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Estimating the incidence rate of enteric (typhoid) fever in India through a multi-center surveillance network of secondary care centers

Submission date
26/03/2020

Recruitment status
No longer recruiting

Registration date
06/05/2020

Overall study status
Completed

Last Edited
09/07/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Enteric fever forms a significant portion of the burden of infectious diseases in developing countries. Caused by Salmonella species (bacteria), it is transmitted through the consumption of food or water contaminated by the excrement of individuals carrying these organisms. Those infected, display symptoms such as fever, weakness, stomach pains, diarrhea or constipation, and rashes. Enteric fever may even be fatal, if left untreated.
In India, this disease still poses a major health risk to the public. Planning measures for its control requires reliable, India-specific epidemiological data on the disease, which is currently lacking. The current study will help fill in such knowledge gaps by estimating the incidence rate and burden of enteric fever occurring at secondary care hospitals in 6 sites across India, over a 24 month period.

Who can participate?
Any patient that has been hospitalized at a healthcare facility involved with the study, who has a fever, and is greater than 6 months of age, irrespective of their gender, may participate. Patients at the study associated healthcare facilities hospitalized with non-traumatic ileal perforations may also participate.

What does the study involve?
At each study hospital. hospitalized patients (> 6 months of age) with a fever or non-traumatic ileal perforations are asked to participate. All participants receive a blood culture. Those whose culture tests positive for either S, Typhi or S. Paratyphi (enteric fever positive) as well as those with ileal perforations, are followed up until the 30th day after their study enrollment to record details such as their treatment, costs and outcomes. The total enteric fever cases that are encountered at each site is then used to calculate the site-specific incidence of the disease. Such surveillance activities will go on for 2 years.
A survey is conducted within clearly demarcated areas at each site. Socio-demographic data as well as details about illnesses/deaths that have occurred in the surveyed households are

collected. This survey will be used to calculate the proportion of those patients who require hospitalization and have a fever but choose non-study hospitals for admission which will in turn be used to adjust the incidence rates for each site.

What are the possible risks and benefits of participating?
The participants will not receive any immediate benefit by taking part in this study. However, the results of this study may help policymakers and researchers better understand how enteric fever can be controlled and therefore lead to its reduction. The participants face no risks by taking part.

Where is the study run from?
1. Rural Development Trust Hospital, Bathalapalli, Andhra Pradesh (India)
2. Post Graduate Institute of Medical Education and Research, Chandigarh (India)
3. Lady Willingdon Hospital, Manali (India)
4. Makunda Christian Leprosy and General Hospital, Bazaricherra (India)
5. Chinchpada Christian Hospital, Navapur (India)
6. Duncan Hospital, Raxaul (India)

When is the study starting and how long is it expected to run for?
February 2018 to April 2020 (updated 25/06/2020, previously: May 2020)

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Dr Jacob John
jacob@nssefi.org

Contact information

Type(s)
Public

Contact name
Dr Jacob John

Contact details
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Type(s)
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Tier2v211072019

Study information

Scientific Title
Surveillance for Enteric Fever in India (SEFI), tier 2 - a hybrid surveillance approach to estimate the burden and incidence of enteric (typhoid) fever in India

Acronym
SEFI

Study objectives
This study aims to estimate the incidence and burden of severe enteric fever in six different settings across India. Such data will enable policymakers to plan suitable control measures against the disease in the country.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 06/12/2017, Postgraduate Institute of Medical Education and Research Institutional Ethics Committee (Room number 6006, 6th floor, Research block B, Post Graduate Institute of Medical Education and Research, Sector 12, Chandigarh, India, 160012; +91 172 2755266; iecpgi@gmail.com), ref: PGI/IEC/2018/000017
2. Approved 15/12/2017, Rural Development Trust Hospital Institutional Ethics Committee (Rural Development Trust Hospital, Bathalapalli, Anantapur, Andhra Pradesh, India, 515661;+91

9177155517; hariharanadha.sarma@gmail.com), ref: RDTHBTP/CERT/ETHICS/2018/002
3. Approved 09/03/2018, Lady Willingdon Hospital Institutional Review Board (Manali, Himachal Pradesh, India, 175131; +91 9816033110; philalex1@gmail.com), ref: LWH/IRB/CL/2018/01
4. Approved 17/11/2017, Emmanuel Hospital Association Institutional Ethics Committee (Emmanuel Hospital Association, 808/92, Deepali Building, Nehru Place, New Delhi, India, 110019; +91 8527747395; jameelageorge@eha-health.org), ref: Protocol Number - 170, Version 2; Protocol number – 168, Version 2; Protocol Number 173, Version 2

Study design
Prospective observational multi-center hybrid surveillance study

Primary study design
Observational

Secondary study design
Hybrid model - hospital based disease surveillance paired with a community based healthcare utilization survey

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Enteric fever

Interventions
The site-specific incidence of enteric fever will be estimated through a hybrid approach - hospital-based surveillance combined with a healthcare utilization survey. Surveillance for enteric fever will be carried out at the designated hospital in each of the six chosen sites, which are the preferred healthcare facilities among their catchment area populations for providing inpatient care for febrile illnesses. All febrile hospitalizations and non-traumatic ileal perforations that occur at these facilities are recruited into the study after collecting informed consent from the patient/patient's parents or guardian. Next, a blood culture is performed and all those recruited patients with a culture positive for either S. Typhi or S. Paratyphi, as well as those who present with a non-traumatic ileal perforation, are followed up until the 30th day after enrollment to document treatment received, costs incurred, and outcome at discharge.

A healthcare utilization study is also carried out in a clearly demarcated catchment area for each of the study hospitals in order to estimate the proportion of febrile patients seeking inpatient care at non-study hospitals. This survey collects data such as socio-demographic characteristics, illness in the past two weeks, and details of hospitalizations and deaths based on a 12-month recall, from approximately 5,000 households (25,000 individuals) in each site's catchment area, via a questionnaire.

Intervention Type

Other

Primary outcome measure
Incidence of enteric fever in each of the study sites over the 24 months of surveillance measured by dividing the number of blood culture-confirmed enteric fever cases with the product of the hospital's catchment population and time period of surveillance. This crude incidence shall then be adjusted for the proportion of febrile patients from the catchment population seeking inpatient healthcare at other facilities, compliance to the study protocol, the sensitivity of blood culture and the probability of enteric fever patients being hospitalized.

Secondary outcome measures
1. Characterization of the clinical spectrum of enteric fever presenting at smaller (<350 beds) hospitals over the 24 months of surveillance- determined through estimating the prevalence of enteric fever among those hospitalized with a febrile illness, the prevalence of complications and severe disease among those presenting to surveillance facilities with enteric fever, and prevalence of antimicrobial resistance among S. Typhi/S. Paratyphi isolates
2. Estimates of the cost of treatment and productivity loss associated with a severe enteric fever over the 24 month period of surveillance- determined through calculating direct and indirect cost-of-illness for severe enteric fever and indebtedness directly attributable to the severe enteric fever illness episodes

Overall study start date
25/04/2017

Completion date
22/04/2020

Eligibility

Key inclusion criteria
For the hospital-based surveillance:
1. Age: greater than six months of age
2. Gender: Both
3. Patients presenting with fever who are hospitalized irrespective of the duration of fever or temperature
4. Patients with non-traumatic ileal perforation irrespective of history of fever or culture confirmation of typhoid

For the healthcare utilization survey:
1. All those who normally reside and are present in the household during the entire period of survey – from the first day of survey to the last day of survey (both days inclusive).
2. All those who were known to be normally residing and had actually stayed in the household during a part of the survey (from the first day of survey to the last day of survey) but were not present at the time of visit of the interviewer.
3. All those who were known to be normally residing in the household and were not present at the time of visit of the enumerator but are expected to return by the last day of survey.
4. Age: all
5. Gender: both

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
150,000

Total final enrolment
137990

Key exclusion criteria
For the hospital-based surveillance:
1. Patients who are not Indian citizens

For the healthcare utilization survey:
1. Visitors to the household

Date of first enrolment
26/02/2018

Date of final enrolment
07/04/2020

Locations

Countries of recruitment
India

Study participating centre
Rural Development Trust Hospital
Kadiri Road
Anantapuramu district
Bathalapalli
India
515661

Study participating centre
Post Graduate Institute of Medical Education and Research
Sector-12
Chandigarh
India
160012

Study participating centre
Lady Willingdon Hospital
Kullu district
Manali
India
175131

Study participating centre
Makunda Christian Leprosy and General Hospital
Karimganj District
Bazaricherra
India
788727

Study participating centre
Chinchpada Christian Hospital
Chinchapads
Nandurbar District
Taluka Navapur
India
425417

Study participating centre
Duncan Hospital
East Champaran District
Raxaul
India
845305

Sponsor information

Organisation
Vellore Christian Medical College Foundation

Sponsor details
Ida Scudder Road
Vellore
India
632004
+91 04162282052
wellcome@cmcvellore.ac.in

Sponsor type
University/education

Website
https://www.vellorecmc.org/

ROR
https://ror.org/020y1sx51

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/09/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author, Dr Jacob John (jacob@nssefi.org), 6 months after the final participant is enrolled into the study. Any requesting party with an analysis plan for the data will be given access. Data analysed as part of the primary results paper shall be made available along with the publication. All data shall be anonymized prior to analysis/sharing. Consent is obtained from all participants.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		23/11/2021	04/03/2022	Yes	No
Results article		20/04/2023	20/04/2023	Yes	No
Protocol file	version 2.0	29/05/2019	09/07/2024	No	No