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'The Superbug is under surveillance' : AMR surveillance tool and proposed solution to fill the gaps in India

by

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PG/21/044

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Post Graduate Diploma in Hospital & Health Management 2021-2023



International Institute of Health Management Research New Delhi

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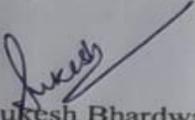
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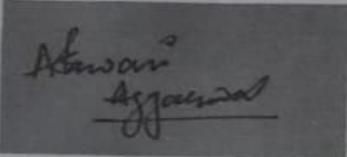
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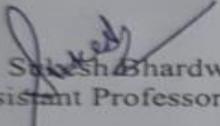

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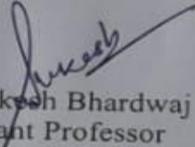
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This is to certify that Ms. Jyoti Yadav student of PGDM (Hospital & Health Management) from International Institute of Health Management Research, New Delhi has undergone internship training at PwC, India from 23rd January 2023 to 21st April 2023.

The Candidate has successfully carried out the study designated to her during internship training and her approach to the study has been sincere, scientific and analytical.

The Internship is in fulfillment of the course requirements. I wish him all success in all his/her future endeavors.

Dr. Sumesh Kumar
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IIHMR, New Delhi


Dr. Suveen Bhardwaj
Assistant Professor
IIHMR, New Delhi

Aknowledgement

I would like to take the opportunity to devote my thanks and express deep sense of gratitude to my IIHMR mentor **Dr. Sukesh Bharadwaj (Assistant Professor)** and organization mentor **Dr. Ashwani Aggarwal (Director, Healthcare team)** and **Dr. Kuntal Mukherjee (Manager)**. I am highly thankful to **Dr. Rana Mehta (Partner- Healthcare)** for providing me the opportunity to work on this assignment. I am greatly indebted to them for providing their valuable guidance, advice, constructive suggestions, positive and supportive attitude and continuous encouragement, without which it would have not been possible to complete the project.

I owe my wholehearted thanks and appreciation to the entire **PwC Healthcare team**

I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards community in coming future.

Jyoti Yadav

TABLE OF CONTENT

| S.No | Content | Page No |
|------|------------------------------|---------|
| 1 | Organization Profile | 7 |
| 2 | Introduction | 8 |
| 3 | Background | 8 |
| 4 | Review of Literature | 9-10 |
| 5 | Objectives | 9 |
| 6 | Research Design &Methodology | 11 |
| 7 | Result and Analysis | 11-20 |
| 8 | Discussion | 21 |
| 10 | Conclusion | 21 |
| 11 | References | 22-23 |

LIST OF FIGURE AND TABLE

| S.No | Figures and tables |
|------|--|
| 1 | Figure 1.1 Dashboard on burden of disease |
| 2 | Table 1.1 to 1.6 are on Burden of antimicrobial resistance |
| 3 | Fig 2.1 GLASS Enrollment |
| 4 | Fig 2.2 Workflow from regional to international level |
| 5 | Fig 2.3 WHONET software model |
| 6 | Fig 2.4 Hospital acquired infection dashboard |
| 7 | Fig 4.1 Vision of Healthcare surveillance |

ORGANISATION PROFILE



PwC, India is a community of solvers combining human ingenuity, experience and technology innovation to deliver sustained outcomes and build trust.

PricewaterhouseCoopers International Limited is a British multinational professional services brand of firms, operating as partnerships under the **PwC** brand. It is the second-largest professional services network in the world and is considered one of the Big Four accounting firms, along with Deloitte, EY and KPMG.

PwC firms are in 157 countries, across 742 locations, with 328,000 people. As of 2019, 26% of the workforce was based in the Americas, 26% in Asia, 32% in Western Europe and 5% in Middle East and Africa. The company's global revenues were \$50.3 billion in FY 2022, of which \$18.4 billion was generated by its Assurance practice, \$20.7 billion by its Tax and Legal practice and \$11.6 billion by its Advisory practice.

In 2014, Google announced its partnership with PwC to drive cloud adoption among businesses. Partnering with Google is part of PwC's decision to begin to move its own business to the cloud. PwC is one of three million business customers using paid services through Google Workspace, previously known as G Suite and Apps for Work.

PwC partners with the United Nations to help keep the international organization's monitoring systems up to date. PwC is also one of the founding partners with the UN Women HeForShe IMPACT 10x10x10 Initiative, launched in 2015, to advance gender equality. The initiative created an online course which aims to increase awareness of unconscious gender bias in corporate life.



Sanjeev Krishan is Chairperson of PwC in India. Previously, he served as the Deals leader. Sanjeev has been with the firm for 29 years, having joined in 1991 as an articled trainee. He became a partner in 2006 and has successfully led the firm's Transactions, Private Equity and Deals business over the years, getting the firm to a pre-eminent position amongst its Private Equity clients and their investee companies. Sanjeev has served in diverse leadership and client service roles and has extensive India and overseas experience in Deals work across a range of sectors, such as technology, consumer and industrial products. Among his prior roles, he was a member of the team that set up the **Transaction Services** practice in India, and has spearheaded the relationship with most global private equity funds, personally looking to raise the firm's focus on numerous funds. Sanjeev did a brief stint with PwC Sweden as part of an International Exchange programme, where he worked with several Private Equity funds and Corporate clients, mostly on cross-border deals.

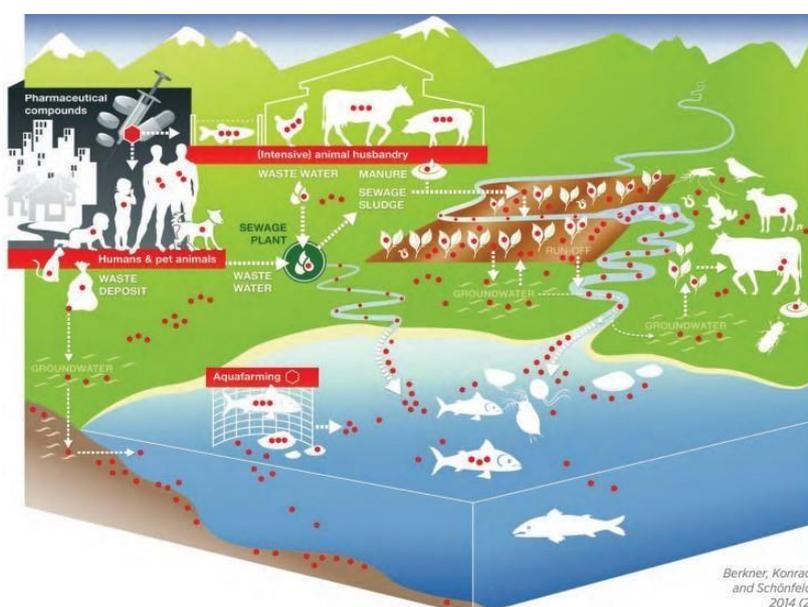
Recently in March 2023 the firm celebrated 150 years of existence.



INTRODUCTION

Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. AMR occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death. As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others. Antimicrobials - including antibiotics, antivirals, antifungals and antiparasitics - are medicines used to prevent and treat infections in humans, animals and plants. Microorganisms that develop antimicrobial resistance are sometimes referred to as “superbugs” (1). <https://www.who.int/health-topics/antimicrobial-resistance>

Antimicrobial resistance is mainly driven by inappropriate use. Global antibiotic consumption in humans has increased by 36% between 2000 and 2010.1 Half of this increased use is regarded as unnecessary, e.g. when antibiotics are used to treat illnesses like common colds that are caused by viruses, where antibiotics have no effect. In many countries, antibiotics can be bought without prescription or do not have underlying standard treatment guidelines. These factors increase antibiotic resistance because of a lack of knowledge of proper antibiotic use (2). https://www.wipo.int/edocs/mdocs/mdocs/en/wipo_who_wto_ip_ge_16/wipo_who_wto_ip_ge_16_inf_2.pdf



Addressing AMR is integral to achieving the Sustainable Development Goals (SDGs). Progress in many of the goals (e.g. improved access to clean water and sanitation, sustainable consumption and production such as more sustainable food production, and appropriate use of antimicrobials in humans and animals) will help to address AMR. However, at the same time, rising levels of AMR will make it more difficult to achieve the goals for health, poverty reduction, food security and economic growth. There is increasing recognition of the relationships between human health, animal health, plant production, food safety and environmental sectors, in both the evolution of the AMR problem and solutions to that problem. To adequately address AMR, it is therefore necessary to take a “One Health” approach, with integrated action from all sectors.

The important antimicrobial bacteria *ESKAPE*, encompassing *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and other *Enterobacter* species.



People living in poverty are more prone to infectious diseases, and resistant infections are more likely to spread in poor living conditions.

AMR in animals increases costs of animal health, infections become untreatable, production decreases and working animals cannot carry out their tasks, affecting the livelihood of farmers and food security.

Lack of access to adequate WASH services is giving rise to the spread of infectious diseases.

RATIONALE OF THE STUDY

1. AMR could push 28.3 million people could be pushed into extreme poverty by 2050 due to high costs of treatment and chronic infections & will loss 4% of GDP.

2. In the fiscal year of 2018–2019 India exported antibiotic ingredients and medicines for a value of **2.4 billion USD**, compared to 268 million USD in 1996–1997. In 2015, study found **the polluted lakes harbored** considerably high proportion of ciprofloxacin resistant and sulfamethoxazole- resistant bacteria. About **80-90% of the world's antibiotics** are made in factories in India and China.

3. India has a large burden of infectious diseases and is one among the largest consumers of antibiotics in the world¹. The efficacy of several antibiotics is threatened by the emergence of resistant microorganisms. Multiple interlinked factors including high burden of disease, poor public health infrastructure, lack of appropriate diagnostic support, poor infection control practices and the tendency of clinicians to continue empirical treatment practices, amplified AMR. Hence a surveillance tool is needed.

OBJECTIVES

PRIMARY:

1. To study the surveillance system in India for Antimicrobial resistance and fill the gaps with proposed solution.

SECONDARY:

1. To estimate the burden of antimicrobial resistance across globe.
2. To define and describe the NARS-Net and ICMR surveillance network and the necessary finding on AMR in India.
3. To conduct SWOT analysis for gaps in the surveillance system.
4. To propose solution to strengthen the surveillance of AMR using current network in India.

REVIEW OF LITERATURE

1. Walia k, et.al (Feb 2013): The Indian Council of Medical Research, in 2013, initiated the Antimicrobial Resistance Surveillance & Research Network (AMRSN) to enable compilation of data on six pathogenic groups on antimicrobial resistance from the country. The overarching aim of this network was to understand the extent and pattern of antimicrobial resistance (AMR) and use this evidence to guide strategies to control the spread of AMR. This article describes the conception and implementation of this AMR surveillance network for India. Also described are the challenges, limitations and benefits of this approach. Data from the Network have shown increasing resistance in Gram-negative bacteria in the hospitals that are part of this network. Combined resistance to third-generation cephalosporins and fluoroquinolones and increasing carbapenem resistance are worrisome, as it has an important bearing on the patients' outcome and thus needs to be addressed urgently. Data generated through this Network have been used to develop treatment guidelines, which will be supportive in harmonizing treatment practices across the tertiary level healthcare institutions in the country. While, the major benefit of having a surveillance system is the collection of real-time accurate data on AMR including the mechanisms of resistance, representativeness to community.

2. NCDC: Under the programme, National AMR Surveillance network (NARS-Net has been established to determine the magnitude and trends of AMR in different geographical regions of the country. The network labs, which include government medical colleges, are supported for capacity building under NARS-Net and are required to submit AMR surveillance data of seven priority bacterial pathogens of public health importance: *Staphylococcus aureus*, *Enterococcus* spp., *Klebsiella* spp., *Escherichia coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*/ *Acinetobacter calcoaceticus* complex, *Salmonella enterica* serotypes Typhi and Paratyphi. Since the year 2020-21, AMR Surveillance has been expanded to include *Candida* spp, from bloodstream infections. Two more bacterial pathogens have been included in the priority pathogens list for AMR surveillance in 2023 namely *Shigella* species and *Vibrio cholerae*.

3. Nan Zohu (Aug 2022): The average GOHI-AMR score for 146 countries is 38.45. As expected, high-income countries (HICs) outperform the other three income groups on overall rankings and all five key indicators of GOHI-AMR, whereas low-income countries unexpectedly outperform upper-middle-income countries and lower-middle-income countries on the

antibiotics-resistant key indicator (ARR) and ARR-subordinate indicators, including carbapenem-, β -lactam-, and quinolone resistance, and even HICs on aminoglycoside resistance. There were no significant differences among the four groups on the environmental-monitoring indicator ($P > 0.05$). GOHI-AMR was positively correlated with gross domestic product, life expectancy, and AMR-related publications, but negatively with natural growth rate and chronic respiratory disease. In contrast to Cyprus, the remarkably lower prevalence of "ESKAPE pathogens" in high-scoring Sweden and Denmark highlights Europe's huge gaps. China and Russia outperformed the other three BRICS countries on all key indicators, particularly India's ARR and Brazil's AMR laboratory network and coordination capacity. Furthermore, significant internal disparities in carbapenem-resistant *Klebsiella pneumoniae* (CRKP) and methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence were observed between China and the USA, with MRSA prevalence both gradually declining, whereas CRKP prevalence has been declining in the USA but increasing in China, consistent with higher carbapenems-related indicator performance in USA.

4. Marol. L. Bayot (2022): Antimicrobial susceptibility testing (AST) is a laboratory procedure performed by medical technologists (clinical laboratory scientists) to identify which antimicrobial regimen is specifically effective for individual patients. On a larger scale, it aids in the evaluation of treatment services provided by hospitals, clinics, and national programs for the control and prevention of infectious diseases. Recently, researchers have had to implement continuous surveillance activities for resistance patterns due to the mutations in bacterial DNA.

5. Kaur J (2021): Growing resistance to antimicrobials has become an important health issue of the 21st century. Many international, national and local approaches are being employed for the control and prevention of antimicrobial resistance (AMR). Among them, surveillance is reported to be the best method to reduce the spread of infection and thereby AMR. An integral component of AMR surveillance is the informatics suite for collection, storage and analysis of surveillance data. *i*-AMRSS is a robust, comprehensive, modular, extensible and intelligent open-source tool piloted in ICMR's AMR Network (31 hospitals and laboratories across India) since 2016. The developed tool has collected more than 280 000 patient records to date.

6. Aggarwal A(2009): The most attractive feature of WHONET is the ability to analyze stored data. The program has a modular configuration that allows customization of software for clinical, epidemiological, and infection control applications. From a single screen, a WHONET user can select the type of analysis to run, the species of bacteria to analyze, the subsets of isolates to include (e.g., all, isolates from urine only, and isolates resistant to gentamicin and from certain locations), and the antimicrobial agents and period to examine. Type of analysis include percentage of data categorized as resistant, intermediate, or susceptible by standard or other breakpoints; distributions of test measurements (zone diameter, minimal inhibitory concentration) in the form of histograms, scatterplots and regression curves besides comparing measurements for different agents or methods for the same isolates.

7. Lancet (2019): Based on predictive statistical models, there were an estimated 4.95 million (3.62–6.57) deaths associated with bacterial AMR in 2019, including 1.27 million (95% UI 0.911–1.71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-Saharan Africa, at 27.3 deaths per 100 000 (20.9–35.3), and lowest in Australasia, at 6.5 deaths (4.3–9.4) per 100 000. Lower respiratory infections accounted for more than 1.5 million deaths associated with resistance in 2019, making it the most burdensome infectious syndrome. The six leading pathogens for deaths associated with resistance (*Escherichia coli*, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) were responsible for 929 000 (660 000–1 270 000) deaths attributable to AMR and 3.57 million (2.62–4.78) deaths associated with AMR in 2019. One pathogen–drug combination, methicillin-resistant *S aureus*, caused more than 100 000 deaths attributable to AMR in 2019, while six more each caused 50 000–100 000 deaths: multidrug-resistant excluding extensively drug-resistant tuberculosis, third-generation cephalosporin-resistant *E coli*, carbapenem-resistant *A baumannii*, fluoroquinolone-resistant *E coli*, carbapenem-resistant *K pneumoniae*, and third-generation cephalosporin-resistant *K pneumoniae*.

8. Niti Aayog Vision 2035 on surveillance: An interdependent federated system of Governance Architecture between the Centre and States 2. Enhanced use of new data collection and sharing mechanisms for surveillance based on unitized, citizen-centric comprehensive Electronic Health Records (EHR) with a unique health identifier (UHID). As well, existing disease surveillance data and information from periodic surveys will complement this information 3. Enhanced use of new data analytics, data science, artificial intelligence, and machine learning, and 4. Advanced health informatics.

METHODOLOGY:

The study is secondary research (Descriptive). Involved mixed approach of Team meetings, Documents review and process mapping.

Research design- This is a secondary research paper that will rely on the analysis of data collected from the web sources (PubMed, Google scholar, WHO and ICMR & NCDC reports).

Data collection- The data for the study is collected from web based and WHO website and ICMR reports. Also, to drive to an integrated solution after analysis.

Data Analysis & data visualization- Tools used are Draw io, MS-Excel, Power BI.

Duration- 2 months

Search terms - Antimicrobial resistance, surveillance, AMR detection & Antibiotic susceptibility testing, AMRSS and India.

RESULT AND ANALYSIS

OBJECTIVE 1: To estimate the burden of antimicrobial resistance across globe.

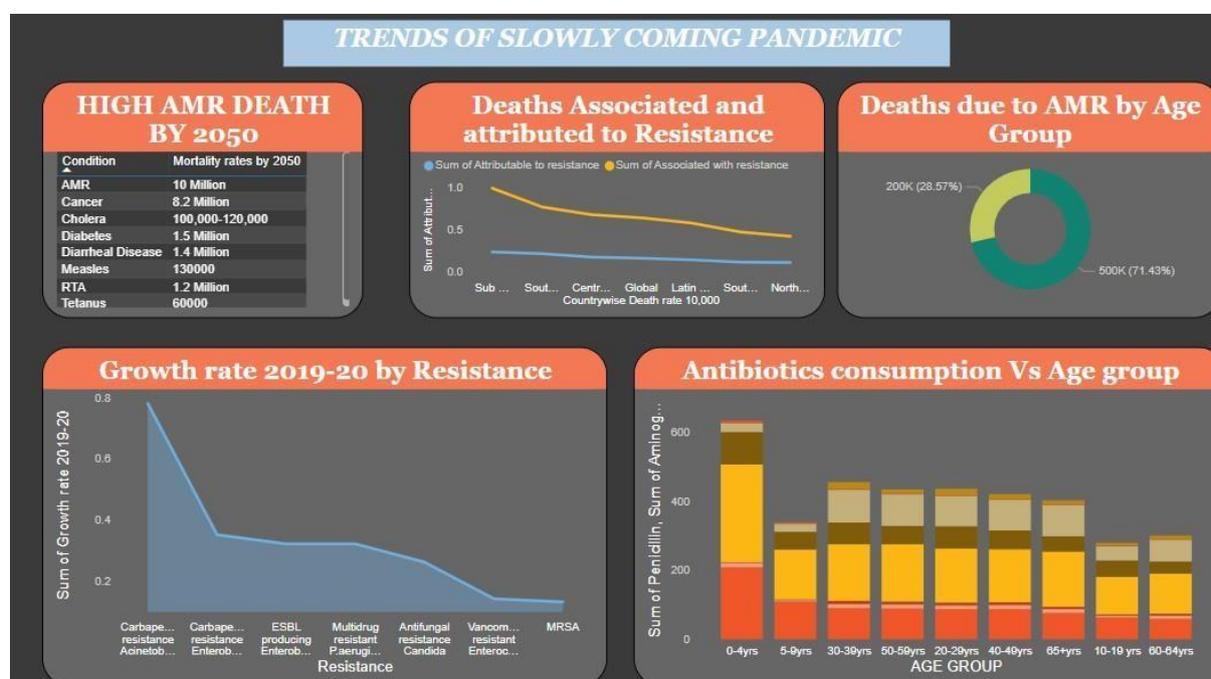


Fig (1.1)- Represents the trends in antimicrobial resistance globally:

1. Overcome all disease by 2050 and cause 10 million deaths.
2. Sub Saharan area followed by South Asian region posses high burden of the disease.
3. 0-4 yrs. possess high burden of the resistance and are even high consumers of antibiotics.
4. Carbapenems- resistant Acinetobacter has shown huge growth rate during 2019-20.

TABLE 1.1

| Condition | Mortality rates by 2050 |
|-------------------|-------------------------|
| Cancer | 8.2 Million |
| Cholera | 100,000-120,000 |
| Diabetes | 1.5 Million |
| Diarrheal Disease | 1.4 Million |
| Measles | 1,30,000 |
| RTA | 1.2 Million |
| Tetanus | 60,000 |
| AMR | 10 Million |

TABLE 1.2

| AGE GROUP | Deaths due to AMR |
|-----------|-------------------|
| All | 5,00,000 |
| Under 5yr | 2,00,000 |

TABLE 1.3

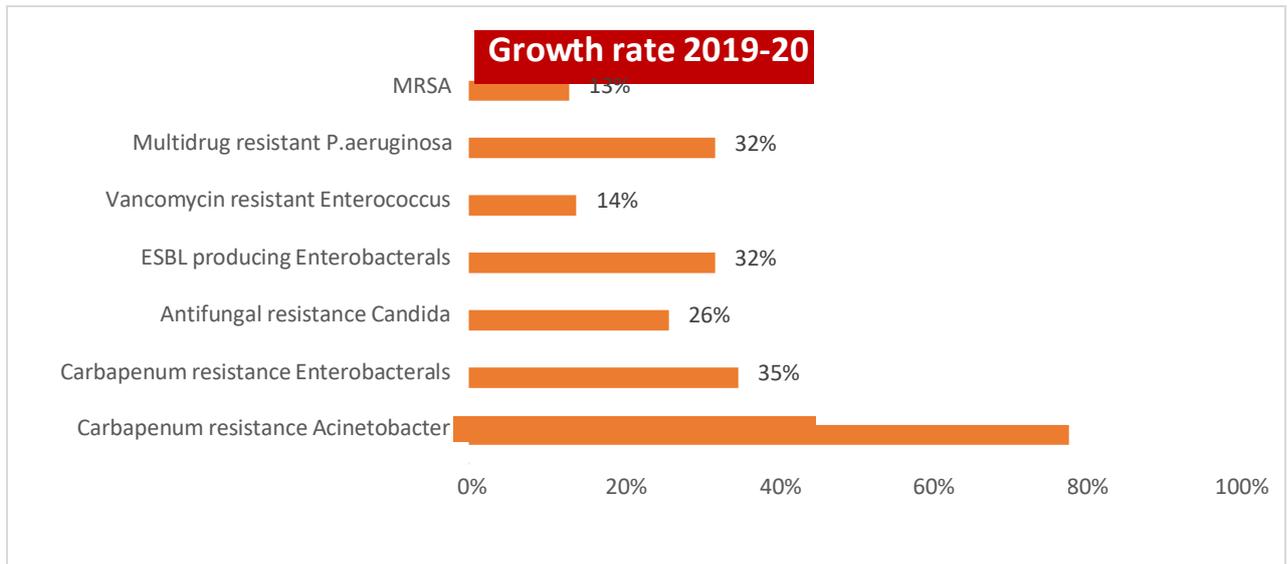


TABLE 1.4

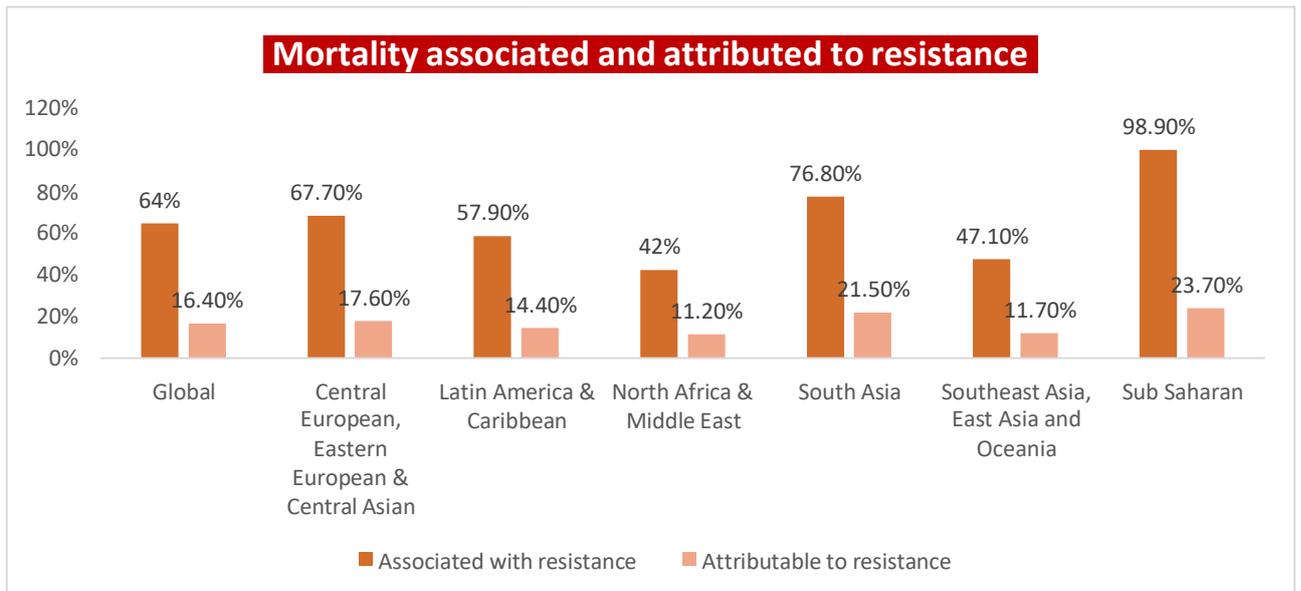


TABLE 1.5

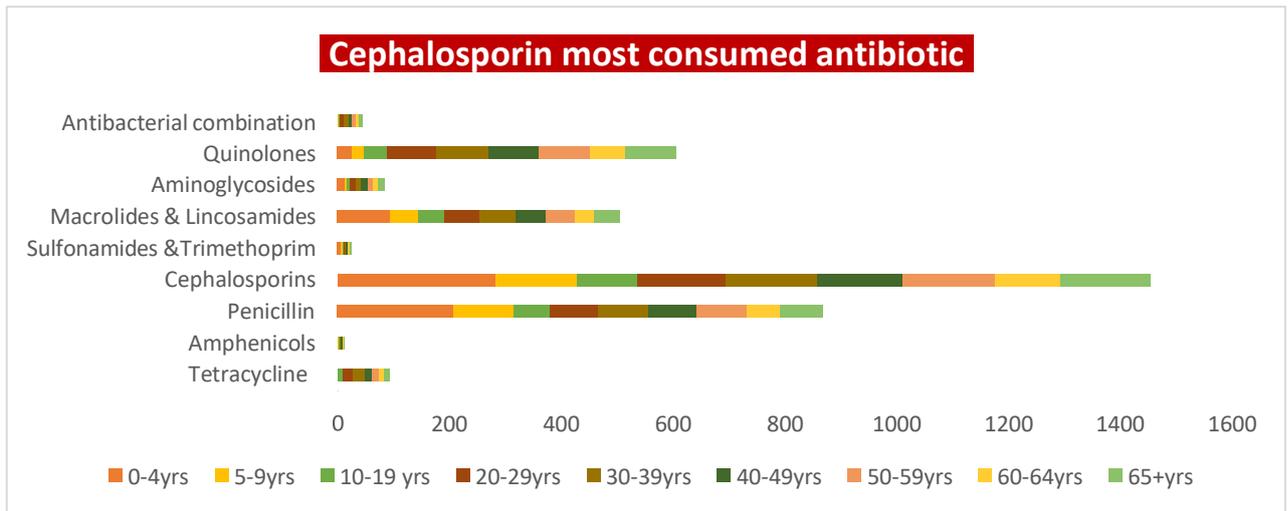
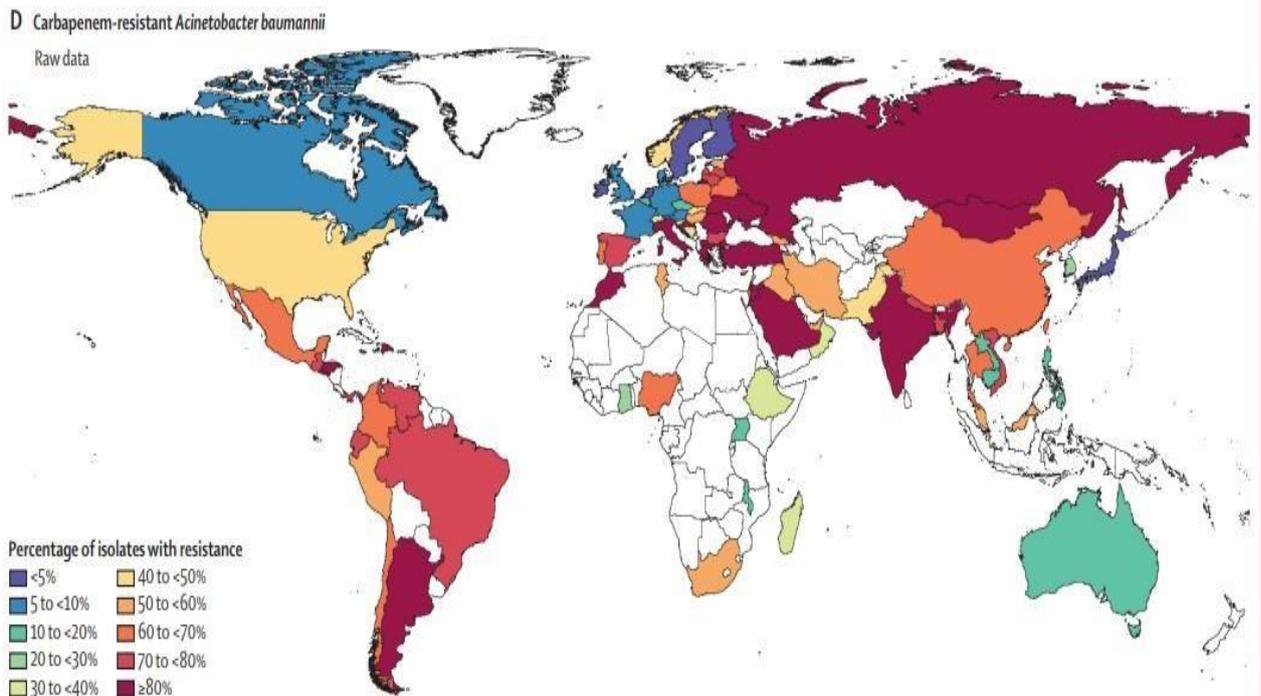


TABLE 1.6

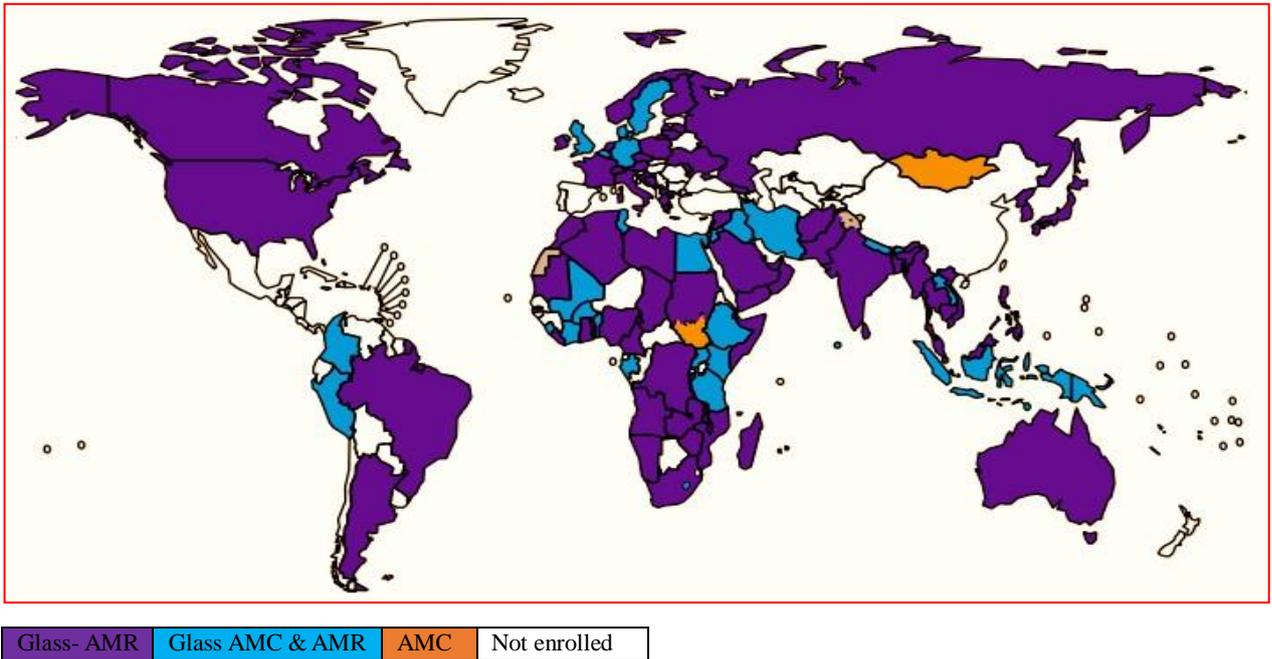
| COUNTRY | Drug Resistance Index | MRSA | 3rd generation Cephalosporin resistant E.coli | Carbapenum resistant klebsiella pneumoniae | 3rd generation Cephalosporin resistant to Klebsiella pneumoniae | Fluoroquinolones resistant E.coli | Carbapenum resistant Acinetobacter Baumannii |
|--------------|-----------------------|------|---|--|---|-----------------------------------|--|
| India | 71 | >50% | >50% | >50% | >50% | >50% | >80% |

The table 1.6 depicts that India has highest Drug resistance of 71 followed by it has heavy burden of all superbugs among which Acinetobacter Baumannii >80%. We really need a robust surveillance system.



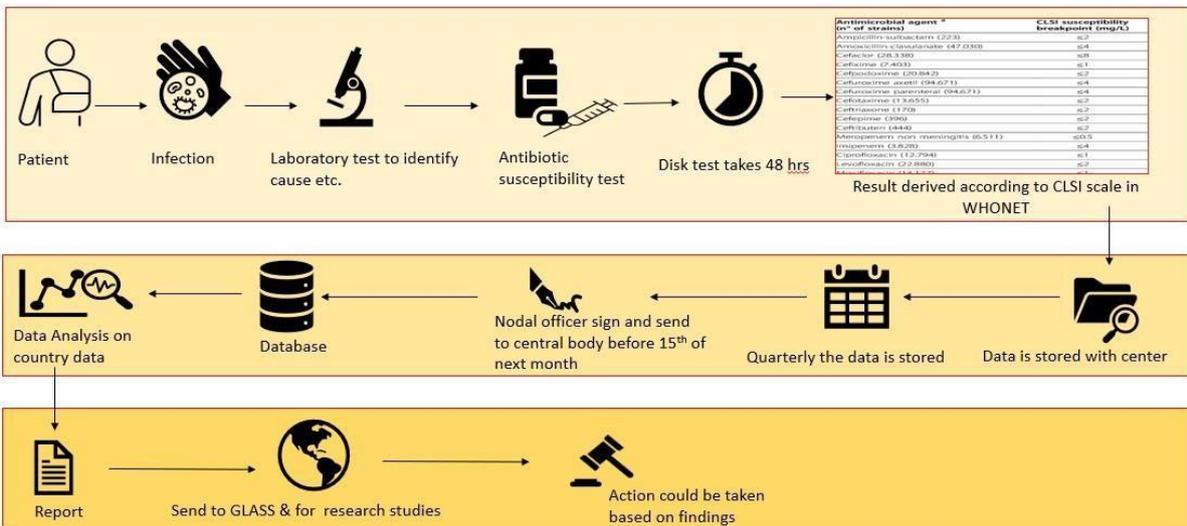
OBJECTIVE 2: To study the NARS-Net and ICMR surveillance network and the necessary finding on AMR in India.

GLASS Global Antimicrobial Resistance Surveillance System (fig 2.1)



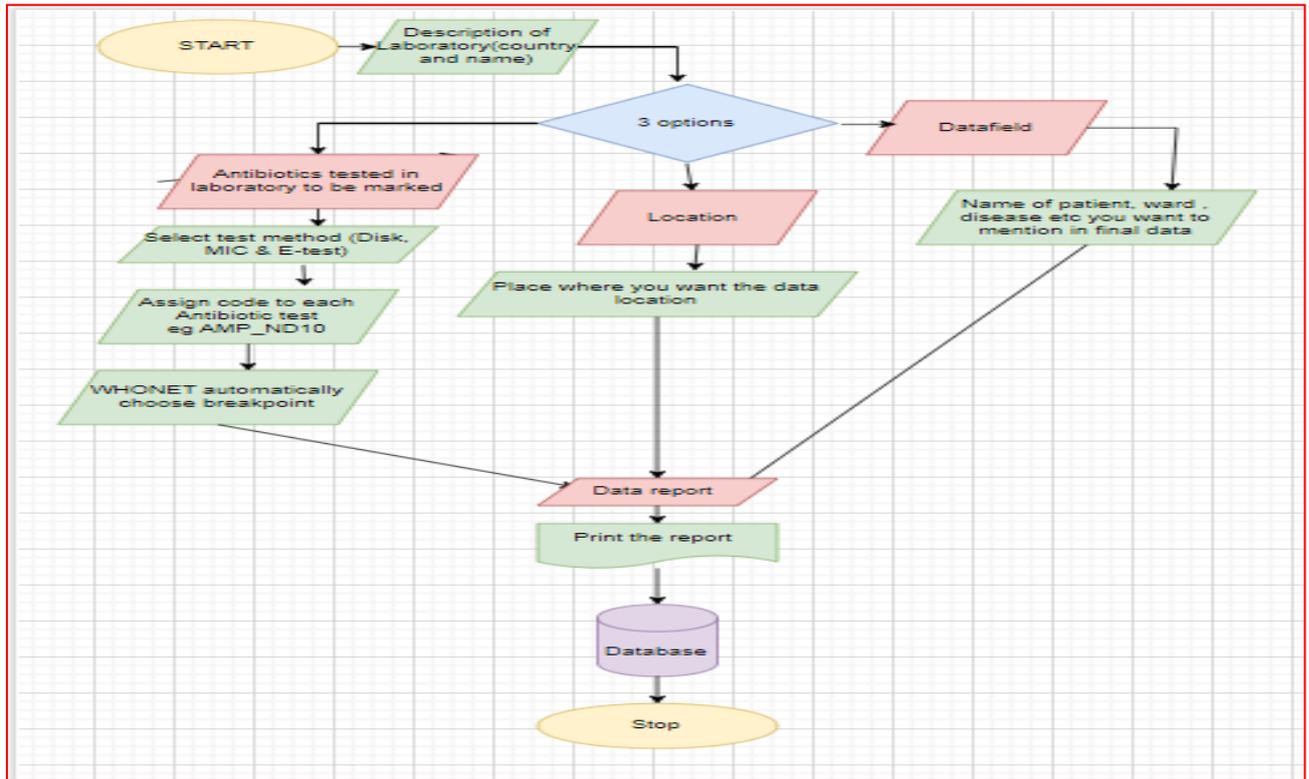
111 countries are enrolled in GLASS-AMR and 33 are enrolled in both AMR and AMC. AMR is antimicrobial resistance and AMC is antibiotic consumption. Montenegro, Mongolia and Sudan are only enrolled in antibiotic consumption.

WORKFLOW DIAGRAM ON ENTIRE SURVEILLANCE FROM REGIONAL TO INTERNATIONAL LEVEL (Fig 2.2)



The positive reports of patient are send and recoreded by WHONET having embeded scale. CLSI is the body whose standards we follow. Quarterly the data is collected and transported to nodal officer for final approval. That's how the data is made to reach the global level.

Process flow of Software WHONET for surveillance: (Fig 2.3)



WHONET is a free available software which is available in 36 language and very easy to integrate in laboratory system.

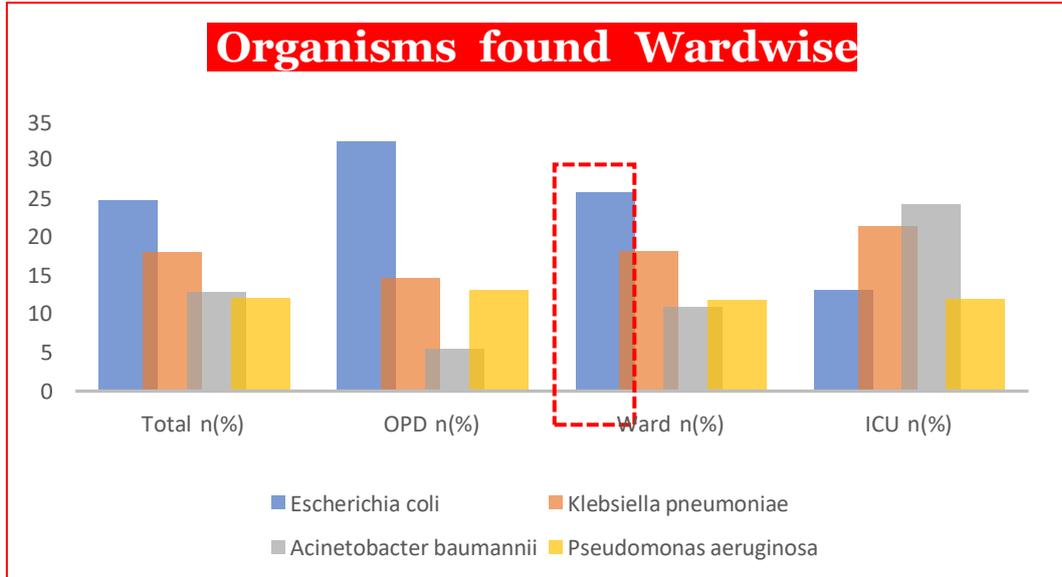
Every medicine is coded for susceptibility and hence it is finally stored and analysed by software.

It can enter, analyse and prepare reports based on results.

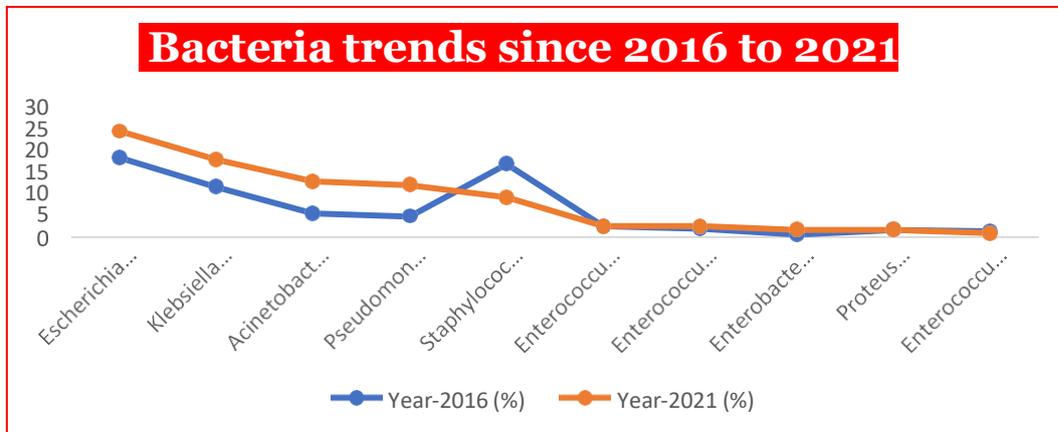
| NCDC NETWORK | ICMR NETWORK |
|------------------------------|---|
| NARS- NET | I-AMRIT |
| Functional in 2017 | Functional since 2015 |
| National coordinating center | Surveillance body |
| No molecular study data | Molecular studies included |
| 36 labs are data center | 20 labs and tertiary hospital provides data |

FINDINGS

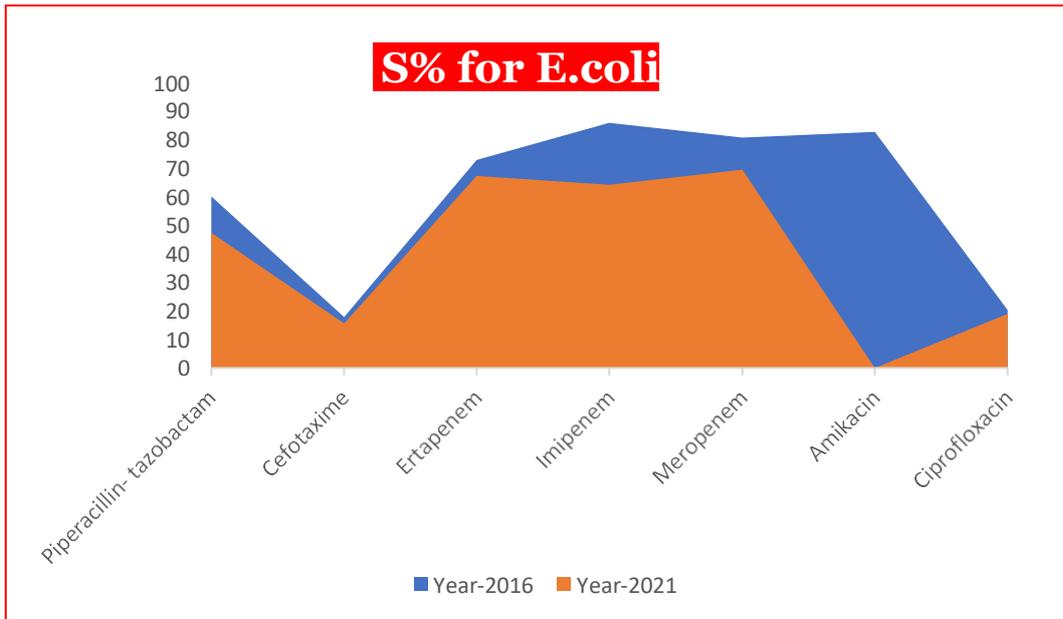
The susceptibility % should be high, the higher the no. higher the rates the medicine is effective against a organism.



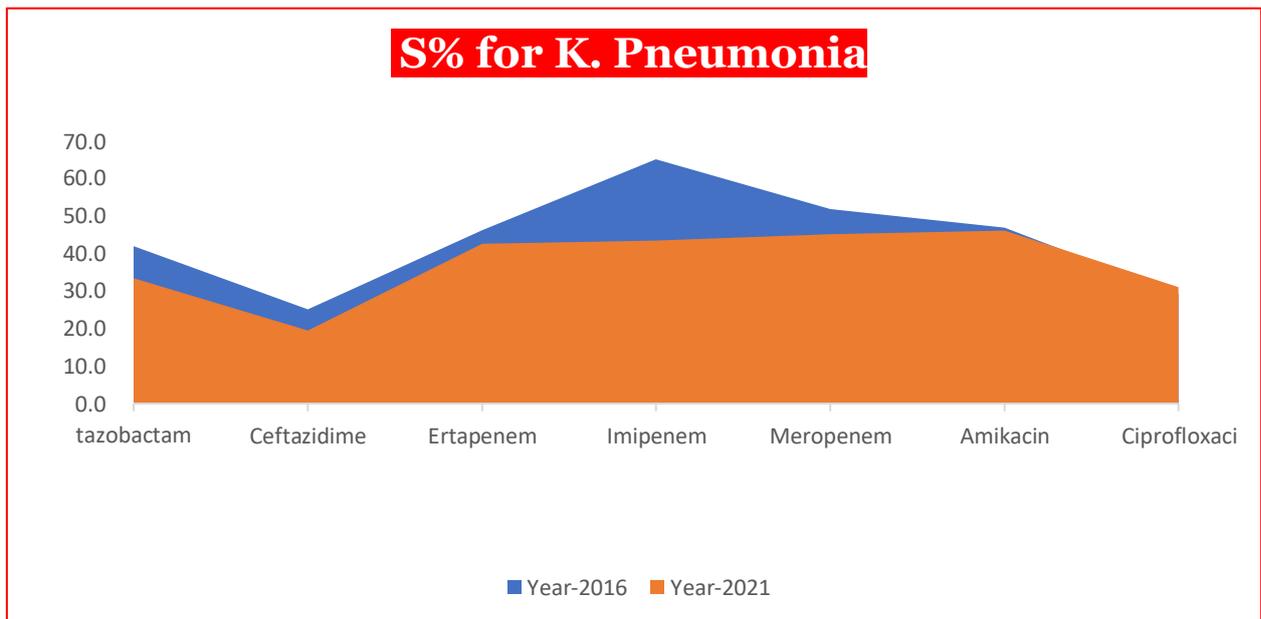
E.coli is prevalent in most samples whereas in ICU A. baumannii is highly found.

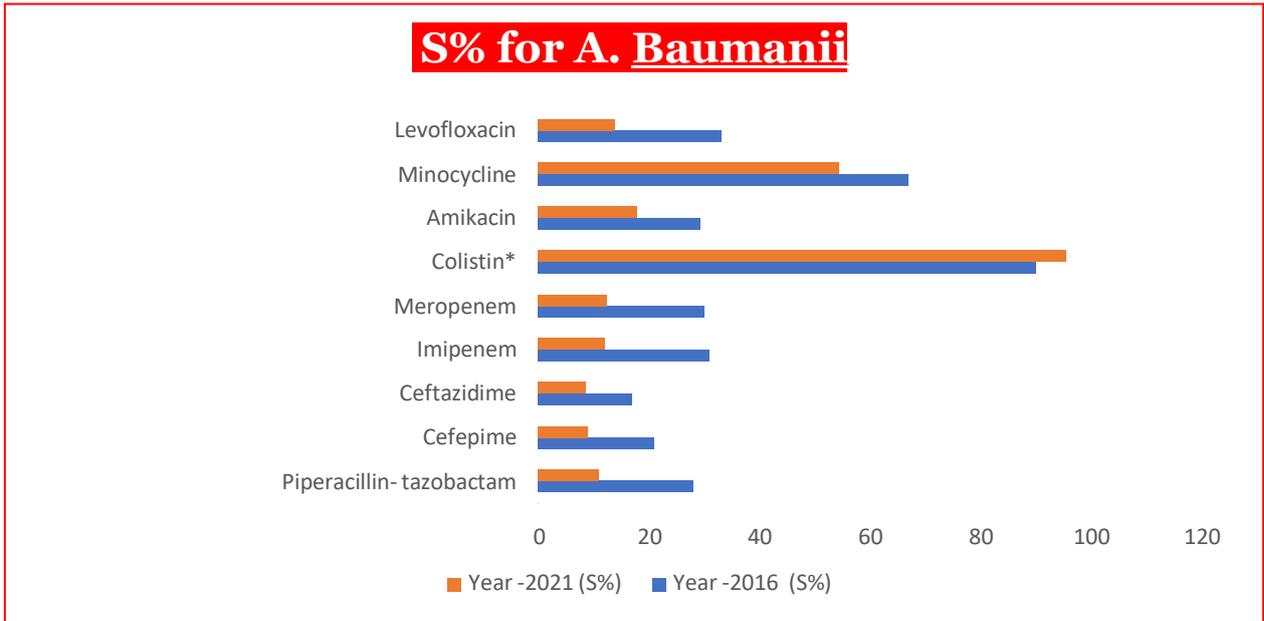


E.coli is highly found in the samples whereas a dip is found in streptococcus.

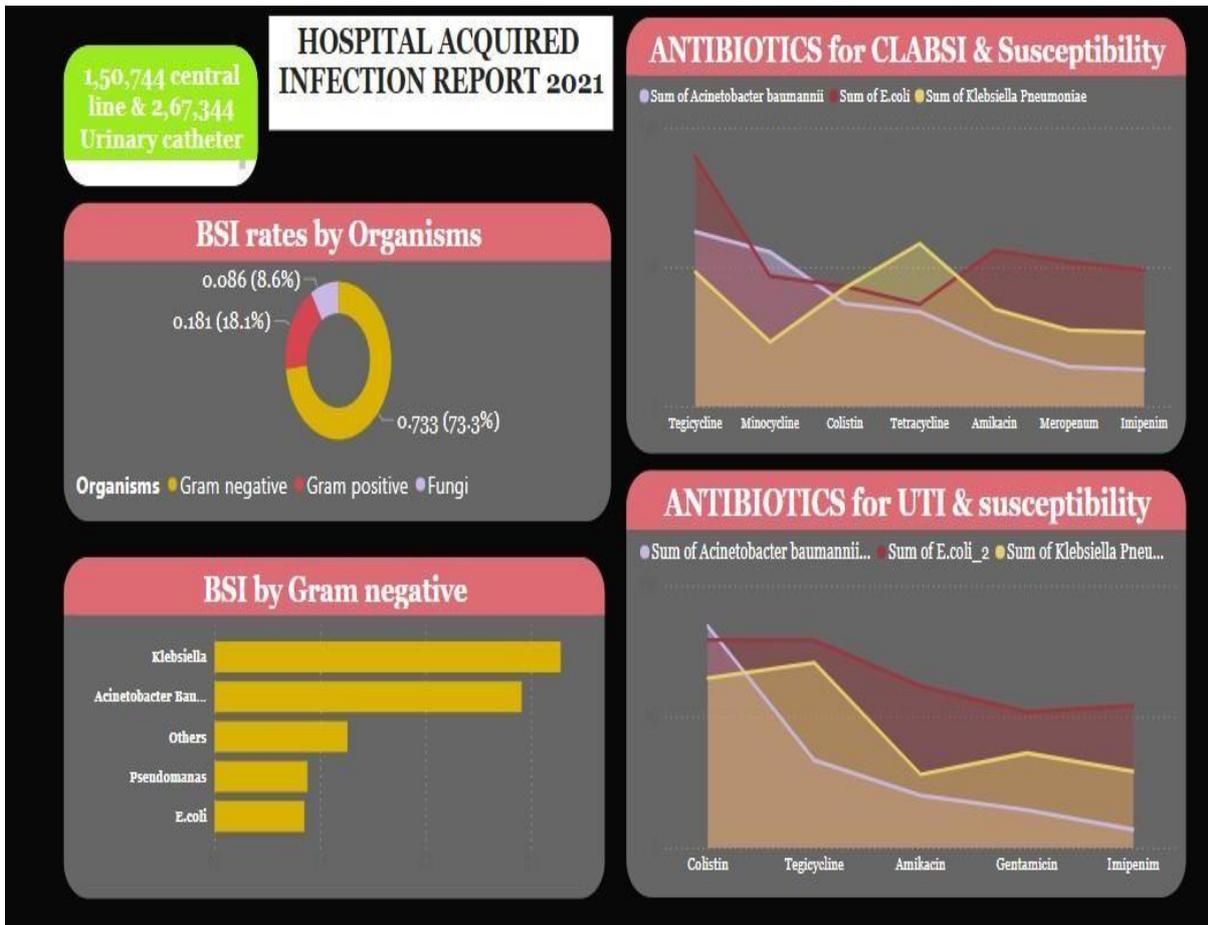


The susceptibility% has decreased





Colistin is effective against A. baumannii but it is highly toxic



Recently this is the first time that HAI were also captured by ICMR in 2021. Fig 2.4

1,50,744 central line and around 2,67,344 urinary catheter associated cases were taken to study. It showed that gram negative bacteria are mainly associated with HAI. Klebsiella pneumoniae is the major cause of blood stream infection. Antibiotic susceptibility has reduced to few like for Acinetobacter.

Klebsiella pneumoniae SHV plasmid is majorly prominent. E.coli CTXM- 15 is majorly prominent.

OBJECTIVE 3: To conduct SWOT analysis for gaps in the surveillance system.

STRENGTH

- Priority pathogen data recorded.
- Ward wise data collection
- Genotypic study done and HAI also included since 2021
- Free software WHONET used to maintain standardization
- Specific nodal centers for specific organism

WEAKNESS

- Population covered is very less.
- Sampling bias (tertiary population)
- Patchy infrastructure (NARS-Net & ICMR)
- Non availability of antibiotic consumption data
- Do not have enough data on Animal surveillance (one health approach)
- Silo data not recorded
- Lack of central repository on data

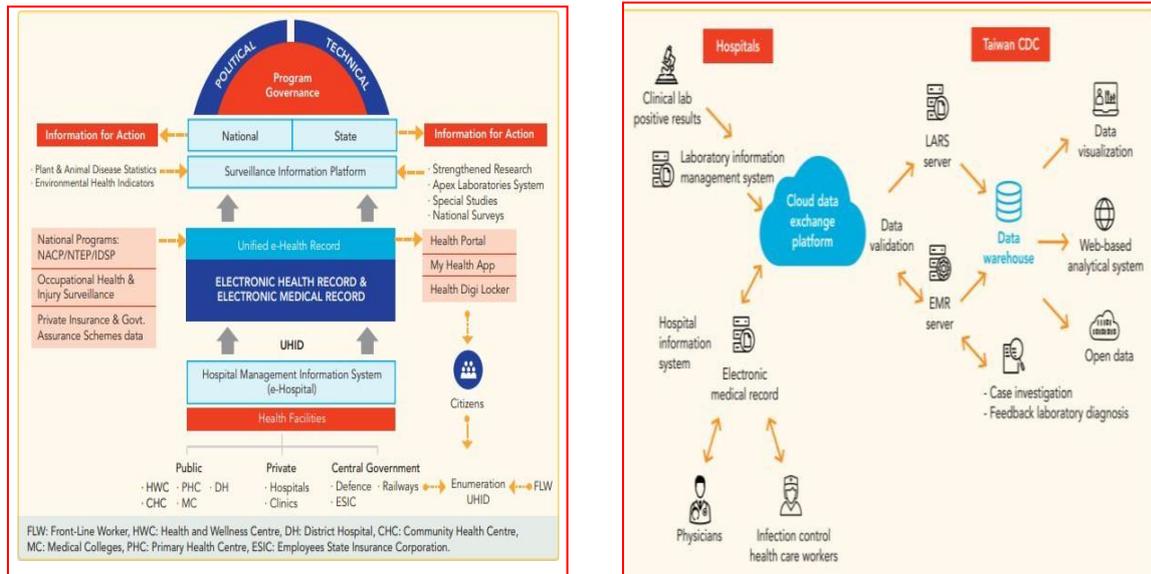
OPPORTUNITY

- Strengthen molecular studies.
- Usage of analysis in generating treatment guidelines specifically for the country.

THREATS

- Over the counter tracking of antibiotics have no record.
- Data privacy and security issues.
- Treatment guidelines are based on foreign research instead of focusing on our inheritance.

OBJECTIVE 4: To propose solution to strengthen the surveillance of AMR using current network in India. Fig 4.1



The vision is that HER will be center for all sort of surveillance. Keeping central repository and masking the identifiers we can cross the information and hence could be used for analysis. A central surveillance platform is the need of the hour present in Taiwan.

Integrated disease surveillance programme/ ABHA

- Geographical data
- Real time data disease based can provide data on Antibiotic consumption

Technology for guidance:

- CDSS
- Antibigram at hospital level

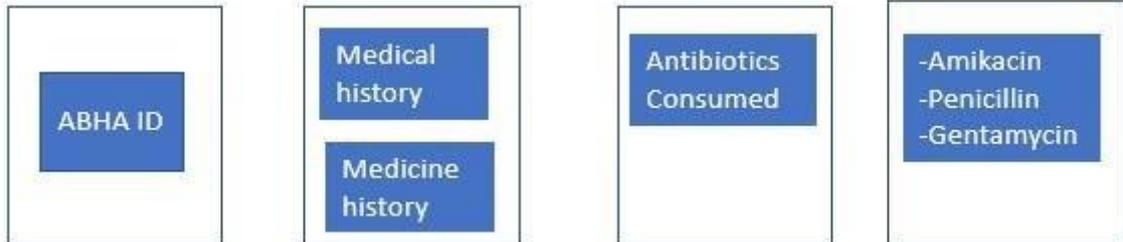
Pharmacovigilance Program network

- Track resistance
- Track treatment based on resistance
- ‘Track and tracing’ quality of drugs based on barcode.
- Diagnostic innovation

PROBLEMS: 1. Antibiotic consumption data not available

2. Geographical data not available

3. Lack of drug repository



1. We can have an app to track the antibiotics consumption history.

2. The application is linked with ABHA and hence can provide geographical data and other demographic details.

3. Doctors can take decision too or CDSS can be integrated to send alerts.

- Escherichia coli was the most commonly isolated pathogen.
- Imipenem susceptibility of E. coli has dropped steadily from 86% in 2016 to 64% in 2021 and that of Klebsiella pneumoniae dropped steadily from 65% in 2016 to 45% in 2020 and was at 43% for the year 2021.
- Resistance to carbapenems in Acinetobacter baumannii was recorded as 87.5% in the year 2021, limiting the availability of available treatment options. In A. baumannii, there is no significant change in the susceptibility trends to all the tested antibiotics compared to last year. Susceptibility to minocycline was close to 50% (45% to 65.6%) making it most susceptible antibiotic after colistin for Acinetobacter baumannii.
 1. AMR burden is heavy in India. We need to work to tackle the situation.
 2. Among all the countries the South Asian countries are carry load of AMR, India is at >50% burden for many microbes.
 3. NARS-NET and ICMR surveillance network capturing the data on resistance for India.
 4. The SWOT analysis shows how silo the structure is and need the PHC and LIS & HIS covered.
 5. Antibigram and CDSS are some of the technological aspects. The centralised repository is the need of the hour.

CONCLUSION

National Action Plan on containment of Antimicrobial Resistance (NAP-AMR) was launched on 19th April, 2017. National AMR surveillance network of state medical college labs (NARS-Net) has been established to generate quality data on AMR for priority bacterial pathogens of public health importance.

Initiated by the ICMR in 2013, AMRSN delivers the accurate estimation of drug resistant infections and patterns of AMR among pathogens of human importance across Indian hospitals.

The promising leads and evidence of AMR brought forth by AMRSN is being used to devise and update the treatment guidelines with the help of collected data. To strengthen the understanding of AMR at multiple levels, ICMR through its AMR surveillance network and various other collaborative research programs is helping to decode the ever-evolving mechanisms of resistance and other targets which could guide the development of new diagnostics, potential drug candidate and drug molecules.

1. The study highlights that AMR is at rise and hence need better digital application at hospital level and national level to track before it is over the head.
2. LIS and HIS can integrate the data for national benefit.
3. Along with this we need tools to diagnose the resistance without consuming time.

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