National Surveillance of Antimicrobial Resistance

Report to Ministry of Health

by

Sri Lanka College of Microbiologists

SLCM ARSP & NLBSA Technical Committees
December 2014
National Surveillance of Antimicrobial Resistance: Report to Ministry of Health by SLCM

Background

Currently, national surveillance on antimicrobial resistance is carried out as two projects by the Sri Lanka College of Microbiologists. The Antibiotic Resistance Surveillance Project (ARSP) which produces data from blood culture isolates was started by the SLCM in a few selected hospitals in 2009 and was expanded to all hospitals with consultant microbiologists by 2013. The parallel project National Laboratory Based Surveillance of Antimicrobial Resistance of significant urine culture isolates (NLBSA) was started following a meeting held in 2011 in the Ministry of Health, with participation of the Director General of Health Services, the DDG/LS, Director (LS), Director (MT&S) and many microbiologists from the hospitals and universities of Sri Lanka. Together, these two projects enable us to gain a broader understanding of the extent of antimicrobial resistance in Sri Lanka.

Implementation plan

Both projects were initiated under the guidance of Steering Committees and a Technical Committee. The Technical Committee designed the way forward in implementing the activity. Decisions were taken on

1) Scope of the activity
2) Data collection & distribution system
3) Needs assessment on fulfilling and sustaining the activity

Scope of the activity and data collection

ARSP

In 2009, at the initiation of ARSP, collecting data which is comparable and is of international standard was difficult due to the non-availability of culture identification systems and the uniformity of antibiotic resistance testing. To overcome these difficulties, the scope of the activities included introducing identification of blood culture isolates to the species level, supplying the essential antibiotic discs, streamlining the supply chain of the Ministry of Health to provide the necessary items to sustain the project and introducing CLSI antibiotic sensitivity testing method in all participant laboratories.
In the first phase of the project, data on all Gram-negative culture isolates were entered into a tailor-made software. A few workshops were conducted by SLCM to train the microbiologists, medical officers (where available) and the technical staff of microbiology laboratories to carry out the project. Data dissemination was planned through scientific presentations and publications.

**NLBSA**

As the initial step in surveillance of antimicrobial resistance in organisms causing UTI, the data on isolates of midstream urine specimens with a colony count of $\geq 10^5$ CFU/ml, was to be entered into WHONET microbiology software in all hospitals with consultant microbiologists and in microbiology departments of medical faculties with diagnostic laboratories. A few workshops were planned and conducted by SLCM to train the microbiologists, medical officers (where available) and technical staff of microbiology laboratories, in order to familiarize them with using WHONET. It was planned to distribute the generated data through the website of SLCM and by oral/poster presentations in the scientific sessions.

**Needs assessment**

A needs assessment was carried out by the SLCM among the expected participant institutes, in order to find out the facilities available and the difficulties that may be encountered. This revealed that many stations had difficulty in entering data due to shortage of manpower and the non-availability of computers.

This issue was discussed with the DDG/LS of the Ministry of Health and a request was made for data entry operators for the laboratories. Although the Ministry of Health does not have cadre provision for data entry operators, a decision was taken to seek support from the heads of institutions to obtain computers and to strengthen human resources in the microbiology laboratories of all hospitals together with Consultant Microbiologists. The DGHS facilitated this by allocating a time slot to the SLCM to discuss this at the regular MoH Directors’ meeting.

**Progress to date**

Following analysis of the needs assessment, the Technical Committee understood the constraints in carrying out the proposed activity but decided to move forward nevertheless because of its importance. While continuing the efforts to strengthen facilities in all microbiology laboratories, it was decided to initiate activities in those institutions where the minimum required facilities were already available.
ARSP

The data of the first phase was analyzed and published in the *Ceylon Medical Journal* in 2013, (See Annex 2 for copy of paper). This data has been used by the WHO in preparation of the AMR report of South East Asia. The 1st phase was followed by the 2nd phase, which started in 2013 with all blood culture isolates. The available data of year 2013 is under analysis now.

NLBSA

For surveillance of AMR on UTI, only the Microbiology laboratories at the Lady Ridgeway Hospital, Colombo North Teaching Hospital, Ragama, Sri Jayawardenapura General Hospital, Nugegoda, BH Angoda (IDH), Peradeniya Teaching Hospital, Faculty of Medicine, Colombo Faculty of Medicine, Ragama and GH Ratnapura were able to commence data entry.

In mid-2014, the SLCM decided to analyze the available data for 2013, and disseminate the results by presentation at the Annual Scientific Sessions of the Sri Lanka College of Microbiologists in September 2014 (See Annex 1 for copy of abstract).

The data was analyzed only in totality and is not age-group specific or disease-entity specific. The susceptibility rates were calculated using the antibiogram reported to clinicians by the laboratories.

Summary findings

*Blood culture isolates*

A total of 599 blood culture isolates were analyzed for the year 2013 (115 from paediatric cases, 484 from adults). 138/599 isolates were from Intensive Care Units. Gram-negative organisms were responsible for 61% of the infections with *E. coli* and *Kleb. pneumoniae* being the commonest. Among Gram-positives, *S. aureus* (49%), *S. pneumonia* (13%), Group B streptococci (10%), Enterococci (9%), and viridans streptococci (6%) were found. Common organisms in ICUs included *S. aureus*, *Acinetobacter*, *E. coli* and *Klebsiella*. Of the *Salmonella* isolates, 36% was *S. paratyphi* while 30% was *S. typhi*.

The rate of resistance in *Acinetobacter* isolates was very high, with 38% showing resistance to cefepenazone salbactam. Among the isolates of *S. aureus*, 53% were MRSA. 95% of *S. pneumoniae* isolates were penicillin resistant by disc diffusion method. 20% of *E. coli* isolates and 28% of *Klebsiella* isolates were ESBL producers. They exhibited carbapenem resistance as
well (E. coli 5-9%, Klebsiella 28-36%). 40% of Salmonella typhi and paratyphi isolates were resistant to ciprofloxacin while 100% of isolates were susceptible to ceftriaxone.

**Urinary isolates**

The results from a total of 1175 significant isolates from four centres (Lady Ridgeway Hospital, Sri Jayawardene pura General Hospital, Faculty of Medicine, Colombo and Faculty of Medicine, Ragama) were analysed. As shown in Table 1, the large majority (n=922, 78.5%) were Gram-negative enteric organisms, commonly known as coliforms. The other causative organisms are as shown in Table 1.

**Table 1. Significant isolates from urinary samples**

<table>
<thead>
<tr>
<th>Organism causing UTI</th>
<th>Number of isolates</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coliforms</td>
<td>922</td>
<td>78.5%</td>
</tr>
<tr>
<td>Enterococcus spp</td>
<td>83</td>
<td>7.0%</td>
</tr>
<tr>
<td>Candida spp</td>
<td>60</td>
<td>5.1%</td>
</tr>
<tr>
<td>Pseudomonas spp</td>
<td>38</td>
<td>3.2%</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>21</td>
<td>1.8%</td>
</tr>
<tr>
<td>Gp B β-haemolytic streptococci</td>
<td>20</td>
<td>1.7%</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>10</td>
<td>0.9%</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>9</td>
<td>0.8%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>7</td>
<td>0.6%</td>
</tr>
<tr>
<td>Staphylococcus saprophyticus</td>
<td>5</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>Total isolates</strong></td>
<td><strong>1,175</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Table 2 shows the number of coliforms tested for antibiotic sensitivity by disc diffusion in the analysed data. None of the 13 isolates of Acinetobacter species tested were sensitive to meropenem while only 55% (16/29) of Pseudomonas spp. were sensitive to meropenem. 74% (60/81) of Enterococcus species were sensitive to ampicillin.
Table 2. Antibiotic sensitivity of coliform organisms

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Number of isolates tested</th>
<th>Number of sensitive isolates</th>
<th>Percentage of sensitive isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meropenem</td>
<td>718</td>
<td>665</td>
<td>92.6%</td>
</tr>
<tr>
<td>Nirofurantoin</td>
<td>873</td>
<td>621</td>
<td>71.1%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>855</td>
<td>601</td>
<td>70.3%</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>883</td>
<td>422</td>
<td>47.8%</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>853</td>
<td>392</td>
<td>46.0%</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>819</td>
<td>341</td>
<td>41.6%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>829</td>
<td>318</td>
<td>38.4%</td>
</tr>
<tr>
<td>Nalidixic acid</td>
<td>866</td>
<td>255</td>
<td>29.4%</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>862</td>
<td>223</td>
<td>25.9%</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>795</td>
<td>92</td>
<td>11.6%</td>
</tr>
</tbody>
</table>

Conclusions and recommendations

Severe infections with blood stream involvement (sepsis / bacteraemias) are caused by both Gram-negative and -positive organisms. *Acinetobacter*, a highly resistant organism with few antibiotic treatment options, is responsible for 1/5th of Gram-negative sepsis observed in ICUs. ESBL production is common in *E. coli* and *Klebsiella* which require therapy with carbapenems in most instances. Carbapenem resistance too has emerged in Gram-negatives.

The common occurrence of MRSA (53%) and ciprofloxacin-resistant *Salmonella* (40%) in typhoid fever, in blood culture isolates should be strongly considered in empiric therapy.

The large majority of UTIs are caused by coliform organisms. The data from four centres revealed a high resistance rate in coliforms against broad spectrum antibiotics like cefotaxime and ciprofloxacin; 7.4% of the coliforms were resistant to meropenem. *Acinetobacter* sp. showed a very high resistance rate even for carbapenems.

The results suggest that nitrofurantoin can still be used for empiric therapy for cystitis and lower urinary tract infections, while ampicillin can be used as empirical therapy to treat UTI due to enterococcus species. However, given that about 1/4th of coliforms are not sensitive to nitrofurantoin, it is strongly recommended that the final choice of anti-microbial agent is based on the results of urine culture and ABST.

It should also be noted that these analyses did not include data on patient age. The data included in the analysis in both projects represented the major hospitals where antimicrobial
resistance is naturally common. These two limiting factors should be taken into consideration whenever the above information is used for patient management.

**Important points to note and lessons learnt**

- Generating data pertaining to antibiotic resistance in the country is an important component in the process of developing rational use of antibiotics. Rational use of antibiotics has the potential to enormously reduce the health budget spent on antibiotics. This has been highlighted by WHO and the Health Ministers of the WHO South East Asia Region who have signed the Jaipur Declaration on AMR.

- Up to now the SLCM has produced data on antibiotic sensitivity patterns in blood culture isolates (through ARSP) and in urinary tract infections (through NLBSA), giving information on serious systemic blood stream infections and UTIs. These data reflect the current trends of antimicrobial resistance, and the organisms involved.

- The available data suggest that antibiotic resistance is alarmingly frequent, and highlights the importance of good antibiotic stewardship.

- Data analysis has been restricted to a few centres so far because many others found data entry difficult due to lack of computers and necessary manpower.

- Generation of accurate national data which can be compared with international data requires strong support from technical experts. Analysis of data available should be done very sensibly to pick the presence of world trends in antibiotic resistance in the country and the existing resistant mechanisms.

- However without a continuous supply chain and without the necessary human resources in laboratories, it is not possible to generate data that is truly representative of the entire country. Therefore strengthening the microbiology laboratories to enable generation of accurate, truly national data, is essential.

**Support required for the future from the Ministry of Health**

Strengthening microbiology laboratories in hospitals is a prime requirement to have a quality output. Further improvement, especially with regard to generation of national data, will be difficult within the existing work platforms. Therefore the following issues are highlighted for necessary corrective action.

1. Large hospitals find data entry difficult due to problems associated with work load, even though they are provided with computer facilities. Some of the larger hospitals still have
very poor infrastructure with no computer facilities. On the other hand, some smaller hospitals have all the required facilities, but quality output is not possible as the required expertise is not available. All these issues hinder generation of high quality national data. Therefore it is suggested that laboratories should be developed in phases, in an organized fashion, paying particular attention to quality assurance. This will automatically lead to a good data generation which will represent the whole country. The Sri Lanka College of Microbiologists will be happy to provide the MoH with any technical inputs that may be necessary for this purpose.

2. Continuous supply of culture media and antibiotic discs are primary requirements to generate quality output from microbiology laboratories. Frequent interruption of supplies greatly disrupts the generation of high quality data. Therefore it is suggested to streamline and strengthen the existing supply chain to meet the minimum requirement of the laboratories.

3. Training of technical staff with a view to improving their quality of work is essential in generating reliable data. Although it may be said that the MOH is trying to achieve this target, the training received by technical staff is neither well-targeted nor oriented towards reaching the goals. Therefore it is suggested to streamline and strengthen the existing system of training given to technical staff, identifying the final target very clearly. Here again the SLCM is willing to support the MoH in identifying appropriate targets and conduct training, etc.

4. A National Antibiotic Policy is essential in order to promote the rational use of antibiotics. We suggest the formulation of a national antibiotic policy with participation of all relevant sectors such as Ministry of Health, Ministry of Livestock, Sri Lanka College of Microbiologists, Sri Lanka College of Physicians etc. This should be followed by development of an implementation plan and a monitoring system. The active support of the SLMC will always be there for this activity. Re-activating the National Alliance for Anti-Microbial Resistance (AMR) in the Ministry of Health, Sri Lanka would also be helpful to carry out this task.
Annex 1. Abstract presented at SLCM Sessions 2014

Only two isolates (3.7%) grew on 3 μg/mL but were inhibited by 6 μg/mL. Both were isolated from patients at the University Hospital. Other (96.3%) isolates had vancomycin MICs of 3.0 μg/mL or below.

More than 50% of the MRSA isolates were resistant to erythromycin (87.03%), clindamycin (79.62%) and ciprofloxacin (57.41%). Resistance to ciprofloxacin was observed in 33.33% and fusidic acid in 35.85% isolates.

Conclusion

Two (3.7%) isolates with highest detected vancomycin MIC of 6.0 μg/mL may fit in to vancomycin intermediate Staphylococcus aureus (VISA) category according to CLSI criteria and needs confirmatory testing. Reduced susceptibility to vancomycin and resistance to other antibiotics are concerns when treating infections caused by MRSA.

OP 15

Analysis of data of urine culture isolates of 2013 sent from four laboratories of National Laboratory Based Surveillance of Sri Lanka College of Microbiologists

Jayatileke SK, Karunarathne GKDP, Perera J, Perera RRP, Wijesooriya WRPL, Sunil-Chandra NP

1Sri Jayewardenepura General Hospital, Nupegoda, 2Lady Ridgeway Hospital for Children, Colombo 8, 3Department of Microbiology, Faculty of Medicine, Colombo, 4Department of Microbiology, Faculty of Medicine, Ragama.

Objectives

1. To determine the etiological agents of midstream urine cultures with a colony count of > 10^5 CFU/mL.
2. To analyse the antimicrobial susceptibility of those isolates.

Method

The National Laboratory Based Surveillance on Antimicrobial Resistance is a collaborative project of the Ministry of Health and the Sri Lanka College of Microbiologists. At the initial phase decided to analyse midstream urine cultures with a colony count of ≥ 10^5 CFU/mL. The specimens were processed according to the standard protocol specified in the laboratory manual in microbiology. Antibiotic susceptibility tests were performed according to the method established in the centre which is either by CLSI method or by Stöke’s comparative disk diffusion method. Data of 2013 sent by the participating laboratories were analysed using WHONET software.

Results

The data was received from four centres. They were Sri Jayewardenepura General Hospital, Lady Ridgeway Childrens’ Hospital, Faculty of Medicine, Colombo and Faculty of Medicine, Ragama.

A Total of 1175 significant isolates were analysed. The majority were Gram negative enteric organisms, commonly known as coliforms, with 922 (78.5%) isolates. The others were Enterococcus species 83 (7%), Candida species 60 (5.1%), Pseudomonas species 38 (3.2%), Acinetobacter species 21 (1.8%), Group B beta-haemolytic Streptococcus 20 (1.7%), coagulase negative Staphylococcus species 10 (0.85%), Streptococcus species 9 (0.8%), Staphylococcus aureus 7 (0.6%), and Staphylococcus saprophyticus 5 (0.4%).

The susceptibility of coliforms were 11.6% (92/795) to ampicillin, 71.1% (621/873) to nitrofurantoin, 25.9% (223/862) to cefalexin, 46% (392/853) to cefuroxime, 29.4% (255/866) to nalidixic acid, 47.8% (422/883) to cefotaxime, 92.6% (665/718) to meropenem, 70.3% (601/855) to gentamicin, 41.6% (341/819) to amoxicillin-clavulanic acid and 38.4% (318/829) to ciprofloxacin.

None of the 13 isolates of Acinetobacter species tested were sensitive to meropenem while only 55% (16/29) of Pseudomonas sp. were sensitive to meropenem.

74% (60/81) of Enterococcus species were sensitive to ampicillin.

Conclusion

Coliforms constitute the commonest organisms causing urinary tract infections (UTI). A high resistance rate was noted in coliforms for broad spectrum antibiotics like cefotaxime and ciprofloxacin. Acinetobacter sp. shows a very high resistance rate even for carbapenems. Ampicillin can be recommended as empirical therapy to treat UTI due to enterococcus species.

OP 16

Detection of antibacterial activity in cerebrospinal fluid

Abeywardena HMW, Thevanesam V, Illangasinghe IMS, Kumari NRW

Teaching Hospital, Peradeniya.

Introduction

Meningitis is caused by a wide variety of infectious and non-infectious agents. Even though majority of infectious cases are caused by viruses, bacterial meningitis remains as a significant problem. It needs prompt and precise management with correct antibiotics which is dictated by accurate microbial identification. In Sri Lanka, microbial diagnosis of meningitis is mainly based on Gram staining and positive culture, for limited availability of antigen detection. This has a lower sensitivity when associated with prior antibiotic usage.