# A retrospective study of patients with blood culture-confirmed typhoid fever in Fiji 2014-15: epidemiology, clinical features, treatment, and outcome

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**Abstract**

**Background:** Typhoid fever is endemic in Fiji. We sought to describe the epidemiology, clinical features, and case fatality risk of blood culture-confirmed typhoid fever from January 2014 through December 2015.

**Methods:** Blood culture positive patients were identified from typhoid surveillance line list.Astandardized case investigation form was used to record data from patients’ medical records.

**Results:** Of542 patients, 518 (95.6%) were indigenous Fijians (iTaukei) and 285 (52.6%) were male. The median (interquartile range) age was 25 (16-38) years. Mean (standard deviation) time from the onset of illness to admission was 11.1 (6.9) days. Of 365 patients with clinical information, 346 (96.9%) had fever, 239 (66.9%) diarrhoea, 113 (33.5%) vomiting, and 72 (30.2%) abdominal pain. There were 40 (11.0%) patients with complications, including 17 (4.7%) with shock and 11 (3.0%) with hepatitis. Nine patients died with case fatality risk of 1.7 %. There was no resistance to first line antimicrobials. Resistance to ciprofloxacin and nalidixic acid was 0.8% (n=3) and 1.4% (n=5), respectively.

**Conclusions:** In Fiji, most blood culture confirmed typhoid fever cases were young adults. Common clinical manifestations were fever and gastrointestinal symptoms. Further studies are required to elucidate factors associated with complications and death.

**Key words**

Antimicrobial susceptibility, Clinical features, Complications, Fiji, *Salmonella* Typhi, Typhoid fever

**Introduction**

Typhoid fever, an infection caused by *Salmonella enterica* subspecies *enterica* serovar Typhi (*Salmonella* Typhi), remains a common infection in low- and middle-income countries.[1](#_ENREF_1),[2](#_ENREF_2) In 2017, it was estimated to cause more than 10 million new cases worldwide,[3](#_ENREF_3) with an estimated 160,000 deaths.[4](#_ENREF_4)

Fiji is an independent island nation in the South Pacific with a 2017 population estimated at 884,887, of which 44.1% lived in rural areas.[5](#_ENREF_5) The two main ethnic groups are iTaukei, Indigenous Fijians (56.8%) and Fijian of Indian Descent (37.5%).[6](#_ENREF_6) Health services are provided mainly by the Ministry of Health and Medical Services (MoHMS). National health service delivery is through four medical Divisions: Central, Western, Northern, and Eastern. Each Division is further divided into Subdivisions, medical areas, and zones. There are three main public hospitals one each in the Central, Northern, and Western Divisions and two specialist hospitals, both based in the Central Division. Primary health care is provided by 19 Subdivisional hospitals, 86 health centres, and 97 nursing stations.[7](#_ENREF_7) Health care in public health facilities are provided free of charge. In addition, there is one private hospital in Suva, Central Division. Several small privately-owned medical centres and clinics exist in all the Divisions.

Passive laboratory surveillance for typhoid fever was established in 2004.[8](#_ENREF_8) Typhoid fever confirmed by culture of blood, stool, pus, or other sterile sites is reported within 24 hours of confirmation by telephone to the Fiji Centre of Communicable Diseases Control (FCCDC) and to treating medical officer in the respective health facility.[9](#_ENREF_9) In addition, all clinically diagnosed typhoid fever patients are reported through the national notifiable diseases surveillance system on a weekly basis.[10](#_ENREF_10) There has been an eight-fold rise in laboratory confirmed cases of typhoid fever detected by passive surveillance form 5.1/100,000 population in 2004[8](#_ENREF_8) to 42.1/100,000 in 2011.[11](#_ENREF_11) Frequent outbreaks have also been reported since 2008.[12](#_ENREF_12), [13](#_ENREF_13) A review of surveillance reports from 2008-2012 found that most culture-confirmed typhoid cases were among young adults with a median age of 24 years and 95% were indigenous Fijians known as iTaukei.[12](#_ENREF_12) Crude typhoid fever incidence was highest among people aged 15 to 29 years at 64/100,000/year.[11](#_ENREF_11), [12](#_ENREF_12) In 2010, the Fiji MoHMS conducted Vi polysaccharide mass vaccination of 65,015 people after a typhoid fever outbreak that followed Tropical Cyclone Tomas.[11](#_ENREF_11), [14](#_ENREF_14) The same year, MoHMS revised the national typhoid fever treatment guidelines, with oral ciprofloxacin 500mg twice daily for 5 days being recommended for uncomplicated typhoid fever and amoxicillin (75 to 100mg /kg for 14 days) for pregnant women.[14](#_ENREF_14) There have been limited recent data regarding the clinical features, complications, and case fatality risk (CFR) of typhoid fever in Fiji. Studies from the 1980s reported high CFR ranging from 2.2% to 5.9%.[15-17](#_ENREF_15) The present study was conducted to provide up-to-date evidence on the clinical features and case fatality in typhoid fever patients as well as the antimicrobial susceptibility patterns of Fiji *Salmonella* Typhi isolates.

**Materials and methods**

Study participants were identified from the FCCDC surveillance line list of patients with culture-confirmed *Salmonella* Typhi infection. The line list incorporates both outbreak and sporadic cases of culture confirmed typhoid fever. We performed a retrospective review of medical records of patients with blood culture-confirmed typhoid fever patients from January 2014 through December 2015. A standardized data collection form was used to record demography (age, sex, ethnicity, residential location), clinical (symptoms, signs, duration of illness, complications, laboratory results), and treatment related information (antimicrobials used, antimicrobial susceptibility patterns of isolates, duration of hospital stay, and death from typhoid). Typhoid fever deaths were identified from review of medical records of cases reported in the passive surveillance. Additional information on deaths was obtained from patient information system (PATIS plus) which is an electronic database that codes mortality according to the International Classification of Diseases, Tenth Revision (ICD 10) through an automated system called Iris (version 4.0).[18](#_ENREF_18) The ICD 10 code used for typhoid deaths was A01.0.

Any typhoid fever patient or typhoid attributable death diagnosed on clinical suspicion only or laboratory confirmed by only stool culture has been excluded.

Consistent with the Fiji 2010 national typhoid management guidelines, an outbreak of typhoid fever was defined as a sudden increase in the number of typhoid fever cases, or the identification of two or more suspected or confirmed cases of typhoid fever in one month in a new area or village.[14](#_ENREF_14)The sudden increase implies any unusually high number of cases compared to the previous reporting period (e.g. the preceding week) or to same week of the previous years. The Fiji MoHMS staff use this threshold to notify or declare outbreak. Data collection was performed from February 2017 through July 2018.

Complications of typhoid

Complications of typhoid fever were defined by the presence of one or more of the following features: i) gastrointestinal bleeding (the presence of occult blood, melena, or visible blood in the stool); ii) intestinal perforation (confirmed at surgery); iii) encephalopathy (delirium, obtundation or coma); iv) haemodynamic shock (systolic blood pressure < 90mmHg and/or diastolic blood pressure < 60 mmHg associated with tissue hypoperfusion); v) myocarditis (tachycardia or bradycardia with an associated abnormality of the electrocardiogram or ultrasound evidence of a pericardial effusion); vi) hepatitis (as indicated by jaundice and/or hepatomegaly with serum transaminases two times above the normal range and vii) a clinical diagnosis of cholecystitis (right upper quadrant pain and tenderness without evidence of hepatitis).[19](#_ENREF_19), [20](#_ENREF_20)

**Laboratory methods**

Blood and stool collected from health centres, Subdivisional, and Divisional Hospitals were cultured at Divisional hospital microbiology laboratories and potential *Salmonella spp.* were identified using standard microbiological methods. Blood cultures were performed using the BaCT/ALERT 3D (Biomerieux, Marcy L’Etoile, France) system. Antimicrobial susceptibility testing to ampicillin, chloramphenicol, ceftriaxone, ciprofloxacin, nalidixic acid, and trimethoprim-sulfamethoxazole was performed by disk diffusion and E-test (BioMerieux, Marcy L’Etoile, France) according to the standards and interpretative criteria of the Clinical and Laboratory Standards Institute.[21](#_ENREF_21)The antimicrobial susceptibility results from the study period were compared with the results collected from the same laboratories in 2004 and 2005.[8](#_ENREF_8)

**Statistical analyses**

Data was analysed using Microsoft Excel (Microsoft Corp. Redmond, WA) and SPSS version 24 (Armonk, NY:IBM Corp.). Overall and specific crude incidence of typhoid fever was calculated using population projections provided by the Fiji Bureau of Statistics (FBoS) for 2014 and 2015. Since FBoS data are not disaggregated for medical Division, crude incidence rates by medical Divisions and Subdivisions were calculated using the 2014 and 2015 population estimates from the MoHMS. CFR was calculated by dividing the number of deaths in blood culture confirmed typhoid patients in 2014 and 2015 by the total number of blood culture positive typhoid patients reported during the same time (n=542) multiplied by 100. Demographic profile, antimicrobial susceptibility pattern, and outcome were assessed among all cases (n=542). Analysis on common clinical presentations, complications, treatment with antimicrobials, and duration of hospital stay was conducted among patients treated in Divisional and Subdivisional Hospitals (n=365). Categorical variables were presented as proportions and the statistical significance of differences was determined using the Chi-square test or Fisher’s exact test with a 95% level of confidence. Continuous variables were described as proportions using mean or median with standard deviation (SD) or interquartile ranges (IQR). Bivariate analyses were performed to assess the clinical and laboratory features between children (age <15 years old) and adults (age **≥** 15 years old) with statistical significance determined at a 0.05%.

**Results**

During the study period 551 instances of culture-confirmed typhoid fever (*Salmonella* Typhi infection) were reported to the FCCDC. Of these, 542 (98.4%) were confirmed by blood culture and we included in the analysis. The demographic characteristics of blood culture confirmed typhoid fever patients are shown in Table 1. Of the 542 patients, 285 (52.6%) were male and 518 (95.6%) were from iTaukei ethnic group. The median (interquartile [IQR]) age was 25 (16-38) years. Children <15 years of age accounted for 118 (21.8%) of the patients. The crude incidence of typhoid fever from passive surveillance was 32.1 and 30.4/100000 population in 2014 and 2015, respectively. The mean age specific crude incidence was 49.1/100000 population per year among people from 15 to 24 years and 12/100,000 population per year among the age group ≥60 years. The Northern Division reported 198 blood culture-confirm typhoid patients for a mean annual crude incidence of 74.2/100,000 population per year. The Western and Central Divisions had mean annual crude incidence of 23.8/100000 population (n=180) and 20.8/100000population (n=158), respectively. At Subdivisional level, the highest mean annual crude incidence of 150.3/100000 population was reported in Ra, Western Division, in 2014 and 170.0/100,000 population in Bua, Northern Division, in 2015. Further analysis of data by the location of patient residence indicated several community outbreaks and clusters. Of 24 typhoid cases reported in Bua Subdivision in 2014, 18 (75%) were from outbreaks in five villages. Similarly, of 51 cases in Suva and 15 cases in Namosi Subdivisions, 22 (43%) and eight (53%) were outbreak-associated, respectively. In 2015, in the Northern and Central Divisions patients reported from community outbreaks accounted for more than half of all cases, such as 11 (55 %) in Namosi, five (62.5%) in Rewa, and eight (72%) in Naitasiri Subdivisions.

**Table 1 Demographic characteristics of typhoid fever patients in Fiji, 2014-2015**

Of 542 patients, 486 (89.7%) were treated in hospitals and 56 (10.3%) were treated in health centres. Clinical information was available for 365 (75.1%) patients who received treatment at Divisional and Subdivisional hospitals. The mean (standard deviation [SD]) time from the onset of illness to admission was 11.1 (6.9) days. The time from onset to admission was 11.1 (SD 5.9) days for males and 10.5 (SD 5.8) days for females (p=0.384), 10.8 (SD 5.8) days for iTaukei and 12.6 (SD 7.0) for Fijians of Indian Descent (p=0.376), and 8.4 (SD 5.9) days for the age group <15 years, and 11.5 (SD 5.1) days for age group ≥ 15 years (p=<0.001). The clinical features of typhoid fever are summarized in Table 2. Fever was reported in 349 (96.9%) of patients. History of diarrhoea and loss of appetite were reported in 239 (66.9%) and 185 (52.0%) of patients, respectively. Among adult patients 160 (58.8%) and 136 (49.8%) gave history of rigors and headache, respectively. On physical examination, conjunctival pallor was reported in 80 (25.2%) patients and jaundice was found in 31 (9.7%) of patients. Abnormal neurologic findings such as confusion, lethargy, or delirium were reported in 21 (6.1%) of patients. At admission, 135 (41.0%) had anaemia (haemoglobin <12 g/dl in adults and < 11g/dl in children under 15 years old) of which 10 patients had severe anaemia; haemoglobin <7 g/dl or needed transfusion (n=8). Leukopenia (white blood cells count <5000x106 cells/L and thrombocytopenia (platelet count <100000cells/L) were reported in 132 (39.8%) and 146 (44.9%) of patients at admission, respectively (Table2).

**Table 2 Clinical and laboratory features of typhoid fever patients in Fiji, 2014-2015**

Of 365 patients, 40 (11. 0%). developed complications. Seventeen (4.7%) had hypovolemic shock, 11 (3.0%) hepatitis, 9 (2.5%) gastrointestinal bleeding, 4 (1.1%) encephalopathy, and 1 (0.3%) myocarditis. Intestinal perforation and cholecystitis were not reported. The mean time to admission among patients with complications was 12.7 (SD 6.9) days and 10.7 (SD 6.9) days in patients with no complications (p=0.137). All patients with complications were from the iTaukei ethnic group. The occurrence of complication did not differ by sex ( 11.9% in females and 10.1% in males, p=0.618) and age group (8.2% in <15 year old and 11.8% in ≥15 years old ,p=0. 432). There were a total of 9 deaths among blood culture confirmed typhoid fever patients . The overall CFR was 1.7%. Among 413 adults, 8 died for an adult CFR of 1.9%. Among 118 children, one died for a child CFR of 0.8%.

Of 365 typhoid fever patients, 290 (79.5%) were treated with ciprofloxacin for the mean duration of 6 (SD 2) days and 80 (21.9%) received ceftriaxone. Other drugs used for treatment of typhoid fever included parenteral ampicillin, oral amoxicillin, and chloramphenicol. Concerning antimicrobial susceptibility, all *Salmonella* Typhi strains were susceptible to ampicillin, trimethoprim-sulfamethoxazole and chloramphenicol (Table 3). Resistance to nalidixic acid identified in 3 (1.4%) of 361 isolates tested and to ciprofloxacin in 3 (0.8%) of 393 isolates tested. No multidrug resistant (MDR) *Salmonella* Typhi was identified during the study period.

**Table 3 Comparison of antimicrobial resistance pattern among *Salmonella* Typhi isolates, Fiji, 2004/05 and 2014/15**

**Discussion**

In a two year retrospective study we found that typhoid fever in Fiji was most common among adolescents and young adults and the iTaukei ethnic group. While typhoid fever disproportionally affects infants and children in high incidence settings,[2](#_ENREF_2), [22](#_ENREF_22) less than one quarter of typhoid fever cases occurred <15 years of age in our study. It is possible that the passive surveillance system for typhoid in Fiji under-ascertains typhoid fever in younger age groups through reluctant to draw blood for culture in this group, low blood volume, and prior antimicrobial use.[23](#_ENREF_23)

In our study, the average duration of illness at time of seeking health care was 11 days, similar to a 1982 study from Fiji that reported a mean duration of illness prior to admission to be 13 days.[16](#_ENREF_16) Other studies from the Oceania reported comparable durations of illness prior to presentation.[24](#_ENREF_24), [25](#_ENREF_25) The clinical features of typhoid in our study were similar to those observed in other studies conducted in endemic countries in Asia, Africa, and the Pacific.[26-28](#_ENREF_26) Fever was the most frequently reported symptom among both children and adults. Consistent with other studies, rigors and headache were commonly reported among adults.[28](#_ENREF_28) Besides the non-specific generalized symptoms, typhoid fever patients in Fiji had a range of gastrointestinal symptoms. Approximately two-third of patients gave history of diarrhoea , half complained of anorexia, one in three reported vomiting, and 20% had abdominal pain. Unlike other studies in Asia and Africa[28](#_ENREF_28) that showed higher occurrence of diarrhoea among children, we did not demonstrate differences in the occurrence of diarrhoea between children and adults. However, constipation was uncommon. The frequent presentation with diarrhoea in Fiji may result in misdiagnosis as diarrhoeal disease. Physical examination findings were non-specific, with high temperature and tachycardia reported in more than half of patients.

In our study, most patients had anaemia and thrombocytopenia at admission. The reported high prevalence of anaemia in children is consistent with results of the recent systematic review of typhoid fever clinical features.[28](#_ENREF_28) However, the prevalence of anaemia in adults was much higher than studies from other endemic settings.[28](#_ENREF_28) Anaemia is common in Fiji and the national nutrition survey conducted in 2015 showed an anaemia prevalence of 63.1% among <5-year-old children and 40.1% among adults.[29](#_ENREF_29) Our participants may have a background anaemia from underlying micronutrients deficiency.

Thrombocytopenia has not been reported as a common presentation of typhoid fever. Its prevalence varied substantially between studies. Some studies in Asia reported thrombocytopenia prevalence of 4.6% -15%.[27](#_ENREF_27), [30](#_ENREF_30) The systematic review of Azmatullah et al.[28](#_ENREF_28)reported a higher prevalence of thrombocytopenia (platelet count <150,000) in sub-Saharan Africa (35%) and East Asia and the Pacific (27%). Typhoid fever patients in Fiji have similar symptoms and hematologic abnormalities such as anaemia and thrombocytopenia as patients suffering from other common febrile illnesses such as dengue and leptospirosis. This could pose further challenge for case management in health centres and Subdivisional hospitals as confirmatory tests are often available only in Divisional hospitals or the public health laboratory in Suva.

The proportion of patients with complications in our study was similar to the global estimate of 10-15%[1](#_ENREF_1), however, the pattern of complications differed. Shock, hepatitis, and anaemia predominated in our study. Intestinal perforation is a late complication that might occur after blood culture is no longer positive therefore might have been missed in our cohort. The CFR of typhoid fever is widely estimated to be <1% with appropriate antimicrobial treatment.[1](#_ENREF_1) Country level studies and systematic reviews reported substantial variation in CFR by age group and geographic region.[28](#_ENREF_28) We found an overall CFR of 1.7% and CFR among adults of 1.9% which is higher than the reported mortality in Asia. Further prospective studies are required better understand the independent risk factors for typhoid fever mortality in Fiji.

Globally, the emergence and rapid spread of the often drug resistant *Salmonella* Typhi H58 lineage has been associated with increased treatment failure and mortality.[27](#_ENREF_27), [31](#_ENREF_31) There is limited literature on the antimicrobial susceptibility pattern of *Salmonella* Typhi strains in Fiji. Dunn et al.[8](#_ENREF_8) in 2005 reported low prevalence of resistance to the first lines drugs ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, ranging from 0.8% to 1.1% (Table 3). Ten years later, the prevalence of resistance to first line drugs remained similar but resistance to nalidixic acid had increased from 0% to 1.4%. In 2010, ciprofloxacin became the first line drug for the treatment for typhoid fever in Fiji. Ciprofloxacin is a restricted drug that is not available over-the-counter from private or public pharmacies. The first ciprofloxacin-resistant strains were reported in 2014 (FCCDC surveillance, unpublished data). The rise in nalidixic acid resistance compared to 2004 is of concern as it is associated with decreased susceptibility to fluoroquinolones.[1](#_ENREF_1) Moreover, there might be under reporting as approximately 30% of samples (mainly from the Northern Division) were not tested for nalidixic acid or ciprofloxacin susceptibility. Other studies in the Pacific also demonstrated low prevalence of antimicrobial resistance.[24](#_ENREF_24), [25](#_ENREF_25) This could suggest that fluoroquinolone resistant and MDR isolates of *Salmonella* Typhi have not yet emerged or been introduced to Fiji or other endemic islands in the Pacific.

Our study has several limitations. Being retrospective, we relied on obtaining data from patient medical records. These were not available for some patients. Furthermore, data were incomplete and were of variable quality in some for whom records were available. Complications, such as intestinal perforation might have been missed as it might occur at the later stage when blood culture is negative. Crude incidence in our study was estimated using the data from passive surveillance, likely underestimating the scale of the typhoid fever problem. We were unable to report on pre hospital antimicrobial use as it was not routinely documented. In addition, some selection bias may be present in the study due to the exclusion of patients whose folders were not available from the health facilities. As a result, we were unable to identify independent factors associated with fatality.

## Conclusions

Our study provides updated information on the clinical features of typhoid fever in Fiji. The majority of blood culture confirmed typhoid fever cases were among young adults. Common clinical manifestations were fever and gastrointestinal symptoms, with high rates of anaemia, thrombocytopenia and complications such as shock and hepatitis among typhoid fever patients admitted to hospital. The reported rate of complications is high despite of low level of antimicrobial resistance, further studies are warranted to investigate factors associated with complications. Our findings revealed that, using the Fiji MoHMS definition, the majority of typhoid fever cases were associated with outbreaks. As per the national typhoid management guidelines, proper investigation of such outbreaks is warranted to identify and treat sub-clinical cases, assess the role of unsafe water and unimproved sanitation facilities in transmission, and to search for chronic carriers of *Salmonella* Typhi who could be implicated in food or water contamination[14](#_ENREF_14). We highlight the potential emerging resistance among *Salmonella* Typhi strains to nalidixic acid and fluoroquinolones. Sustained typhoid fever clinical and laboratory surveillance is vital to monitor this important disease threat, including the impact of prevention and control efforts.

**Authors contribution**

AGS, CMP conceived the study. AGS, CMP, JAC, RAS, EKM, and RN designed the study protocol. AGS and VR performed data collection and data entry. AGS performed data analysis, AGS drafted the manuscript. JAC, CMP, RAS, EKM, AJ and RN critically reviewed and appraised the manuscript. All authors read and approved the final manuscript.

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**Competing interest**

None declared

**Ethical approval**

The study was approved by the Fiji National Health Research and Ethics Committee (2016.87.NW). This was a retrospective medical folder review with subsequent analysis of anonymised data and individual patient consent was not required.

**Reference**

Uncategorized References

1. Crump JA, Sjolund-Karlsson M, Gordon MA, et al.; Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. *Clin Microbiol Rev* 2015;**28**(4):901-37. doi: 10.1128/CMR.00002-15

28/4/901 [pii].

2. Mogasale V, Maskery B, Ochiai RL, et al.; Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. *Lancet Glob Health* 2014;**2**(10):e570-80. doi: 10.1016/S2214-109X(14)70301-8

S2214-109X(14)70301-8 [pii].

3. Disease GBD, Injury I, Prevalence C; Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;**392**(10159):1789-1858. doi: 10.1016/S0140-6736(18)32279-7.

4. Collaborators GBDCoD; Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;**392**(10159):1736-1788. doi: 10.1016/S0140-6736(18)32203-7.

5. FIBOS. *Fiji Islands Bureau of Statistics. Population and housing census 2017*. <http://www.statsfiji.gov.fj/index.php/2017_Population_and_Housing_Census_Release_1.pdf> (Date Accessed 2018 Accessed, date last accessed)

6. FBOS; Population and housing census 2007. . In:Statistics FBos (ed). Suva, Fiji Islands 2008.

7. MoHMS; Fiji Ministry of Health and Medical Services. Annual Report 2016. Suva Fiji 2017.

8. Dunn J, Pryor J, Saketa S, et al.; Laboratory-based Salmonella surveillance in Fiji, 2004-2005. *Pac Health Dialog* 2005;**12**(2):53-9.

9. MoHMS; Communicable diseases surveillance and outbreak management guidelines. Fiji Ministry of Health and Medical Services. Suva, 2010.

10. MoHMS; Communicable diseases surveillance and outbreak management guidelines. Fiji Ministry of Health and Medical Services. . Suva, Fiji, 2016.

11. Scobie HM, Nilles E, Kama M, et al.; Impact of a targeted typhoid vaccination campaign following cyclone Tomas, Republic of Fiji, 2010. *Am J Trop Med Hyg* 2014;**90**(6):1031-8. doi: 10.4269/ajtmh.13-0728.

12. Thompson CN, Kama M, Acharya S, et al.; Typhoid fever in Fiji: a reversible plague? *Trop Med Int Health* 2014;**19**(10):1284-92. doi: 10.1111/tmi.12367.

13. Kumar SA, Jacob A, Enari M, et al.; The incidence of typhoid fever in Fiji from 1995-2009. *Fiji Journal of Public Health* 2012;**1**(1):31-36.

14. MoHMS; Guidelines for the Diagnosis, Management and Prevention of Typhoid Fever. Fiji Ministry of Health and Medical Services. . Suva , Fiji 2010.

15. Ram P, Mataitoga V, Seruvatu L, et al.; Typhoid Fever in Fiji in 1982: I: Epidemiological aspects *Fiji Medical Journal* 1983;**September /October** 124-129.

16. Naidu V, Kapadia V, Boladuadua A, et al.; Typhoid Fever in Fiji in 1982: III clinical cases at colonial war memorial hospital. *Fiji Medical Journal* 1983;**September/October** 134-137.

17. Narayan Y, Lal M, Foi J, et al.; Typhoid Fever in fiji in 1982: II: clinical cases at the Levuka hosptal. *Fiji Medical Journal* 1983;**September/October** 130-133.

18. WHO.; International Statistical Classification of Diseases and Related Health Problems. . Geneva:World Health Organization., 2010.

19. Parry CM, Hien TT, Dougan G, et al.; Typhoid fever. *N Engl J Med* 2002;**347**(22):1770-82. doi: 10.1056/NEJMra020201

347/22/1770 [pii].

20. Bhan MK, Bahl R, Bhatnagar S; Typhoid and paratyphoid fever. *Lancet* 2005;**366**(9487):749-62. doi: 10.1016/S0140-6736(05)67181-4.

21. CLSI; Performance standards for antimicrobial disk susceptibility tests. Clinical and Laboratory Standards Institute. . 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2006.

22. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, et al.; A study of typhoid fever in five Asian countries: disease burden and implications for controls. *Bull World Health Organ* 2008;**86**(4):260-8. doi: S0042-96862008000400010 [pii].

23. MoHMS; Annual report 2015, Pathology department, microbiology section of CWM hospital (unpublished). 2016.

24. Lane RJ, Holland D, McBride S, et al.; Enteric fever in the Pacific: a regional retrospective study from Auckland, New Zealand. *Intern Med J* 2015;**45**(2):148-55. doi: 10.1111/imj.12644.

25. Olsen SJ, Kafoa B, Win NS, et al.; Restaurant-associated outbreak of Salmonella typhi in Nauru: an epidemiological and cost analysis. *Epidemiol Infect* 2001;**127**(3):405-12.

26. Thriemer K, Ley B, Ame SS, et al.; Clinical and epidemiological features of typhoid fever in Pemba, Zanzibar: assessment of the performance of the WHO case definitions. *PLoS One* 2012;**7**(12):e51823. doi: 10.1371/journal.pone.0051823

PONE-D-12-19228 [pii].

27. Parry CM, Thompson C, Vinh H, et al.; Risk factors for the development of severe typhoid fever in Vietnam. *BMC Infect Dis* 2014;**14**:73. doi: 10.1186/1471-2334-14-73

1471-2334-14-73 [pii].

28. Azmatullah A, Qamar FN, Thaver D, et al.; Systematic review of the global epidemiology, clinical and laboratory profile of enteric fever. *J Glob Health* 2015;**5**(2):020407. doi: 10.7189/jogh.05.020407

jogh-05-020407 [pii].

29. NFNC; 2015 Fiji national nutrtion survey results National Food and Nutrition Centre and Ministry of Health and Medical Services 2016.

30. Limpitikul W, Henpraserttae N, Saksawad R, et al.; Typhoid outbreak in Songkhla, Thailand 2009-2011: clinical outcomes, susceptibility patterns, and reliability of serology tests. *PLoS One* 2014;**9**(11):e111768. doi: 10.1371/journal.pone.0111768

PONE-D-14-15431 [pii].

31. Bhutta ZA; Current concepts in the diagnosis and treatment of typhoid fever. *BMJ* 2006;**333**(7558):78-82. doi: 333/7558/78 [pii]

10.1136/bmj.333.7558.78.

**Table 1 Demographic characteristics of typhoid fever patients in Fiji, 2014-2015**

|  |  |  |
| --- | --- | --- |
| **Demography** | **n/total (%)** | **Mean crude incidence (per 100,000 population)** |
| **Sex** |  |  |
| Male | 285/542 (52.6) | 31.9 |
| Female | 257/542 (47.4) | 29.3 |
| **Ethnicity** |  |  |
| iTaukei | 518/542 (95.6) | - |
| Fijian of Indian Descent | 14/542 (2.6) | - |
| Other | 10/542 (1.8) | - |
| **Age group** |  |  |
| 0-4 | 34/531 (6.4) | 19.3 |
| 5-14 | 84/531(15.8) | 25.6 |
| 15-24 | 147/531(27.7) | 49.1 |
| 25-39 | 139/531(26.2) | 35.8 |
| 40-59 | 108/531(20.3) | 28.2 |
| 60+ | 19/531 (3.6) | 12.0 |
| **Medical Division** |  |  |
| Central | 158/542 (26.2) | 20.8 |
| Eastern | 6/542 (1.1) | 7.6 |
| Northern | 198/542 (36.5) | 74.2 |
| Western | 180/542 (33.2) | 23.8 |
| **Level of management** |  |  |
| Divisional hospital | 206/542 (38.0) | - |
| Sub divisional hospital | 284/542 (52.4)) | - |
| Health centre | 56/542 (10.3) | - |

**Table 2 Clinical and laboratory features of typhoid fever patients in Fiji, 2014-2015**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Features** | **Total**  n/total (%) | **<15 years**  n/total (%) | **≥** **15 years**  n/total (%) | ***P* value** |
| **Signs and symptoms** |  |  |  |  |
| History of fever | 349/360(96.9) | 82/84 (97.6) | 267/276 (96.9) | NS |
| Diarrhoea | 239/357(66.9) | 52/83(62.7) | 187/274(68.2) | NS |
| Loss of appetite | 185/356(52.0) | 48/81(59.3) | 137/275(49.8) | NS |
| Rigors | 182/353(51.6) | 22/81 (27.2) | 160/272 (58.8) | <0.001 |
| Headache | 154/353(43.6) | 18/80(22.5) | 136/273 (49.8) | <0.001 |
| Vomiting | 119/355(33.5) | 25/81 (30.9) | 94/274 (34.3) | NS |
| Abdominal pain | 72/354(20.3) | 20/80(25.0) | 52/274(19.0) | NS |
| Cough | 64/358 (17.9) | 20/83(24.1) | 44/275(17.9) | NS |
| Constipation | 17/360 (4.7) | 6/84(7.1) | 11/276 (4.0) | NS |
| Conjunctival pallor | 80/317(25.2) | 19/73 (26.0) | 61/244(25.0) | NS |
| Jaundice | 31/318(9.7) | 2/72(2.8) | 29/246(11.0) | 0.02¶ |
| Organomegaly† | 8/343 (2.3) | 4/82 (4.9) | 4/261(1.5) | NS ¶ |
| **Haematology** |  |  |  |  |
| Anaemia\* | 135/329 (41.0) | 38/77(49.4) | 97/252(38.5) | NS |
| Leukopenia¥ | 132/332 (39.8) | 36/77(46.8) | 96/255(37.6) | NS |
| Thrombocytopenia‡ | 146/325 (44.9) | 39/75(52.0) | 107/250(42.8) | NS |

NS: not significant

¶ Fisher’s exact test, †Include hepatomegaly and splenomegaly, \*hemoglobin < 11g/dl for under 15 years and hemoglobin <12gm/dl for individuals ≥ years . ¥white blood cell count < 5,000x106cells/L, ‡platelet count <100,000cells/L

**Table 3 Comparison of antimicrobial resistance pattern among *Salmonella* Typhi isolates, Fiji, 2004/05 and 2014/15**

|  |  |  |
| --- | --- | --- |
| **Antimicrobial** | **Resistance( 2004/05)**[**7**](#_ENREF_7)  n/total (%) | **Resistance (2014/15)**  n/total (%) |
| Ampicillin | 3/272(1.1) | 0/544 (0) |
| Chloramphenicol | 2/272 (0.7) | 0/544 (0) |
| Trimethoprim-sulfamethoxazole | 2/263 (0.8) | 0/544 (0) |
| Doxycycline | 3/209 (1.4) | 0/2 (0) |
| Nalidixic acid | 0/207 (0) | 5/361(1.4) |
| Ciprofloxacin | Not done | 3/393(0.8) |