Efficacy of Ceftriaxone and adding Moxifloxacin in treating Enteric fever

IB Reza, MM Rishad, N Noor, KAK Azad, HAM Ahasan, QT Islam

Dr. Ishrat Binte Reza

Assistant professor

Dept of Medicine

PMCH

Introduction

- Enteric Fever (EF) is a human-restricted disease caused by the *Salmonella enterica* serovar Typhi (*S*. Typhi) and Paratyphae (*S*. Paratyphi), which is associated with significant morbidity and mortality when untreated [1].
- The disease is transmitted through a fecal-oral route via contaminated food and water[2].
- It is highly endemic in developing countries, mainly in Asia and Africa [2].
- According to the WHO, the estimated global incidence of EF is about 21 million cases, resulting in more than 200,000 deaths annually[3].
- In Bangladesh estimated incidence rates is 252 per 100,000 people yearly [4].

- In the past, Enteric fever responded extremely well to other types of antimicrobial agents such as chloramphenicol, some of the Fluroquinolones(ciprofloxacin, ofloxacin), cotrimoxazole.
- MDR (*Ampicillin, chloramphenicol, Trimethoprim-sulfamethoxazole*) enteric fever prevalence is around **17% in Bangladesh** [5]
- Recently XDR(*MDR,Fluroquinolones,3rd generation cephalosporin*) enteric fever has become an emerging problem in south Asia mainly (Pakistan, Nepal) and Africa [5].
- Despite all, fortunately Ceftriaxone is a drug of choice for enteric fever in our country till now.
- Currently, single-drug regimens exhibit prolonged fever clearance time (FCT), imposing a great burden to the development of antibiotic resistance and the chronic carriage of the pathogens.

- Despite emergence of resistance to some of fluroquinolones, Moxifloxacin shows sensitivity in culture media.
- Fourth generation Fluroquinolones: Moxifloxacin when combined with a ceftriaxone act synergistically on the intra- and the extra-cellular compartments of the bacteria respectively.
- In this study we had few patients who continued to have a fever above 103°F despite ceftriaxone therapy(2gmi.v 12hrly) for 5 days and we combined oral moxifloxacin(400mg) on 6th day with inj. ceftriaxone regime and assessed their response.
- The aim of our study was to assess the efficacy of ceftriaxone in the treatment of enteric fever and also to observe the response of combined therapy in poor responders.

Objectives:

- 1.To observe anti-microbial sensitivity patterns of salmonella typhae and paratyphae.
- 2.To monitor the efficacy of Ceftriaxone.
- 3. To assess response after adding moxifloxacin in ceftriaxone regime in patients whose fever persisted above 103°F after five days .

Materials and methods

- Study design: Quasi Experimental Study
- Study place: Popular Medical college and Hospital
- Study duration: 6 months(Jul to Dec’23)

- • Inclusion criteria:

Fever for atleast 3 days and blood culture positive for salmonella typhae and paratyphae.

Age > 18yrs

- • Exclusion criteria:

Blood culture negative for salmonella typhae and paratyphae.

Age<18yrs

Pregnancy and lactating mother

Any history of drug hypersensitivity to cephalosporines and fluroquinolones

- Study population: Hospitalized
- Total No: 40 patients

Group A:

Fever below 103°F on 5th day

No of pt 30

Treated with Inj Ceftriaxone alone

Group B:

Fever above 103°F on 5th day

No of patient 10

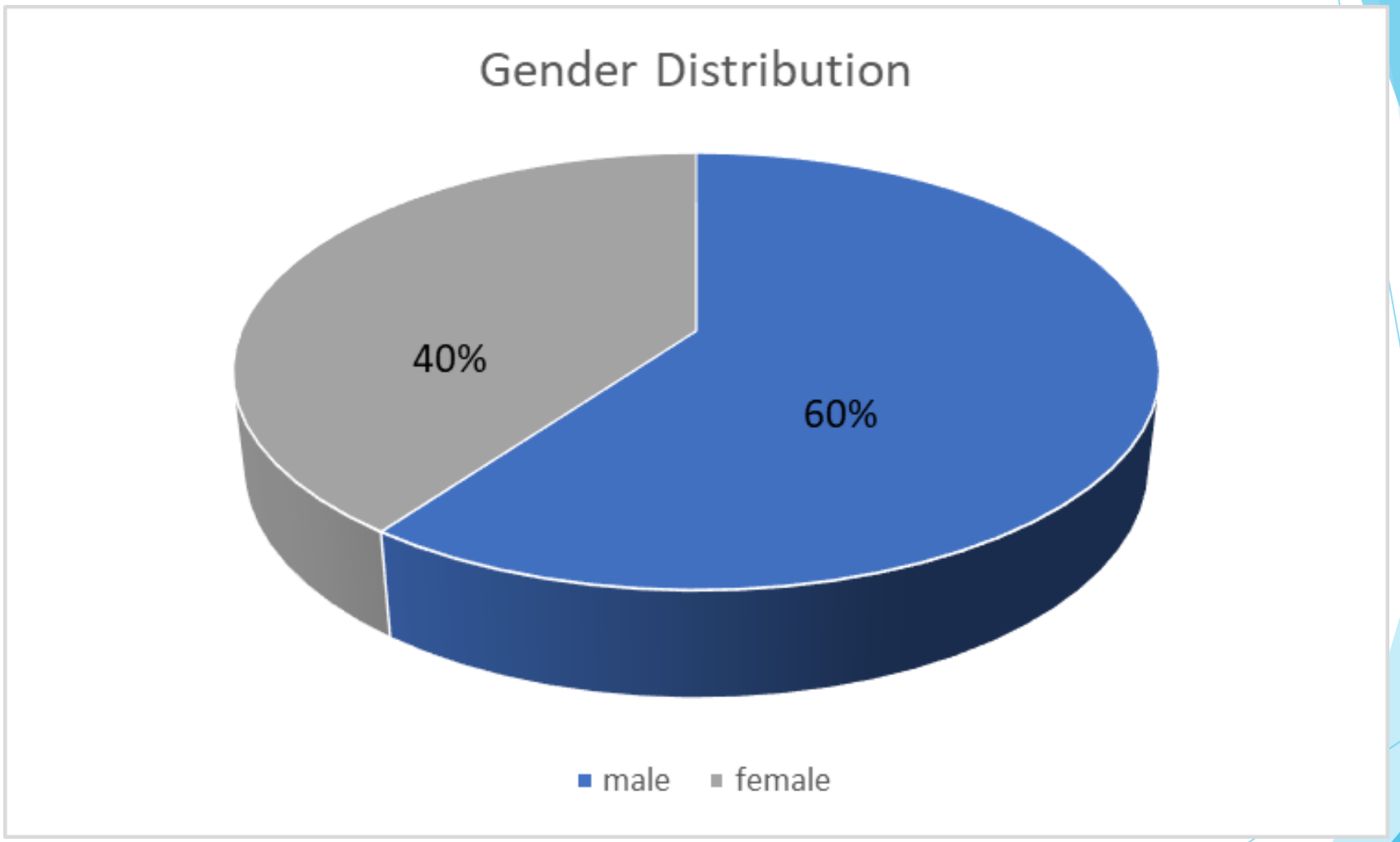
Treated with Inj. ceftriaxone and add on oral moxifloxacin on 6th day

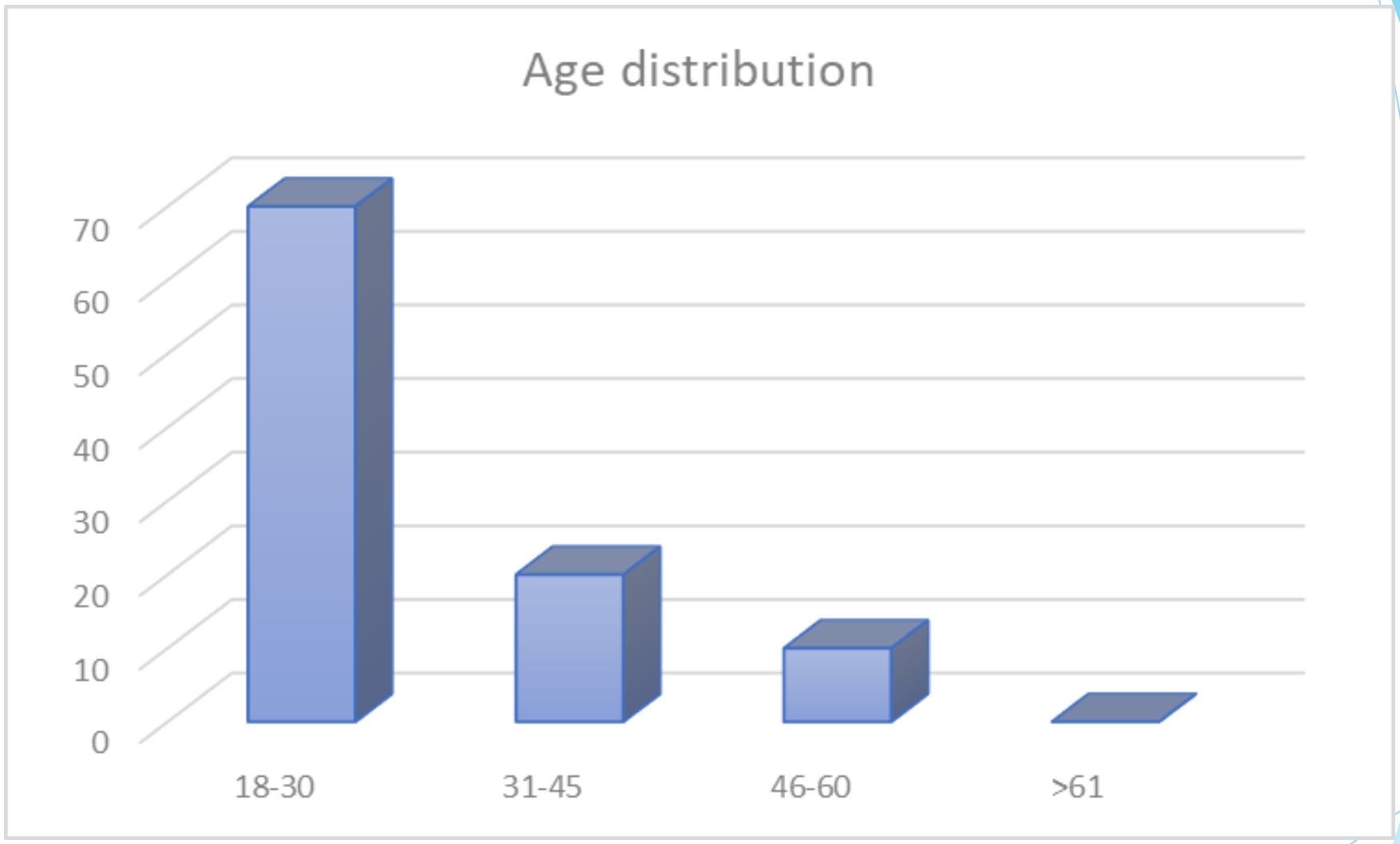
- Operational Definition :

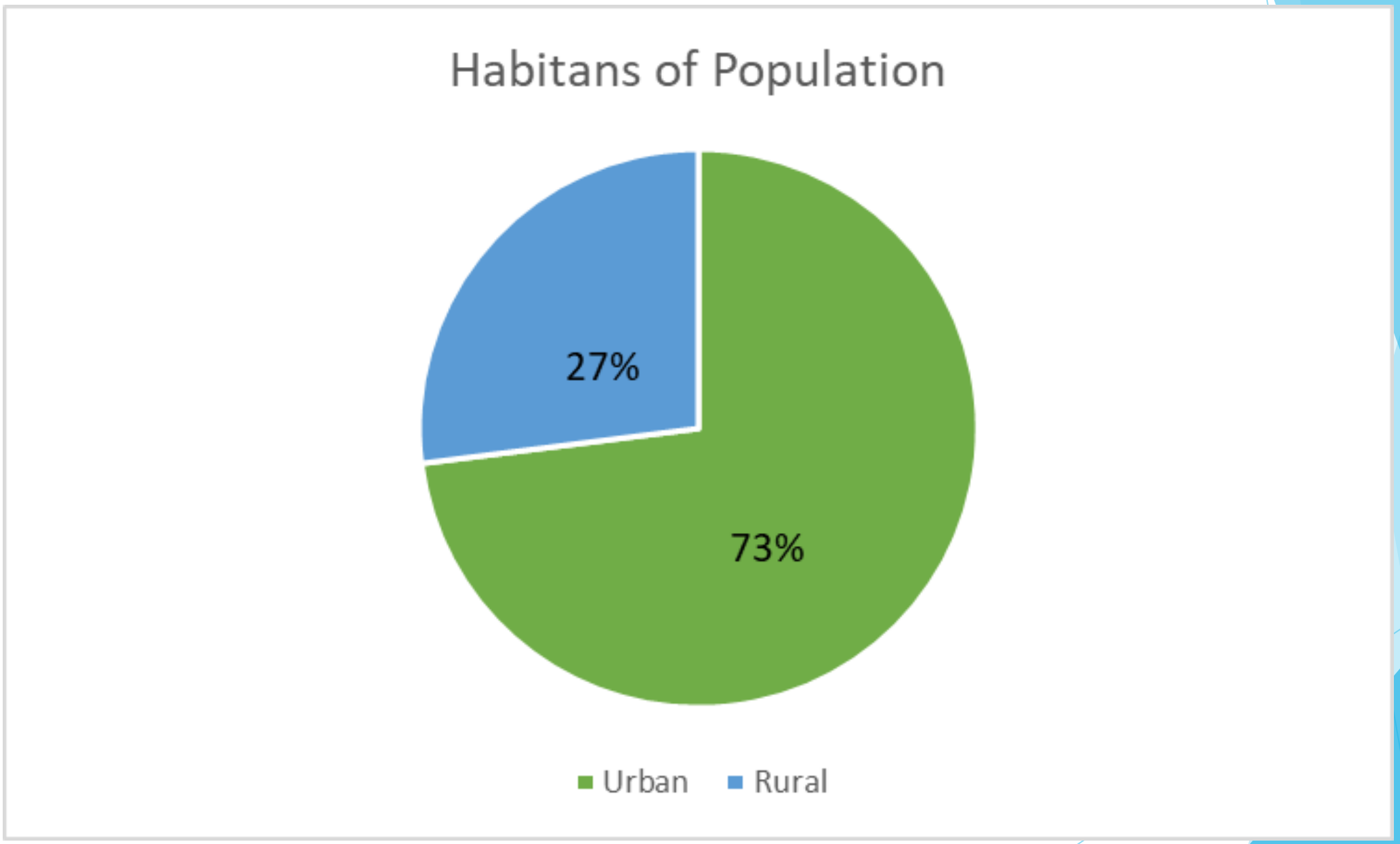
Defervescence: Defined as the number of days required for abatement of fever after starting the antibiotics.

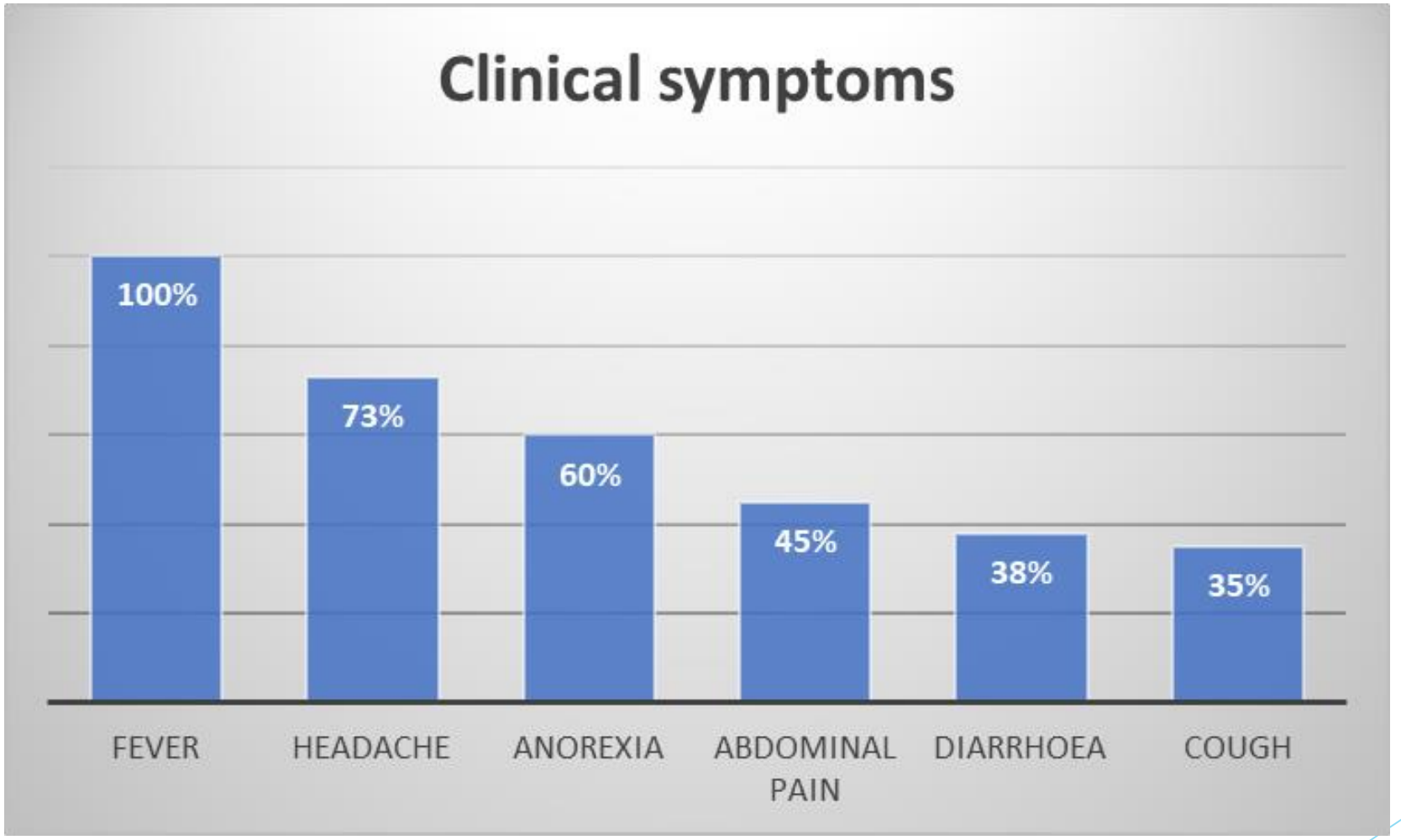
Data Analysis: stat version 16

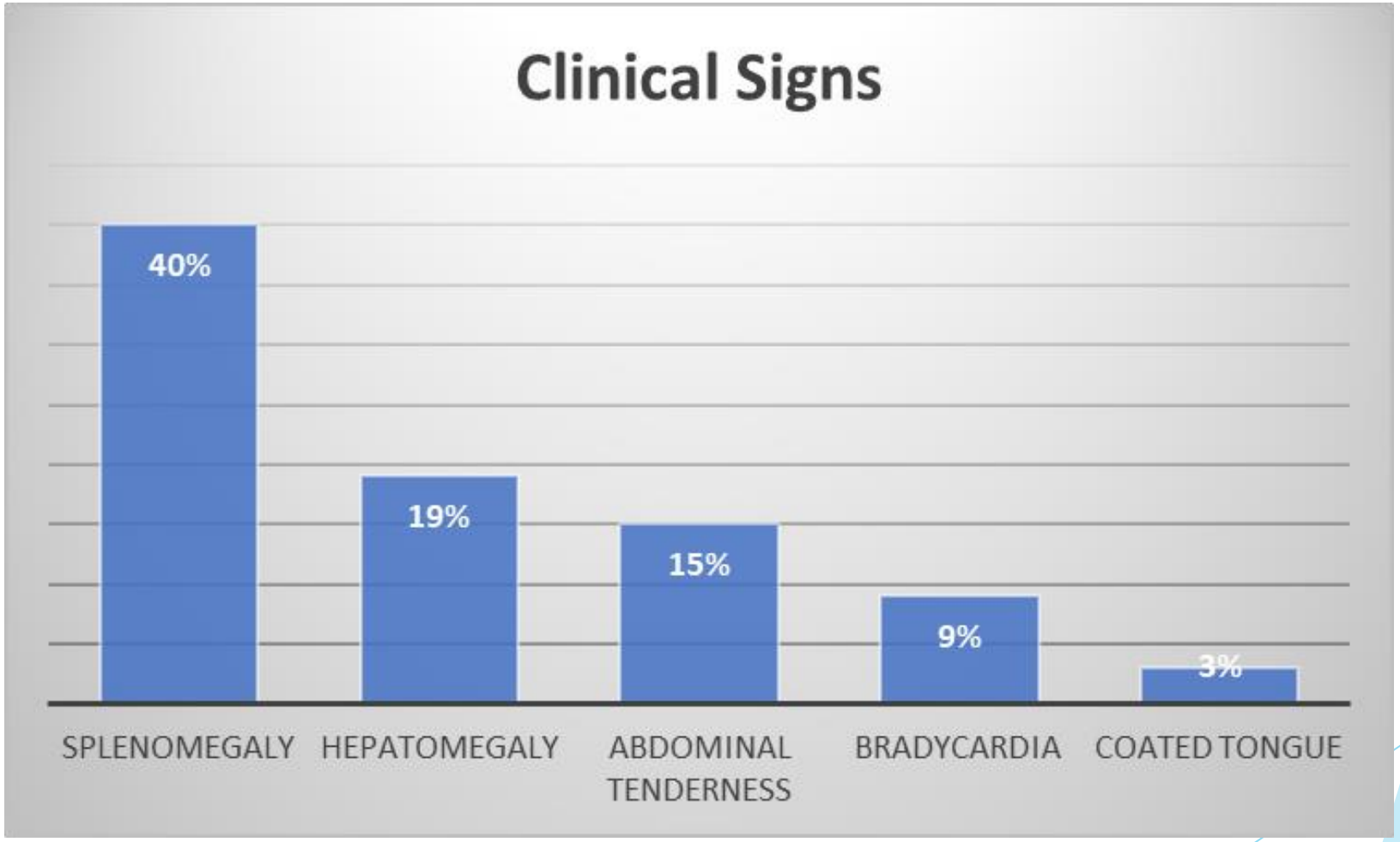
RESULT

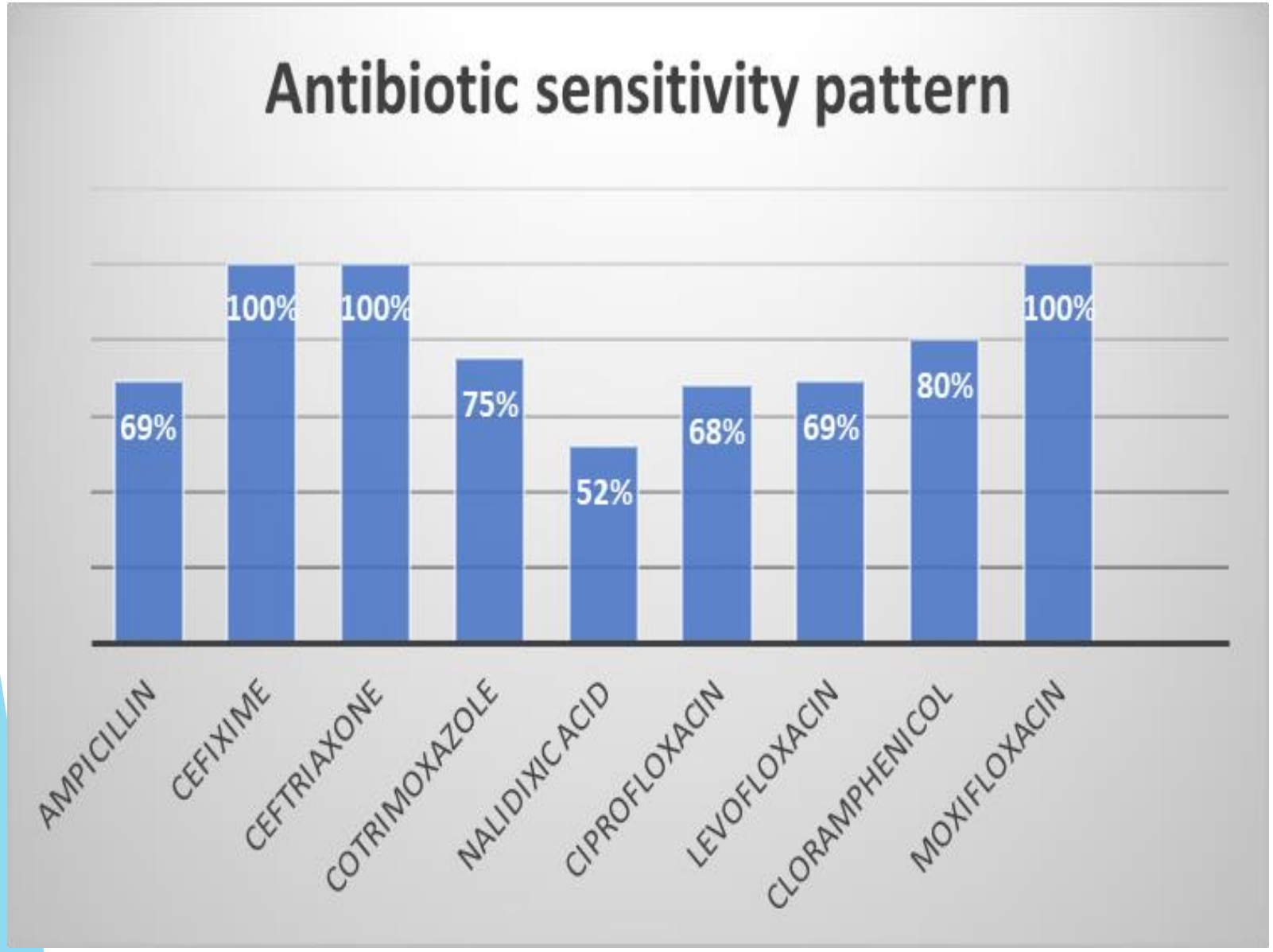

Gender Distribution
40%
60%
male
female


Age distribution
70
60
50
40
30
20
10
0
18-30
31-45
46-60
>61


Habitans of Population
27%
73%
Urban
Rural


Clinical symptoms
100%
73%
60%
45%
38%
35%
FEVER
HEADACHE
ANOREXIA
ABDOMINAL PAIN
DIARRHOEA
COUGH


Clinical Signs
40%
19%
15%
9%
3%
SPLENOMEGALY
HEPATOMEGALY
ABDOMINAL TENDERNESS
BRADYCARDIA
COATED TONGUE



Gender 16 Yrs/Male
Red By PROF. DR. H.A.M. NAZMUL AHASAN, FCPS, FRCP (Glasg), FRCP (Edin), FRCP (London), MACP (USA)
Report Date 20/02/2024
Report Status Final

MICROBIOLOGY REPORT

BLOOD FOR C/S (FAN METHOD)

Identification and susceptibility tests with MIC done by VITEK 2 Compact, Fully Automated Microbial Identification and Antibiotic Susceptibility System (BioMerieux S.A. France).

CULTURE & SENSITIVITY REPORTS

Organism 1 Salmonella ser Typhi

Antibiotic Name	MIC	Interpretation	Break Point
Amikacin	>=2 mcg/ml	Resistant	>=64
Cefixime	<=0.25 mcg/ml	Sensitive	>=4
Cefoxitin	>=4 mcg/ml	Resistant	>=32
Ceftazidime	<=1 mcg/ml	Sensitive	>=16
Ceftriaxone	<=1 mcg/ml	Sensitive	>=4
Ciprofloxacin	1 mcg/ml	Resistant	>=1
Ertapenem	<=0.5 mcg/ml	Sensitive	>=2
Gentamicin	>=1 mcg/ml	Resistant	>=16
Imipenem	<=0.5 mcg/ml	Sensitive	>=4
Meropenem	<=0.5 mcg/ml	Sensitive	>=4
Norfloxacin	2 mcg/ml	Sensitive	>=16
Ofloxacin	1 mcg/ml	Intermediate	>=2
Piperacillin-tazobactam	<=4 mcg/ml	Sensitive	>=128
Trimethoprim/Sulfamethoxazole	<=20 mcg/ml	Sensitive	>=80
Amoxicillin-Clavulanic Acid	<=2 mcg/ml	Sensitive	>=32

Moxifloxacin = Sensitive (Disc diffusion method)

Prof. Dr. Mushtaque Ahmed
FCPS (Micro). M. Phil (Viro). MBBS.
Popular Medical College

By: Md. Sanaullah Printed By: RASHID.M Printed at 20/02/2024 17:30

Day of defervescence of Group A (n=30)

Day of defervescence	No of patients	Percentage
4th	2	7%
5th	5	17%
6th	7	23%
7th	12	40%
8th	3	10%
9th	1	3%

Day of Defervescence of Group B(n=10)

Day of defervescence	No of patients	Percentage(%)
7th	1	10
8th	6	60
9th	3	30

Take home message

- Ceftriaxone is a well-established and effective treatment for enteric fever.
- Response to treatment and time to defervescence is increasing in patients despite highly sensitive ceftriaxone therapy.
- This delay is setting alarm bells for escalating resistance in salmonella. In near future dual therapy may be needed.
- Moxifloxacin can be good choice as an add on therapy.
- While preliminary results are promising, more research is needed.

- References:

1. Tharwani ZH, Kumar P, Salman Y, Islam Z, Ahmad S, Essar MY. Typhoid in Pakistan: Challenges, efforts, and recommendations. Infection and Drug Resistance. 2022 Jan 1:2523-7.
2. Ram PK, Naheed A, Brooks WA, Hossain MA, Mintz ED, Breiman RF, Luby SP. Risk factors for typhoid fever in a slum in Dhaka, Bangladesh. Epidemiology & Infection. 2007 Apr;135(3):458-65.
3. https://www.who.int/news-room/fact-sheets/detail/typhoid
4. Forster DP, Leder K. Typhoid fever in travellers: estimating the risk of acquisition by country. Journal of Travel Medicine. 2021 Dec;28(8):taab150.
5. mora N, Shrestha S, Neuberger A, Paran Y, Tamrakar R, Shrestha A, et al. (2018) Open label comparative trial of mono versus dual antibiotic therapy for Typhoid Fever in adults. PLoS Negl Trop Dis 12(4): e0006380. https://doi.org/10.1371/journal.pntd.0006380

Thank you