700	13	0.4	126	2.8	.	2.2	1.9	5.1	2.2	2.9	59	0	.	0	.	.	.	.	.	0	1
76	173000	15	1.1	134	3.6	23	2	0.2	7	3.3	140	97	0	.	0	.	.	.	.	.	1	.
82	35000	12	1.5	138	3.9	13	3.1	2.5	6	2.3	220	131	0	.	0	.	.	.	.	.	1	1
85	105000	.	1.5	136	3.7	20	1.3	0.2	7.4	3.5	82	63	0	.	0	.	.	.	.	.	1	.
84	29000	11	2.8	140	4.4	9	5.6	2.4	6.8	2.4	299	89	0	.	.	.	.	.	.	.	1	1
68	45000	14	5.1	143	3.7	10	0.7	0.1	4.8	2	454	167	0	.	0	0	40	320	0	0	0	0
94	102000	.	6.9	135	4.5	10	3	2.2	4.9	2.2	115	71	0	.	0	.	.	.	.	.	1	1
70	110000	.	0.9	132	3.5	27	0.8	0.3	7.6	3.8	58	35	0	.	0	.	0	0	0	0	1	.
60	90000	.	0.9	135	4.3	22	0.4	0.2	7.3	3.8	22	10	0	.	0	0	.	.	.	.	0	0
87	14000	14	1.1	134	4.1	13	0.5	0.2	4.5	1.6	141	41	.	.	.	.	.	.	.	.	1	1
14	63000	11	0.9	140	3.6	28	0.5	0.2	7.3	4.6	277	123	0	.	0	.	0	0	0	0	0	1
50	45000	13	1.9	139	3.9	13	4.9	2.7	7.2	3.3	90	27	0	.	0	0	.	.	.	.	1	.
88	36000	11	1.5	129	3.6	23	0.7	0.2	5.9	3.2	201	49	0	.	0	.	160	640	0	0	0	.
44	114000	18	4.3	134	3	14	4.3	1.6	6.3	3.2	217	113	0	.	0	0	.	.	.	.	0	0
79	66000	29	2.6	138	4.2	13	1.8	1.4	5.5	3	1231	435	0	.	.	.	.	.	.	.	0	0
53	75000	14	9.9	133	4.9	14	4.6	3	6.3	2.8	40	44	1	.	1	1	.	.	.	.	1	.
69	136000	12	1	126	2.9	18	2.2	1.6	6.8	3	362	110	0	.	0	.	.	.	.	.	1	1
71	18000	14	1.3	138	3.7	17	6.5	5.4	5.1	2.5	424	184	0	.	.	.	.	.	.	.	0	1
84	120000	20	2.4	131	3.2	17	3.3	0.3	6.9	3.6	246	187	0	.	0	.	.	.	.	.	0	.
72	125000	26	1	121	2.7	23	0.5	0.1	6.7	4.1	87	46	0	.	.	.	0	0	0	0	0	.
54	75000	32	2.3	141	4.1	11	7.2	5.7	5.3	3.2	348	75	0	.	0	0	0	0	0	0	0	0
54	174000	.	1	137	3.8	21	0.7	0.2	7.8	4.5	481	391	0	.	0	0	160	160	0	0	.	.
77	255000	13	2.4	129	4.2	13	0.5	0.2	8.9	3.8	119	39	0	.	0	.	.	.	.	.	.	0

69	35000	11	6.9	137	5.2	14	4	3.1	7.3	2.9	135	39	0	.	0	0	.	.	.	.	1	0
76	48000	13	1.1	132	2.9	21	1.5	1.2	6.9	3.3	327	169	0	.	0	.	.	.	.	.	1	.
28	10000	10	1.4	132	4.7	22	0.7	0.2	7.2	4	73	18	0	.	.	.	.	.	.	.	0	0
14	43000	11	1.3	140	4.3	18	1.6	0.6	7.7	3.7	80	18	0	.	.	.	.	.	.	.	0	1
58	6000	12	0.7	137	4.6	21	0.7	0.2	5.6	2.5	44	12	1	.	1	.	.	.	.	.	.	.
55	52000	20	2.7	143	4.3	15	3.1	2.7	5.7	3	72	25	0	.	.	.	0	0	0	0	0	0
69	167000	.	1.4	127	3.7	20	0.5	0.2	6.8	3.7	66	75	0	.	.	.	.	.	.	.	.	.
77	97000	.	1	124	3.6	19	3.6	3	7.2	3.6	103	107	0	.	0	0	0	0	0	0	1	.
49	59000	.	.	.	.	.	0.5	0.2	6.1	3.1	24	12	1	.	1	1	0	0	0	0	.	.
91	15000	11	3	127	5.6	12	1.1	0.2	6.7	2.2	71	66	1	.	1	.	0	80	0	0	.	.
33	61000	.	1	133	4.1	19	0.5	0.3	7.7	4.1	474	209	0	.	.	.	.	.	.	.	0	1
74	22000	.	2.1	136	3.7	16	3.8	2.7	7	3.6	168	159	0	.	.	.	.	.	.	.	1	.
95	200000	.	1.3	132	4.7	20	1	0.1	8.2	3.5	41	42	0	.	0	0	0	40	20	0	1	1
77	24000	17	1.3	134	4.2	14	0.7	0.2	6.6	2.1	122	147	0	.	0	0	.	.	.	.	1	1
79	24000	12	7.5	129	4.6	17	29	27	6.3	3.2	140	83	1	.	1	.	.	.	.	.	.	0
64	19000	14	3.4	128	4	19	23	21	5.9	2.4	54	13	1	1	1	1	.	.	.	.	.	.
58	21000	13	1.5	131	5.2	18	1.3	0.4	5	2.3	78	30	1	2	1	.	.	.	.	.	.	.
60	31000	.	1.1	.	.	.	0.5	0.2	6	3.3	83	59	1	.	1	1	.	.	.	.	.	.
98	9000	.	1.3	134	3.3	21	16	0.2	5.2	2.4	68	24	1	3	1	1	.	.	.	.	.	.
70	7000	.	1.2	137	4.7	22	2.9	1.6	5.7	2.8	108	58	1	1	1	1	.	.	.	.	.	.
69	16000	.	0.7	134	3.2	22	18	15	6.1	2.9	39	13	1	.	.	.	.	.	.	.	.	.
79	8000	.	1	138	5.1	10	2.3	1.3	6	3.3	42	71	1	2	1	1	.	.	.	.	0	.
65	200000	.	1.3	127	4.9	10	.	.	.	.	.	.	0	.	.	.	0	0	0	0	0	0
86	102000	.	5.3	120	4.9	13	2	0.9	7.7	2.8	209	102	0	.	0	.	.	.	.	.	1	.
55	157000	.	0.9	126	3.5	22	0.4	0.2	6.3	1.9	71	37	0	.	0	0	20	0	20	0	1	1
71	50000	16	0.7	132	5.6	20	0.8	0.2	8.6	3.8	27	37	0	.	.	.	.	.	.	.	1	1
81	49000	.	1.5	130	4.1	23	0.5	0.2	7.7	3.7	139	252	0	.	.	.	.	.	.	.	1	.
79	260000	15	12	132	3	11	0.2	0.1	6.9	3.7	24	7	.	.	.	.	.	.	.	.	0	0
81	81000	.	0.9	139	3.9	20	0.4	0.2	7.1	3.4	85	28	.	.	.	.	.	.	.	.	.	.
87	157000	16	15	133	3	5	0.4	0.3	5.9	3.3	59	7	0	.	.	.	0	0	0	0	0	1
54	193000	13	1.1	135	4.8	28	0.2	0.1	7.6	3.3	70	.	0	.	0	.	0	20	320	40	.	1
70	144000	.	1	133	3.5	21	0.6	0.4	7.9	4.3	132	129	0	.	0	0	0	0	0	0	.	.
59	160000	.	0.8	131	3.6	25	0.4	0.4	6.7	2.8	37	28	0	.	0	.	20	0	0	0	1	.
73	27000	13	0.9	134	3.7	18	1.2	0.5	6.1	2.9	148	104	0	.	0	0	.	.	.	.	1	0
94	152000	.	1.2	125	3.4	.	1.2	0	7.4	3.4	75	71	0	.	.	.	.	.	.	.	1	.
93	17000	15	1.1	139	3.8	16	0.4	0.2	5	2.1	74	27	0	.	.	.	.	.	.	.	1	.
45	15000	.	1.3	137	4	17	1.1	0.9	5.6	2.3	75	39	1	2	.	.	.	.	.	.	.	.
90	200000	.	1	131	3.2	.	3.2	1	5.6	2.3	36	20	1	.	1	1	.	.	.	.	0	.
72	30000	12	2.9	130	4.2	11	5.7	3.9	4.7	1.7	221	87	0	.	0	.	.	.	.	.	1	.
87	66000	16	6.9	133	4.7	11	1.9	0.2	6.9	3	208	114	0	.	0	0	.	.	.	.	1	1
90	13000	14	7.6	128	4.1	7	5.8	5.1	7.9	2.2	205	30	0	.	0	.	.	.	.	.	1	0
93	164000	14	6	133	8.5	7	25	20	5.3	2.4	124	122	0	.	0	0	320	#####	2560	640	0	0
84	27000	13	4.9	118	5.3	14	31	30	4.9	2.4	194	44	1	1	1	.	.	.	.	.	.	.
82	151000	18	2.2	132	4.9	12	0.9	0.2	4.5	1.6	237	94	0	.	0	.	0	0	0	0	1	.
89	119000	.	4.7	129	3.8	17	0.8	0.2	6.6	2.9	60	51	0	.	.	.	.	.	.	.	1	.
47	91000	.	1.8	131	3.9	18	4.3	3.6	7.4	3	98	102	0	.	0	.	.	.	.	.	.	.
81	9000	.	1.3	132	4.2	20	0.1	0	6.2	2.2	218	34	0	.	0	0	0	0	0	0	1	.
39	36000	13	0.9	136	3.8	25	0.4	0.2	6.1	3.4	183	137	0	.	0	0	.	.	.	.	0	1
76	19000	.	1.2	.	.	.	0.5	0.1	7.1	3.3	21	11	0	.	0	0	40	0	0	0	0	.
77	73000	.	1.7	132	3.9	22	2.4	0.4	6.8	3.8	40	27	1	.	1	0	.	.	.	.	.	.
60	600000	18	2.8	130	4.4	10	0.4	0.2	5.8	2.2	235	29	0	.	0	.	.	.	.	.	1	0

85	61000	15	7.2	134	5.3	6	5.3	3.1	6.2	2.7	141	54	0	.	0	.	.	.	.	.	0	0
90	77000	.	5.6	130	4.3	16	0.5	0.1	6.2	2.4	123	53	0	.	.	.	0	10	80	0	1	0
80	22000	.	3.1	131	3.7	11	2.6	0.3	7.6	3	185	43	0	.	0	.	.	.	.	.	1	.
92	146000	11	4.7	129	4.4	14	0.5	0.2	6.4	3.3	49	11	0	.	0	.	.	.	.	.	1	.
77	91000	14	0.7	130	4.2	14	2.3	0.8	5.9	1.9	140	53	1	.	1	1	.	.	.	.	.	.
70	15000	17	8.6	135	4.1	14	26	18	6.1	2	95	26	1	.	1	1	.	.	.	.	.	.
91	60000	17	2	132	3.7	12	1.1	0.2	4	1.8	159	57	0	.	.	.	.	.	.	.	0	0
77	64000	13	1.2	132	4.3	2.8	2.1	2.1	6.4	2.6	132	97	0	.	0	.	0	0	0	0	1	.
79	94000	14	2.5	138	3.8	14	0.5	0.2	6.1	2.5	86	39	0	.	0	.	.	.	.	.	1	.
34	18000	14	4	125	4.6	8	1.8	1.3	5	2.4	355	177	1	.	1	1	.	.	.	.	0	.
82	115000	13	1.9	133	2.8	21	0.7	0.3	6	2	251	75	0	.	0	.	.	.	.	.	1	0
84	60000	14	3	125	3.8	9	2.1	0.2	5.1	2.2	60	14	0	.	0	.	.	.	.	.	0	0
61	8000	11	1.3	136	4.9	17	28	28	5.1	2.7	51	22	1	.	1	1	.	.	.	.	.	1
53	237000	16	1.4	136	3.8	14	0.6	0.2	7.7	4	103	19	0	.	0	.	.	.	.	.	0	.
62	117000	.	1.5	121	4.2	18	0.4	0.2	8.3	3.6	198	180	.	.	.	.	.	.	.	.	1	1
78	44800	12	1.6	112	4.5	17	0.4	0.2	5.3	3.7	15	11	.	.	.	.	.	.	.	.	0	0
83	91000	13	1.1	118	3.3	.	1.2	0.7	5.3	3.3	298	90	0	.	0	.	.	.	.	.	0	1
90	21000	33	3.6	133	4.6	22	1.5	0.6	7.1	2.3	20	36	0	.	0	0	.	.	.	.	0	1
74	41000	11	0.9	124	3.2	27	1.1	0.9	7.4	3	140	120	0	.	0	.	.	.	.	.	0	0
65	15000	.	2.9	135	4.5	16	7.4	3.5	6	2.7	134	61	1	.	1	1	0	20	0	0	.	.
58	9000	13	1.1	138	3.6	19	0.4	0.2	7.4	3.3	120	74	0	.	0	.	.	.	.	.	1	1
89	49000	.	1	124	3.4	20	0.5	0.2	7.7	2.8	109	33	0	.	0	.	.	.	.	.	1	.
88	163000	17	6.3	127	5.7	10	6.2	3.2	6.6	2.4	68	24	0	.	0	0	0	40	0	0	0	0
94	14000	12	1.4	137	5.1	13	0.8	0.4	5.4	1.4	101	20	0	.	.	.	.	.	.	.	1	0
63	31000	15	1.1	138	4.5	16	7	4	7.8	4.1	2008	1039	0	.	0	0	.	.	.	.	0	0
95	2E+06	29	1.5	125	5.2	13	0.5	0.2	5.7	2.4	479	116	0	.	0	.	.	.	.	.	0	0
55	36000	14	2.1	140	4.8	10	2.1	0.8	6.3	2.9	1583	592	0	.	.	.	.	.	.	.	0	1
57	69000	12	4.7	133	5.8	10	18	13	6	2.4	127	31	1	.	1	1	.	.	.	.	.	.
67	11000	9.5	1.2	128	5.5	22	10	9.5	5.6	2	39	20	1	.	1	1	.	.	.	.	.	.
58	16000	11	0.8	138	3.4	18	0.5	0.1	5.3	2.8	61	40	0	.	0	.	.	.	.	.	0	0
94	61000	11	2.2	128	3.8	12	6.5	5.5	6.5	2.6	298	111	0	.	0	0	.	.	.	.	1	0
91	13000	15	1	137	3.8	14	13	13	5.3	2.1	44	19	1	.	1	1	.	.	.	.	.	.
72	90000	28	2.8	146	5	11	8.9	7.4	5.2	1.9	225	73	0	.	0	.	.	.	.	.	1	.
64	20000	16	4.9	121	5.7	7	18	12	7.2	3.5	113	61	1	1	1	1	.	.	.	.	.	.
77	112000	.	1.8	140	4.4	18	1.1	3	5.9	2.7	23	28	0	.	0	0	.	.	.	.	0	.

Aa	Lep	SL	UC	UB	UB	USpg	Up	UN	Ule	URE	UW	Ca	Gr	BC	UC	Dur	UCr	UNa	UK	UCl	UPL	DBU	DCr	Buc	DCy	DNa
0	0	.	0	1	3	1.02	5	0	0	0	2	0	0	0	.	0	.	.	.	.	.	.	4.9	.	5.1	.
0	0	.	1	1	3	1.01	6	0	0	2	6	0	0	0	0	0	48	88	18	58	1.8	88	4.8	18	3	132
0	.	.	.	.	.	.	.	.	.	4	0	0	0	0	0	0	83	93	29	77	0.3	46	1	46	2.4	124
0	0	.	1	2	3	1.03	5	0	0	99	0	0	0	0	.	0	86	52	31	39	0.9	256	6.8	37	13	133
0	0	.	0	1	3	1.02	5	0	0	99	6	2	1	0	0	0	152	16	44	21	0.3	.	.	.	.	.
0	0	.	.	.	.	.	.	.	.	6	8	5	1	0	.	0	.	.	.	.	.	6	0.7	8.6	1.1	137
0	0	.	.	.	.	.	.	.	.	6	8	5	1	0	0	.	63	50	9	44	0.5	19	1.2	16	1.5	137
0	0	0	.	.	.	.	.	.	.	10	12	5	1	0	0	.	49	75	19	72	0.6	62	1.2	52	2.1	134
1	0	0	0	1	3	1.01	6	0	0	20	0	0	0	0	.	0	40	95	37	94	4.5	.	6.7	.	5.8	138
.	.	.	.	.	.	.	.	.	.	4	35	5	1	0	0	0	80	3	39	18	1.3	97	1.6	61	2.5	132
0	0	.	.	.	.	.	.	.	.	40	6	.	0	0	.	.	80	85	28	82	0.1	.	1.7	.	2.8	130
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	.	24	104	12	105	0.6	147	2.2	67	3.5	147
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	.	60	153	21	159	0.4	43	1	43	1	136
.	0	0	.	.	.	.	.	.	.	12	6	0	0	0	.	0	57	196	21	166	0.6	20	0.6	33	1.4	137
.	.	0	.	.	.	.	.	.	.	6	5	5	1	0	0	.	63	38	34	84	0.6	45	0.9	50	1.9	141
.	0	.	.	.	.	.	.	.	.	12	3	2	1	0	.	.	64	106	40	74	0.8	.	.	.	.	.
0	.	.	0	0	0	1.02	5	0	0	10	6	5	1	0	0	0	74	32	45	40	2.1	137	3	46	4.1	128
0	0	.	.	.	.	.	.	.	.	12	2	0	0	0	.	0	.	.	.	.	.	47	2.6	18	3.6	124
0	0	0	.	.	.	.	.	.	.	6	2	0	0	0	.	.	19	102	13	118	1.1	38	1.1	35	1.8	127
0	.	.	.	.	.	.	.	.	.	2	8	1	1	0	.	.	20	142	13	143	0.8	18	0.9	20	2.2	120
.	.	.	.	.	.	.	.	.	.	3	5	5	1	0	.	.	47	34	17	46	0.9	32	0.9	36	1.3	178
0	.	0	.	.	.	.	.	.	.	6	4	5	1	0	.	.	20	76	8	76	0.1	.	0.9	.	1.4	138
.	.	.	.	.	.	.	.	.	.	0	2	0	0	1	.	.	178	21	30	27	1.3	54	1.4	39	1.8	131
.	0	0	0	0	2	1.01	6	0	0	4	2	0	0	0	.	0	104	97	23	77	0.5	75	4.6	16	5.9	136
1	0	0	.	.	.	.	.	.	.	2	5	5	1	0	.	.	39	99	13	94	5.7	116	2.4	48	2.7	140
.	.	0	.	.	.	.	.	.	.	.	.	.	0	0	.	0	33	138	21	147	0.2	30	0.7	43	2.1	121
.	.	.	.	.	.	.	.	.	.	4	4	5	1	0	.	.	.	.	.	.	.	28	0.9	31	1.3	134
0	0	.	0	0	3	1.01	7	0	0	25	4	1	1	0	0	0	95	3	26	67	5.3	31	0.6	52	1.5	141
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	0	113	138	11	160	0.9	29	1.1	26	1.1	136
0	0	0	0	0	1	1.01	6	0	0	0	4	5	1	0	.	0	.	.	.	.	.	202	4.1	49	7	149
.	.	.	.	.	.	.	.	.	.	8	15	5	1	0	0	.	149	117	35	157	0.8	42	0.9	47	1.5	144
1	0	0	.	.	.	.	.	.	.	.	.	.	0	0	.	.	38	110	33	124	0.6	80	1.1	73	2	140
0	0	.	.	.	.	.	.	.	.	99	15	2	1	1	0	0	115	30	30	26	3.2	.	.	.	.	.
0	0	0	.	.	.	.	.	.	.	8	4	2	1	0	.	.	38	107	18	94	1.2	230	6.4	36	6.7	108
.	.	.	0	1	1	1.01	7	0	0	6	2	1	1	0	0	.	49	190	16	213	0	9	0.8	11	1	136
0	0	0	0	0	0	1.03	6	1	0	3	4	2	1	0	.	.	101	22	23	38	0.2	29	0.8	36	1.4	122
1	0	0	.	.	.	.	.	.	.	.	.	.	0	0	0	.	95	60	23	68	0.1	.	.	.	.	.
1	0	.	0	0	0	1.01	6	0	0	.	.	.	0	0	.	.	96	69	42	56	0.7	97	2.2	43	3	130
.	0	.	.	.	.	.	.	.	.	2	6	5	1	0	0	.	90	8	42	16	0.7	124	1.8	69	2.5	120
.	.	.	.	.	.	.	.	.	.	2	2	0	0	1	.	0	101	88	18	79	0.6	43	1.7	25	1.6	128
0	0	0	0	0	3	1.01	6	1	0	12	4	0	0	0	0	0	80	42	48	58	0.6	.	6.7	.	.	134
0	0	0	.	.	.	.	.	.	.	6	10	5	1	0	.	0	32	143	12	110	8.4	.	4.2	.	3	188
.	0	.	0	1	2	1.02	6	0	0	12	2	0	0	0	.	0	38	73	8	62	0.7	204	11	18	3.5	127
0	0	0	0	1	1	1.01	6	0	0	5	10	0	0	0	0	0	55	161	28	190	0.8	24	0.7	34	1.7	136
0	0	.	0	0	1	1.01	7	0	0	99	99	0	0	0	1	0	28	2	13	17	0.3	85	1.3	67	2.4	145
.	0	0	2	0	3	1.01	6	0	0	12	4	5	1	0	0	.	8	97	9	74	13	111	3.6	31	2.3	144
.	0	0	0	0	0	1.02	7	0	0	12	4	0	0	0	0	0	24	78	8	54	4.1	42	2.2	19	1.4	130
0	0	.	.	.	.	.	.	.	.	.	.	.	0	0	.	0	13	106	8	81	1.6	.	1.7	.	1.3	117
.	.	0	.	.	.	.	.	.	.	4	8	0	0	1	0	.	185	97	28	94	0	13	1	13	1	113
0	.	.	.	.	.	.	.	.	.	5	6	5	1	0	.	.	22	90	13	85	1.7	65	2.3	28	1.9	128

0	0	0	.	.	.	.	.	.	.	2	4	0	0	0	0	.	46	50	57	48	2.1	291	7	42	6.2	148
.	.	.	0	0	1	1.01	6	0	0	2	0	0	0	0	0	0	70	61	34	59	1.2	.	1.2	.	1.7	134
1	.	0	.	.	.	.	.	.	.	0	5	0	0	0	.	0	35	56	3	42	0	16	1.2	13	1.3	135
0	.	0	0	0	2	1.01	6	0	0	20	5	5	1	0	.	0	37	97	15	94	0.1	25	1.6	16	1.6	142
.	.	.	.	.	.	.	.	.	.	2	2	0	0	.	.	0	63	178	28	217	0	13	0.7	19	0.9	136
0	0	0	0	1	2	1.02	6	0	0	6	0	0	0	0	.	.	43	114	31	113	0.4	.	.	.	.	.
.	.	0	.	.	.	.	.	.	.	0	2	0	0	1	.	.	173	22	39	30	0.5	37	1.5	25	1.8	128
.	.	.	0	1	1	1.01	6	0	0	2	2	0	0	0	.	0	77	33	14	48	0.6	20	0.8	25	1.4	132
.	.	.	0	0	1	1.01	6	3	0	.	.	.	0	0	.	.	39	75	6	70	0.1	16	1.1	15	2	138
.	.	.	.	.	.	.	.	.	.	5	5	5	1	0	.	.	39	140	12	159	0.5	69	1.3	53	1.6	133
0	.	0	.	.	.	.	.	.	.	.	.	.	0	.	.	0	162	30	24	38	0.1	26	0.9	29	1.1	139
.	.	.	0	1	2	1.01	6	0	0	10	6	0	0	0	.	.	62	73	11	60	0.5	.	2	.	1.8	138
0	0	0	.	.	.	.	.	.	.	4	4	0	0	1	.	.	39	59	8	52	0.1	22	1.1	20	1.6	131
0	.	.	0	0	2	1.01	6	1	1	6	4	5	1	0	.	0	105	11	36	30	0.8	84	1.1	76	2.7	135
1	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	0	43	99	12	73	1.6	321	8.7	37	5.5	129
.	.	.	0	2	3	1.01	6	0	0	99	6	0	0	0	.	.	54	74	12	66	0.7	.	1.8	.	1.5	.
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	0	79	135	40	159	0	.	0.8	.	1.1	.
.	.	.	0	1	1	1.01	9	0	0	6	0	0	0	0	.	.	103	129	18	118	0.5	.	1.4	.	1.2	.
.	.	.	.	.	.	.	.	.	.	0	1	0	0	0	.	0	24	182	8	203	0.2	21	1	21	1	134
.	.	.	.	.	.	.	.	.	.	4	20	5	1	0	.	.	34	185	23	206	1.1	.	1	.	0.9	.
.	.	.	.	.	.	.	.	.	.	8	4	5	1	0	.	.	57	103	19	141	0.4	.	0.7	.	1.3	.
.	0	.	.	.	.	.	.	.	.	6	2	0	0	0	.	0	27	111	17	104	1.2	62	0.9	69	1.2	137
0	0	0	2	0	1	1.01	6	0	0	20	2	0	0	0	1	.	59	139	6	97	1.3	.	.	.	.	136
.	.	.	0	1	2	1.01	7	0	0	12	0	2	1	0	.	.	177	34	37	21	0.3	.	3.1	.	4.1	.
0	0	0	.	.	.	.	.	.	.	0	4	0	0	0	.	.	63	100	12	52	0.3	23	0.8	29	2.1	125
1	1	.	.	.	.	.	.	.	.	6	4	0	0	0	.	.	125	29	24	41	0.5	.	1	.	2.2	.
.	.	.	.	.	.	.	.	.	.	3	8	0	0	0	1	.	163	152	24	151	0	21	1	21	1.4	137
0	0	0	0	0	3	1.01	6	0	0	25	3	0	0	0	1	0	37	73	8	71	1.4	242	8.9	27	3.4	126
.	.	.	.	.	.	.	.	.	.	.	.	.	0	1	.	0	.	.	.	.	.	34	0.8	43	1	139
1	0	.	0	0	3	1.01	6	0	0	6	3	2	1	0	.	0	28	127	6	118	1.1	358	17	21	5.6	138
0	0	.	.	.	.	.	.	.	.	0	0	0	0	0	.	0	46	106	18	76	0	40	1.1	36	1.9	133
.	.	.	.	.	.	.	.	.	.	6	12	0	0	1	1	.	37	47	9	45	0.4	18	1.4	13	1.3	129
.	.	.	.	.	.	.	.	.	.	40	4	0	0	0	.	.	91	243	8	223	0.1	14	0.9	16	1.4	126
0	0	0	0	2	2	1.02	6	0	0	10	2	1	1	0	.	.	171	22	##	157	1	54	0.8	68	1.5	134
.	.	.	.	.	.	.	.	.	.	2	0	0	0	0	.	.	151	55	48	80	1	25	1	25	1.6	127
.	0	.	.	.	.	.	.	.	.	35	35	0	0	0	1	.	24	120	10	127	0.9	23	0.8	29	1.5	134
.	.	.	.	.	.	.	.	.	.	2	6	0	0	0	.	.	95	171	15	169	0.4	34	1.4	24	1.5	125
.	0	.	0	1	1	1.02	6	0	0	3	0	1	1	0	.	.	106	88	81	101	0.3	32	0.7	46	1	127
.	0	.	0	1	3	1.01	6	0	0	50	10	1	1	0	.	.	58	199	24	213	2.2	.	1.2	.	2	144
1	0	0	.	.	.	.	.	.	.	.	.	.	0	0	0	0	137	61	47	23	1.7	185	7.9	23	4.6	136
0	0	.	.	.	.	.	.	.	.	12	0	0	0	0	0	.	123	68	24	28	0.7	.	6.6	.	7.4	132
0	0	.	0	2	2	1.01	6	0	0	10	6	0	0	1	.	0	46	60	15	54	1	102	4	26	3.9	121
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	0	52	23	37	28	0.8	166	2.9	57	0.9	123
.	.	.	.	.	.	.	.	.	.	3	3	0	0	0	.	0	72	86	17	58	0.6	85	1.6	53	2.6	150
.	0	.	1	1	2	1.01	6	0	0	12	8	0	0	0	0	.	82	38	11	26	0.5	91	2.1	43	3.3	131
.	.	.	0	3	1	1.03	6	0	0	3	0	0	0	0	.	.	165	151	28	200	0.6	39	1.4	28	2	136
.	.	.	0	0	2	1.01	6	0	0	12	2	0	0	0	.	.	42	166	39	196	0.4	53	0.9	59	1.6	141
1	0	0	.	.	.	.	.	.	.	0	0	0	0	0	.	0	63	129	20	161	0.1	23	0.9	26	0.8	138
.	0	0	0	0	2	1.01	6	0	0	12	0	0	0	0	.	0	53	45	11	49	0.2	27	1.2	23	1.4	136
.	.	.	.	.	.	.	.	.	.	20	99	0	0	0	0	.	63	143	15	148	0.3	28	1.2	23	1.2	137
0	0	0	.	.	.	.	.	.	.	4	10	0	0	0	0	0	82	18	27	19	1.2	144	4.7	31	4.7	145

0	0	0	0	1	2	1.01	6	0	0	10	4	0	0	0	.	0	41	111	24	93	2	156	8.1	19	16	132
0	.	0	0	0	0	1.01	6	0	0	12	12	0	0	0	.	.	52	102	19	102	0.7	68	2.4	28	2.2	140
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	.	76	16	35	14	1.4	114	1.6	71	3.5	152
.	.	.	0	0	3	1.01	6	0	0	20	4	0	0	0	.	0	42	79	24	87	1.9	104	6	17	5.3	123
.	.	.	0	0	2	1.01	6	0	0	8	6	0	0	0	.	0	29	79	26	65	2.8	122	3.2	38	1.2	132
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	.	38	116	12	99	4.2	.	10	.	4	142
1	0	0	.	.	.	1.01	7	.	.	35	20	1	1	0	.	.	5	46	4	40	1.2	.	.	.	.	.
.	.	.	0	0	2	1.01	6	0	0	8	8	2	1	0	.	.	36	193	26	217	2.2	30	0.8	38	1.7	133
.	.	.	.	.	.	.	.	.	.	15	50	1	1	0	.	.	43	117	14	53	0.2	19	0.6	32	1.5	136
.	0	.	0	0	3	1.01	6	0	0	10	2	0	0	0	.	0	30	89	27	71	3.4	198	6.6	30	6.2	136
0	0	0	0	0	3	1.01	6	0	0	2	4	0	0	0	1	0	.	.	.	.	.	67	2.2	30	3.3	130
0	0	.	.	.	.	.	.	.	.	28	8	2	1	0	.	0	31	97	32	98	3.3	.	5.3	.	5.4	140
0	.	0	.	.	.	.	.	.	.	2	3	2	1	.	.	0	80	37	32	36	0.9	79	1.3	61	2.3	130
.	.	.	0	0	0	1.02	6	0	0	0	0	0	0	0	.	0	28	107	9	119	0.6	15	0.8	19	1.1	139
0	0	0	1	0	2	1.02	6	0	2	.	.	.	0	0	.	.	68	177	28	196	1	34	1.1	31	1.1	126
0	0	.	.	.	.	.	.	.	.	0	0	1	1	0	.	0	69	41	40	37	2.2	46	3	15	2.4	142
0	0	0	0	0	3	1.01	6	0	0	20	3	0	0	0	.	0	.	.	.	.	.	.	1.4	.	.	148
0	0	0	0	0	3	1.01	6	0	0	99	0	0	0	0	.	0	22	130	16	135	5.2	101	4.4	23	4.9	140
0	0	0	.	.	.	.	.	.	.	12	2	2	1	0	.	.	17	40	9	43	5.7	24	0.9	27	1.7	111
.	.	.	.	.	.	.	.	.	.	30	4	0	0	0	.	.	.	.	.	.	.	68	1.5	45	1.6	123
1	.	.	.	.	.	.	.	.	.	3	10	5	1	0	.	.	102	8	24	17	4	54	0.8	68	1.4	131
.	.	.	.	.	.	.	.	.	.	.	.	.	0	0	.	.	41	179	20	222	1.2	18	0.8	23	1.9	112
0	1	0	.	.	.	.	.	.	.	6	4	0	0	0	0	0	34	71	25	65	1	368	6.1	60	4.2	119
0	0	0	0	0	2	1.01	6	0	0	12	0	0	0	0	.	.	18	78	14	78	0.5	37	0.8	46	1.7	115
1	0	0	.	.	.	.	.	.	.	2	2	0	0	0	.	0	71	104	17	125	0.4	96	1	96	1.3	118
0	0	0	.	.	.	.	.	.	.	6	2	0	0	0	.	.	.	.	.	.	.	70	1.1	61	1.5	137
1	0	0	.	.	.	.	.	.	.	8	12	0	0	0	.	0	.	.	.	.	.	45	2.5	18	2.1	147
.	.	.	1	0	2	1.01	7	0	0	6	4	0	0	0	.	0	59	69	22	38	2.5	189	5.3	36	6.2	135
.	.	.	.	.	.	.	.	.	.	0	4	0	0	0	.	0	59	50	25	45	1.1	78	0.3	260	1.9	132
1	0	0	.	.	.	.	.	.	.	0	4	0	0	0	.	0	.	.	.	.	.	12	0.7	17	0.9	139
0	0	0	.	.	.	.	.	.	.	4	8	5	1	0	.	0	38	33	5	31	0.6	64	0.6	107	2.8	130
.	.	.	0	3	0	1.01	6	0	0	4	99	0	0	0	.	0	52	136	11	98	0.5	35	0.6	58	1.3	134
.	.	.	0	1	3	1.01	5	0	0	4	12	0	0	.	.	0	59	96	22	111	1.6	168	3.5	48	4.6	146
.	.	.	0	1	3	1.01	5	0	0	10	4	5	1	0	.	0	.	.	.	.	.	.	.	.	.	.
.	.	.	2	0	2	1.02	6	0	0	6	2	0	0	0	.	.	.	.	.	.	.	.	.	.	.	.

DCl	RFl	FEN	CXl	AB1	AB2	AB3	Ion	Diur	Tx	Cr(	cr1	cr2	cr3	cr4	cr5	cr6	cr7	cr14	cr21	cr28	Hd
.	.	.	2	Doxic	Ceftri	.	Yes	Furos	Yes	5	.	.	8.6	8.5	.	.	.	.	.	.	Yes
91	8.8	6.7	4	Doxic	Azithr	Pipra	Yes	No	No	7	3.3	4.5	4.2	4.9	4	3.2	2.8	1.9	.	.	Yes
97	1.1	0.9	0	Doxic	Azithr	Ceftri	No	No	No	1	.	0.8	.	0.8	.	.	.	.	.	.	No
103	4.1	3.1	4	Doxic	Azithr	Mero	Yes	No	Yes	5	5.2	6.7	3.7	3.6	3	4.1	4	.	.	.	Yes
.	.	.	2	Azithr	Mero	.	Yes	Furos	No	5	3.9	.	.	.	.	.	.	.	.	.	Yes
104	.	.	0	Doxic	Ceftri	.	No	No	No	1	.	0.7	.	.	.	.	.	.	.	.	No
105	1	0.7	0	Doxic	Azithr	Ceftri	No	No	No	1	1.3	1.1	.	.	.	.	.	.	.	.	No
107	1.8	1.4	0	Doxic	Ceftri	.	No	No	No	.	1.1	.	.	.	.	.	.	.	.	.	No
104	.	.	0	Doxic	Mero	.	No	Furos	Yes	4	.	6.1	.	6.7	.	.	11	3.1	.	.	Yes
109	0.1	0.1	2	Doxic	Azithr	Pipra	Yes	No	No	2	.	1.1	1	.	.	.	.	.	.	.	No
104	.	.	0	Doxic	Azithr	Pipra	No	No	No	2	2.1	2.7	1.8	.	1	.	.	.	.	.	No
117	9.5	6.5	4	Doxic	Azithr	.	No	No	No	4	3.8	2.5	.	.	.	.	.	.	.	.	No
102	2.6	1.9	0	Doxic	Ceftri	.	No	No	No	1	.	1	.	.	.	.	.	.	.	.	No
96	2.1	1.5	4	Doxic	Azithr	Pipra	No	Furos	No	1	.	.	.	.	.	0.6	.	.	.	.	No
110	0.5	0.4	2	Doxic	Azithr	Pipra	Yes	Furos	No	1	0.7	0.7	0.8	0.6	.	0.6	.	.	.	.	No
.	.	.	0	Doxic	Ceftri	.	Yes	No	No	1	0.6	0.6	0.6	.	.	.	.	.	.	.	No
97	1.3	1	4	Cifran	Clox	.	Yes	No	No	2	1.9	2.6	2.5	2.6	.	1.7	1.5	.	.	.	No
86	.	.	3	Doxic	Mero	.	Yes	No	No	2	.	1.9	.	.	.	.	.	.	.	.	Yes
104	5.9	4.7	5	Doxic	.	.	No	No	No	2	1.1	1	.	.	.	.	.	.	.	.	No
97	6.4	5.3	0	Doxic	.	.	No	No	No	1	.	.	.	.	1	.	.	.	.	.	No
114	0.7	0.4	0	Doxic	Azithr	.	Yes	No	No	1	0.8	0.7	0.8	0.7	.	.	.	.	.	.	No
110	3.4	2.5	5	Doxic	Pipra	.	No	Furos	No	1	.	.	.	0.7	.	.	.	.	.	.	No
99	0.2	0.1	0	Gatifl	.	.	No	No	No	1	.	.	0.8	.	.	.	.	.	.	.	No
100	4.3	3.2	2	Doxic	Cefap	.	No	Furos	No	6	.	7.7	6.3	5.4	5	.	.	9.2	.	.	Yes
108	6.1	4.4	2	Doxic	Azithr	Mero	Yes	No	No	1	.	2.3	2.2	2.3	.	.	.	.	.	.	No
98	2.9	2.4	0	Doxic	Azithr	.	No	No	No	1	.	0.7	.	.	.	.	.	.	.	.	No
107	.	.	5	Doxic	Gatifl	.	No	No	No	1	.	0.9	.	.	.	.	.	.	.	.	No
109	0	0	2	Doxic	Azithr	Mero	Yes	Furos	Yes	0	.	0.6	0.6	0.5	1	0.4	0.4	.	.	.	No
107	1.3	1	4	Doxic	Azithr	.	Yes	No	No	1	1.1	1.1	0.9	0.8	1	.	.	.	.	.	No
116	.	.	4	Doxic	Azithr	Pipra	Yes	No	Yes	2	3.7	2.8	.	.	.	.	.	.	.	.	Yes
106	0.7	0.5	4	Doxic	Azithr	Pipra	No	Furos	No	2	1.2	1	0.8	0.8	.	.	.	.	.	.	No
105	3.2	2.3	4	Doxic	Azithr	Pipra	No	No	No	3	2.5	2.5	1.8	1.3	.	.	.	.	.	.	No
.	.	.	4	Doxic	Azithr	Mero	Yes	No	Yes	5	.	5	4.7	5	5	6	2.1	.	.	.	Yes
92	18	17	4	Doxic	Mero	.	Yes	No	No	7	6.6	5.1	.	.	.	.	.	.	.	.	No
102	3.1	2.3	5	Doxic	Ceftri	.	No	No	No	1	.	.	0.8	.	.	.	.	.	.	.	No
83	0.2	0.1	5	None	.	.	No	Furos	No	1	.	.	.	0.8	.	.	.	.	.	.	No
.	.	.	4	Doxic	Azithr	Mero	No	No	No	1	1.6	1.6	1	0.8	1	.	.	.	.	.	No
107	1.6	1.2	0	Doxic	Ceftri	.	No	No	No	1	2.2	.	.	.	.	.	.	.	.	.	No
106	0.2	0.1	5	Doxic	Azithr	Pipra	No	No	No	2	2.5	2.5	2.5	1.7	1	.	.	.	.	.	No
105	1.5	1.2	5	Doxic	Ceftri	.	No	No	No	2	.	1.5	1.2	.	.	0.9	.	.	.	.	No
100	3.5	2.6	5	Doxic	Pipra	Mero	Yes	Furos	Yes	4	.	5	5.9	6.9	7	7.9	8.9	.	.	.	No
108	19	10	5	Doxic	Azithr	Pipra	Yes	No	Yes	5	.	.	.	.	.	.	.	.	.	.	No
107	21	17	0	Doxic	Artes	.	No	No	No	10	9.6	11	10	9.7	7	4.9	.	.	1.9	1.5	No
113	2.1	1.5	4	Azithr	Pipra	.	Yes	No	No	1	.	1	1	.	.	0.7	.	.	.	.	No
110	0.1	0.1	0	Doxic	Azithr	Pipra	No	No	Yes	1	1.2	1.4	1.4	1.2	1	1.1	0.8	.	.	.	No
106	44	30	2	Doxic	Mero	.	Yes	No	Yes	2	2.2	3.6	3.9	4.1	.	.	.	.	.	.	No
92	7.1	5.5	4	Doxic	Azithr	Mero	Yes	No	No	1	.	2.7	2.3	3.3	2	3.9	5	.	.	.	Yes
93	.	.	2	Doxic	Pipra	.	No	No	No	2	1.7	1	0.9	.	.	.	.	.	.	.	No
97	0.5	0.5	0	Gatifl	.	.	No	No	No	1	.	1	.	.	.	.	.	.	.	.	No
87	9.4	7.4	4	Doxic	Azithr	Cifran	Yes	No	No	2	2.4	1.8	.	.	.	.	.	.	.	.	No

95	7.6	5.1	4	Doxic	Pipra	.	Yes	No	No	7	5.8	5.9	6.6	.	.	.	.	.	.	.	No
109	1.1	0.8	4	Doxic	Azithr	Pipra	Yes	No	No	1	1.2	1	.	0.8	.	0.8	.	.	.	.	No
102	1.9	1.4	0	Doxic	Ceftri	.	No	No	No	1	.	.	.	1.2	.	.	.	.	.	.	No
109	4.2	3	0	None	.	.	No	No	No	1	.	.	.	1.6	.	.	.	.	.	.	No
104	2	1.5	6	Artesu	Clinda	.	No	No	No	1	.	.	.	0.7	.	.	.	.	.	.	No
.	.	.	5	Doxic	Azithr	Pipra	Yes	No	No	3	.	1.5	.	.	1	0.7	.	.	.	.	No
92	0.2	0.2	0	Doxic	Gatifl	.	No	No	No	1	.	.	1.3	.	.	.	.	.	.	.	No
96	0.3	0.3	5	Doxic	Ceftri	.	No	No	No	1	.	0.8	.	.	.	.	.	.	.	.	No
105	2.1	1.5	0	Chlore	.	.	No	No	No	.	.	.	1.1	.	.	.	.	.	.	.	No
108	4.7	3.5	5	Artesu	Ceftri	.	No	No	No	3	2.5	1.6	1.1	.	.	.	.	.	.	.	No
105	0.2	0.1	0	None	.	.	No	No	No	1	0.9	.	.	.	.	.	.	.	.	.	No
103	2.4	1.7	4	Doxic	Azithr	Ceftri	No	No	No	2	1.8	1.6	.	.	.	.	.	.	.	.	No
101	1.7	1.3	0	Doxic	Azithr	Ceftri	No	No	No	1	.	.	0.9	.	.	.	.	.	.	.	No
111	0.1	0.1	4	Doxic	Azithr	Mero	No	No	Yes	1	1.4	1	0.8	0.7	.	.	.	.	.	.	No
101	20	16	5	Doxic	Artes	Pipra	No	No	No	8	8	6.6	6.9	4.2	4	3.2	2.6	.	.	.	Yes
.	2.5	.	5	Doxic	Artes	Ceftri	No	No	No	3	2.7	1.8	.	.	1	1.3	1.3	.	.	.	No
.	1.4	.	0	Doxic	Artes	.	No	No	No	2	.	0.8	0.8	.	.	0.8	.	.	.	.	No
.	1.8	.	5	Chlore	Artes	Lumir	No	No	No	1	1.4	.	.	.	.	.	.	.	.	.	No
106	7.6	5.7	0	Doxic	Artes	Pipra	No	No	No	1	.	0.7	.	.	.	.	.	.	.	.	No
.	.	.	0	Doxic	Artes	Pipra	Yes	No	Yes	1	1.4	1	.	.	.	.	.	.	.	.	No
.	1.3	.	5	Doxic	Artes	Ceftri	No	No	No	1	.	0.7	.	.	.	.	.	.	.	.	No
105	3.7	2.7	5	Doxic	Doxic	Pipra	No	No	Yes	1	.	0.9	0.6	0.6	1	.	.	.	.	.	No
100	.	.	3	Azithr	Ceftri	.	No	No	No	1	0.7	.	.	.	.	.	.	.	.	.	No
.	.	.	2	Doxic	Pipra	.	No	No	No	5	4.5	3.1	2.1	.	.	.	.	.	.	.	No
83	1.3	1	5	Doxic	Ceftri	.	No	Furos	No	1	.	.	0.9	.	.	.	.	.	.	.	No
.	0.2	.	2	Doxic	Azithr	Pipra	No	No	No	1	.	1	.	.	.	.	.	.	.	.	No
101	0.9	0.7	0	Doxic	Ceftri	.	No	No	No	1	.	1	.	.	1	.	.	.	.	.	No
97	18	14	0	Pipra	.	.	No	No	No	12	.	5.8	5	3.4	2	1.9	.	.	.	.	Yes
102	.	.	0	Gatifl	.	.	No	No	No	1	.	.	.	.	1	.	.	.	.	.	No
104	76	55	4	Doxic	Azithr	Pipra	No	No	No	15	16	14	10	12	10	9.7	7.1	.	.	.	Yes
86	2.5	1.9	0	Doxic	Ceftri	.	No	No	No	1	.	.	1.4	.	.	.	.	.	.	.	No
100	1.8	1.4	0	Gatifl	.	.	No	No	No	1	.	.	1.3	.	.	.	.	.	.	.	No
97	2.4	1.9	5	Doxic	Gatifl	.	No	No	No	1	.	0.8	.	.	.	.	.	.	.	.	No
103	0.1	0.1	5	Doxic	Azithr	Ceftri	No	No	No	1	.	1.6	.	.	.	.	.	.	.	.	No
.	0.4	0.3	5	Doxic	.	.	No	No	No	1	1	.	.	.	.	.	.	.	.	.	No
98	4	3	4	Doxic	Azithr	.	Yes	No	No	1	0.8	0.8	.	.	.	.	.	.	.	.	No
106	2.5	2	0	Doxic	Artes	.	No	No	No	1	1.2	.	.	.	.	.	.	.	.	.	No
99	0.6	0.5	0	Chlore	.	.	No	No	No	1	0.7	.	.	.	.	.	.	.	.	.	No
124	4.1	2.9	4	Doxic	Azithr	Pipra	No	No	No	3	.	2	1.6	.	1	0.9	.	.	.	.	No
102	3.5	2.6	4	Doxic	Azithr	Pipra	Yes	No	No	7	6.6	6.2	.	.	.	.	.	.	.	.	Yes
103	3.7	2.8	4	Doxic	Azithr	Mero	Yes	No	Yes	8	.	4.9	2.4	2.1	2	1.3	1	1	.	.	No
97	5.2	4.3	0	Doxic	Azithr	Gatifl	No	No	No	6	6	4.5	2.8	4.3	.	.	3.3	.	.	.	Yes
85	1.3	1	4	Doxic	Artes	Pipra	Yes	No	No	5	.	.	.	.	.	.	.	.	.	.	Yes
121	1.9	1.3	2	Doxic	Azithr	Pipra	No	No	Yes	2	.	1.5	1.2	1.1	.	.	.	.	.	.	No
100	1	0.7	0	Doxic	Azithr	.	No	No	No	5	3.6	2.1	1.1	1	.	.	.	.	.	.	No
104	1.3	0.9	0	Doxic	.	.	No	No	No	2	1.4	.	.	.	.	.	.	.	.	.	No
111	3.6	2.5	3	Doxic	Azithr	Ceftri	Yes	No	No	1	0.9	.	0.8	.	.	.	.	.	.	.	No
102	1.8	1.3	0	Doxic	Doxic	Ceftri	No	No	Yes	1	.	.	.	1.1	.	.	.	.	.	.	No
101	.	.	0	Doxic	.	.	No	No	No	1	.	.	.	.	.	.	.	.	.	.	No
107	2.7	2	0	Doxic	Artes	Pipra	Yes	No	No	2	1.1	1.2	.	1.2	.	.	.	.	.	.	No
92	1	0.7	5	Doxic	Azithr	.	Yes	No	Yes	3	3	.	.	.	.	.	.	.	.	.	No

97	22	17	4	Merop	.	.	Yes	Furos	No	7	.	.	.	.	.	.	.	.	.	.	No
111	4.7	3.4	2	Doxic	Azithr	Pipra	No	No	No	6	5.5	.	.	3.5	3	2.3	1.6	.	.	.	No
120	0.3	0.2	1	Doxic	Azithr	Pipra	No	No	No	3	4	2.9	2	1.6	.	1.5	1.3	.	.	.	No
93	11	9.2	4	Doxic	Mero	.	Yes	Furos	No	5	5.2	5.2	6	7.2	8	8.8	6.8	.	.	.	Yes
106	8.7	6.6	1	Doxic	Artes	Pipra	Yes	Furos	Yes	1	.	1.6	2.5	3.1	3	3.5	3.1	1.6	.	.	No
108	32	22	2	Doxic	Artes	Pipra	No	No	Yes	9	.	8	6.2	7.6	5	5.2	7.5	.	.	.	Yes
.	.	.	4	Doxic	Azithr	Pipra	Yes	No	Yes	2	2	1.2	0.7	.	.	.	.	.	.	.	No
102	4.3	3.2	1	Doxic	Azithr	.	No	No	No	1	0.9	0.6	0.6	.	.	.	.	.	.	.	No
99	1.6	1.2	4	Doxic	Azithr	Mero	No	No	No	3	2.9	1.6	0.9	.	1	0.6	.	.	.	.	No
90	20	14	4	Doxic	Azithr	Pipra	Yes	No	Yes	4	4.5	4.1	6.1	6.5	8	9.4	9.5	.	.	.	Yes
101	.	.	4	Doxic	Azithr	Mero	Yes	No	No	2	1.7	1.5	2.4	2.7	4	4.1	4.4	.	.	.	No
98	17	12	4	Doxic	Pipra	.	Yes	No	Yes	3	4	4.6	4.5	2.7	.	.	.	.	.	.	No
98	0.6	0.5	5	Doxic	Artes	Ceftri	No	No	Yes	1	.	2.2	.	.	.	.	.	.	.	.	No
105	3.1	2.2	5	Doxic	.	.	No	No	No	1	.	.	.	1	.	0.9	.	.	.	.	No
88	2.9	2.3	0	Doxic	Ceftri	.	No	No	No	2	.	.	.	.	1	.	.	.	.	.	No
88	1.8	1.3	0	Doxic	Azithr	Pipra	Yes	No	Yes	2	1.3	1.4	2.7	.	.	.	.	.	.	.	Yes
95	.	.	0	Doxic	.	.	Yes	Furos	No	1	.	.	.	.	.	1.2	1.3	.	.	.	No
106	26	19	4	Doxic	Azithr	Mero	Yes	No	Yes	4	5.1	2.5	2.5	4	.	.	.	.	.	.	Yes
92	2.1	1.9	0	Doxic	Azithr	Ceftri	No	No	No	1	.	.	0.9	.	.	.	.	.	.	.	No
104	.	.	5	Doxic	Artes	Ceftri	No	No	No	3	1.6	1.4	.	.	1	.	.	.	.	.	No
101	0.1	0.1	1	Doxic	Azithr	Ceftri	No	No	Yes	1	1	1	0.8	.	1	.	.	.	.	.	No
99	3.5	3.1	0	Doxic	Azithr	Ceftri	No	No	No	1	.	0.8	.	.	.	.	.	.	.	.	No
101	.	.	5	Doxic	Pipra	.	No	No	No	6	.	.	.	6.1	6	4.6	3.1	.	.	.	No
108	3.5	3	5	Doxic	Azithr	.	No	No	No	1	1.3	0.9	.	0.7	1	.	.	.	.	.	No
96	1.5	1.2	0	Doxic	Ceftri	.	No	No	No	1	.	1	.	.	.	.	.	.	.	.	No
114	.	.	2	Doxic	Pipra	.	Yes	No	No	2	1.7	.	.	.	.	.	.	.	.	.	No
106	.	.	4	Doxic	Azithr	Pipra	Yes	No	No	2	2.5	.	.	.	.	.	.	.	.	.	Yes
104	6.2	4.6	0	Doxic	Artes	Pipra	No	No	Yes	5	.	3.3	5.6	4.7	7	.	.	.	.	4.5	Yes
107	0.3	0.2	2	Doxic	Artes	Ceftri	No	No	No	1	0.4	1	.	0.6	.	.	.	.	.	.	No
110	.	.	0	None	.	.	No	Furos	Yes	1	0.7	.	.	.	.	.	.	.	.	.	No
102	0.5	0.4	0	Doxic	.	.	No	No	No	2	1.7	0.4	.	.	.	.	.	.	.	.	No
99	1.6	1.2	1	Artesu	Clinda	Lumit	No	No	Yes	1	0.8	0.9	0.9	0.8	1	0.7	.	.	.	.	No
116	5.8	4	4	Doxic	Azithr	.	Yes	Furos	Yes	3	.	2.9	2.8	3	4	.	.	.	.	.	Yes
.	.	.	4	Doxic	Artes	.	No	No	Yes	5	.	3.9	4.2	4.1	6	.	.	.	.	.	Yes
.	.	.	4	Azithr	Pipra	.	No	No	No	2	.	1.1	.	.	.	.	.	.	.	.	No

Hdn	HD	Dur	Ind	Fre	Typ	Acc	Hep	Sur	RIF	RIF	RIFF	RIFN	ARF	ARF	ERI	EAR	ARFN	VellSc	Lian0
1	Yes	0	Hyper	Inter	SLE	Femo	Rigid	0	3	3	3	3	3	1	3	1	1	.	.
1	Yes	0	Metab	Inter	Reg	Femo	Rigid	1	3	3	3	3	3	1	3	1	1	1	0.41
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	3	1	0	1	0.21
5	No	5	Metab	Inter	Reg	Femo	Salin	1	3	3	3	3	3	1	3	1	1	1	0.48
1	Yes	0	Metab	Inter	SLE	Femo	Salin	0	3	3	3	3	3	1	.	.	1	1	0.59
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.91	0.05
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	0.98	0.22
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	1	0.17
4	Yes	7	Anuria	Inter	Reg	Femo	Salin	1	3	3	3	3	3	1	3	1	1	0.99	0.18
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	3	1	1	1	0.4
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.54
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.62
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	1	0.24
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.29
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	0.8	0.16
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	.	.	1	1	0.62
.	Yes	.	.	.	.	.	.	.	3	2	3	3	3	1	3	1	1	1	0.17
2	Yes	0	Anuria	Inter	SLE	Femo	Rigid	0	2	2	2	2	2	1	3	1	1	1	0.31
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.34
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	1	0.38
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.91	0.37
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.11
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	0.69	0.18
5	Yes	5	Metab	Inter	Reg	Femo	Rigid	1	3	3	3	3	3	1	3	1	1	0.94	0.15
.	No	.	.	.	.	.	.	.	3	2	3	3	3	1	3	1	1	1	0.43
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	1	0.26
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.86	0.27
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	1	0.62
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	1	0.52
3	Yes	1	Hyper	Inter	SLE	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.69
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	0.92	0.39
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.67
1	Yes	0	Metab	Inter	Reg	Femo	Salin	0	3	3	3	3	3	1	.	.	1	0.98	0.33
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.37
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	1	0.36
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.7	0.27
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	.	.	1	1	0.68
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	3	1	1	0.98	0.13
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	3	1	1	1	0.5
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	2	1	1	0.93	0.38
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	.	.	1	1	0.62
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	.	.
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	0.99	0.36
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	0.98	0.58
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	3	1	1	1	0.58
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	.	.
3	Yes	7	Anuria	Inter	SLE	Femo	Rigid	0	3	3	3	3	3	1	1	1	1	1	0.44
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	1	1	1	0.96	0.42
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.52	0.18
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	0.99	0.28

.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.59
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	2	1	1	1	0.57
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	1	1	1	0.74	0.19
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	2	1	1	0.95	0.13
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.96	0.39
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	.	.	1	1	0.76
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	2	1	1	1	0.3
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.37
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	0.9	0.22
.	No	.	.	.	.	.	.	.	3	2	3	3	3	1	2	1	1	1	0.27
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.84	0.17
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.49
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	1	0.17
.	No	.	.	.	.	.	.	.	1	2	2	2	1	1	3	1	1	1	0.67
2	Yes	2	Uremi	Daily	Reg	Femo	Rigid	1	3	3	3	3	3	1	3	1	1	0.96	0.32
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	2	1	1	1	0.25
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	0	0	1	0.91	0.3
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.84	0.18
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.96	0.32
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	0	0	1	0.98	0.43
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.44
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.39
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	.	.	1	1	0.35
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.66
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	1	0.43
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	1	0.35
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	1	1	1	0.9	0.21
1	Yes	0	Uremi	Inter	Reg	Femo	Rigid	1	3	3	3	3	3	1	3	1	1	0.97	0.33
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.77	0.11
4	Yes	5	Metab	Inter	Reg	Femo	Rigid	1	3	3	3	3	3	1	3	1	1	0.97	0.48
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	0.97	0.24
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	1	1	1	0.91	0.1
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.4
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.33
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	0.99	0.24
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	1	0.59
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.73	0.18
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	1	0.51
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.63
2	Yes	1	Metab	Inter	Reg	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.37
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.46
2	Yes	1	Hyper	Inter	Reg	IJV	Salin	1	3	3	3	3	3	1	3	1	1	0.98	0.42
1	Yes	0	Metab	Daily	SLE	Femo	Salin	0	3	3	3	3	3	1	0	0	1	1	0.36
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	3	1	1	0.99	0.24
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.37
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	2	1	1	0.99	0.34
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	1	0.27
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	0.69	0.19
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	1	1	1	0.99	0.32
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	1	1	1	1	0.39
.	.	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.56

.	3	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.45
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.33
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.74
7	Yes	12	Uremi	Inter	SLE	Femo	Rigid	0	3	3	3	3	3	1	3	1	1	1	0.38
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	1	1	1	1	0.48
8	Yes	9	Metab	Inter	Reg	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.65
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	.	.	1	0.99	0.44
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	0.99	0.51
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	2	1	1	1	0.51
5	Yes	6	Metab	Inter	Reg	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.68
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	.	.
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.58
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	3	1	1	1	0.41
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	0	0	1	1	0.29
.	No	.	.	.	.	.	.	.	1	1	1	1	1	1	0	0	1	1	0.12
1	Yes	0	Metab	Inter	SLE	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.53
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	.	.	1	.	.
3	Yes	3	Metab	Inter	SLE	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.78
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	2	1	0	1	0.4
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.48
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.99	0.42
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	1	0.46
.	No	.	.	.	.	.	.	.	3	3	3	3	3	1	3	1	1	1	0.32
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	1	0.37
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	0.97	0.22
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	2	1	1	.	.
1	Yes	0	Metab	Inter	SLE	Femo	Salin	0	3	2	3	3	3	1	2	1	1	1	0.76
3	Yes	3	Metab	Inter	Reg	Femo	Salin	1	3	3	3	3	3	1	3	1	1	1	0.36
.	No	.	.	.	.	.	.	.	0	1	1	1	0	0	2	1	1	1	0.53
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	0	0	0	1	0.45
.	No	.	.	.	.	.	.	.	2	2	2	2	2	1	3	1	1	1	0.49
.	No	.	.	.	.	.	.	.	0	0	0	0	0	0	1	1	0	1	0.68
3	Yes	2	Metab	Inter	SLE	Femo	Salin	0	3	3	3	3	3	1	3	1	1	1	0.65
4	Yes	3	Metab	Inter	SLE	Femo	Salin	0	3	3	3	3	3	1	.	.	1	1	0.79
.	No	.	.	.	.	.	.	.	1	2	2	2	1	1	.	.	1	1	0.17