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Antibiotic Resistance in Laboratory acquired infections-A Review

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ABSTRACT: *Laboratory acquired infection occur globally. These infections are caused by multiple parasites and pathogens belonging to bacteria, fungi and the viruses. Laboratory acquired infections in laboratories of research and development; production installations and academic sectors i.e., teaching labs vary, but do contribute to morbidity and mortality with respect to their occurrence. The health status of a lab worker or technician is an important factor in keeping the community health as these acquired infections easily get introduced into the community. The current review gives an overview about the laboratory acquired infection, their past and the complications that are being faced in their control and management. The review focuses on one of the major problem now being faced in the lab acquired infections that is antibiotic resistance.*

Key words*: Lab acquired infections, Antibiotics, resistance, Mechanism of resistance*

INTRODUCTION

The safety of the lab environment and the people working in the facility are usually referred under the description of "Laboratory Biosafety", which is an essential, assertive process to ensure the safety of the lab from microbial contamination or introduction of any kind of infection, focusing not only on the environment of the lab but also towards the workers, technicians and its transfer to the general public of a community, ultimately getting introduced into the overall environment (Nobel , 2011).

The contamination arises due to the active manipulations conducted in the products or in the live organisms. Usually this is observed in labs pursuing academic research, industrial and clinical studies (Noble, 2015). The infection acquired while working in the lab or such facility is termed as laboratory acquired infection. The laboratory acquired infections or LAIs are defined as:

"An infection obtained through the laboratory or due to its related activities, during the handling of the biological agents".

The LAIs can be symptomatic or asymptomatic. Although the rate of infection

of LAIs is not as frequent, but still can occur and are considered as a possibility. For an infection of such nature to occur, the portal of entry for invasions by the microorganisms becoming easy due to the following exposures:

1. Sharp injuries; caused by sharp objects such as contaminated broken glass, pointed objects and needle stick injuries.

2. Inhalation; the aerosols containing the biological agents are usually dispersed and suspended in the air and can reside in the air for longer period of time.

3. Ingestion; due to accidents while working in the lab e.g., spillage or due to poor use of personal protective equipment.

4. Exposure of mucous membrane; the exposure of mucous membrane can also result in the infection acquisition.

The laboratory acquired infections can be categorized on the basis of the nature of occupation into the following two major categories (Wedum, 1997):

a. Primary risk: It involves people directly working with the microorganisms i.e., scientific personnel and assistants.

b. Secondary risk: It involves people that get exposure indirectly from the lab i.e., caretakers, cleaners, sweepers and dishwashers etc.

Epidemiology of LAIs:

The characterization of worker's infection to be as laboratory acquired is based on the assumption that the infection has occurred only due to the exposure within the lab, and that no circumstances could have accounted for such an infection (Herwaldt, 2001; Kahn, 2004). The laboratory workers are considered to be at high risk when it comes to acquiring an infection as they are directly or indirectly exposed to the microbes while working in the lab environment. Many cases of morbidity and mortality have been reported related to LAIs in the literature, highlighting its importance (Kahn, 2004).

Although there is clearly the chances of occupational risk for lab workers to acquire an array of infection but studies reveal that the incidence, prevalence and exposure related rate of the infection can be minimized by following specific interventions and by adopting work safety.

History of LAIs:

The first survey of laboratory acquired infections was made after 30 years of the first case of typhoid reported as laboratory acquired, indicating a slow start in the epidemiological review of infections (Wedum, 1997).

Kisskalt in 1915, through a questionnaire sent to his colleagues in Europe, collected information of 50 cases of typhoid fever infections, acquired from labs. The data had information dating back to 1885. The information showed 6 fatalities, with 23 cases of known cause, while 16 out of 23 cases were caused due to pipette (Kisskalt, 1915).In another study conducted in 1929, Kisskalt reviewed 59 new cases of typhoid fever and 24 cases of infections caused by other agents.

Draese conducted subsequent reviews during, 1937-39 in Germany, clearly depicted the prime cause of infection in a lab was due to ingestion because of oral pipetting, followed by used of syringe via spray or injection (Draese, 1937-39).

Reinhardt, an Austrian Physician, reported 21 different types of mechanical pipettors and highlighted the use of mechanical pipettes to overcome the problems faced by the use of oral pipette (Reinhardt, 1918).

To avoid laboratory infections the improvement in the infrastructure of the lab was observed with the efforts to improve the in-house facilities and the introduction of "protective microbiological cabinets" was one of the most important biosafety measures that were adopted for the first time in 1919 in Germany (Fricke, 1919). While, its use in the U.S; was not notable until 1940s (Wedum, 1997).

McCoy in 1930 reported 11 cases with 1 fatality of psittacosis that occurred in a period of 2 months. The epidemiological study conducted by Hornibrook et al.,, included analysis of 15 infection cases of Q fever (with 1 fatality) at NIH, in a period of 51 days (Hornibrook et al., 1940).

It was in 1956, that a government regulation was published to prevent infection getting acquired from the labs. For this, prohibition on the use of mouth pipetting, drinks, tobacco, food and chewing gum in the laboratory were made.

With the publication of first significant study in this area, in 1953, multiple studies have been conducted since the past 60 years (Chen et al., 2009; Evans et al., 1990; Fichet et al., 2004). Sulkin and Pike published a survey which included 5000 American laboratories. With the updates provided in 1961, 1965 and 1976, the survey clearly showed the importance of laboratory acquired infection and the need to consider it (Sewell, 1995).

During 1930-1974, 3,921 laboratories were cited for several mortality and morbidity cases. The mortality reported was 4.1%, while 58.8% infections were reported from research facilities, 17.3% from diagnostic facilities, 3.4% were due to the generation of biological products from the industry, 2.7% included from teaching facilities while the remaining17.8% were from an unspecified source (Sulkin, and Pike, 1951).

Sulkin in 1961, reported many bacterial infections that were being acquired during working in the lab, by use of a pipette. The microorganism reported included; *Salmonella enterica* serovar Typhi causing typhoid, *Brucella*, *Corynebacterium diphtheriae*, Salmonella, Shigella, *Vibrio cholera*, *Bacillus anthracis*, *Meningococcus*, *Streptococcus*, *Hemophilus Influenzae*, *Leptothrix*, *Treponema pallidum* and *Francisella tularensis* (Sulkin, 1961). Among viruses, *Rubulavirus* (Sulkin, 1961), *Coxasackievirus*, viral hepatitis (including *Hepatitis A*, *Hepatitis B* and *Hepatitis C*) (Kuh, 1950), *Venezuelan equine encephalitis* (Johnson and Kadull, 1966), *Chikungunya virus* (Shah, 1965) and *Orientia tsutsugamushi* (Van den Ende, 1946).

Four series of studies conducted during the years, 1971 and 1991, concluded that major laboratory acquired infections are caused in the clinical facilities, occurring majorly in the workers of microbiology lab, followed by those offering autopsy service. The level of incidence of these infections reduced 80% within the period of 20 years.

In 1991, 8 out of 26 microbiologists were reported to be ill due to *Brucella melitensis*, despite the fact; that there had

been no isolation conducted of the microbe in the preceding 3 years (Salerno et al., 2004).

In another case reported, a child (approximately 6 years old) indicates the presence of laboratory acquired infection. The boy was reported to have come in contact with open plate, and was observed to have developed colitis along with hemolytic uraemic syndrome, despite the fact, that his hands were washed. *Escherichia coli* strain was O157:117 involved in lab technician cases reported with infection (Misra et al., 2001).

With the advancement in technology and improved methods, the laboratories are now becoming safer and better but it is tempting to conclude that with the improvements, there is lack of active monitoring and proGrams, that can show the actual number of accidents and the infections caused while working in the lab facility. Due to this, there tends to be a limited range of data reported in the literature and the databases (Griffith et al., 2000).

The occurrence of uncommon infection being reported as common, while those caused commonly (such as *S. aureus*) are rarely reported as lab acquired clearly shows that the listing reflects minority of the infections that actually occur (Sewell, 1995).

Two hundred cases of laboratory acquired infections due to parasites have been reported from 1929 to 1999 (Herwaldt and Juranck, 1993; Herwaldt, 2001). It was reported that sharp injuries were a common factor that caused the acquisition of the infection, during studying and manipulation of research animals, e.g., while preparing blood smears for malaria.

The role of lab equipment in acquiring infections was also highlighted and studied. Although the safety centrifuges were described originally in 1935 but the accidental contamination of the lab personnel, the literature was been reported regularly (Fiori et al., 2000; Hall, 1975). Although other instruments are also involved in causing contamination, if not attended properly, the centrifuges are considered important as the frequency, of acquiring an infection of centrifuge users increases; as the spillage is a common factor involved, while using a centrifuge and therefore can easily cause aerosol contamination (Hambleton and Dedonato, 1992).

During 1979-2004, 1141 cases of laboratory acquired infections were reported in the U.S., highlighting *Mycobacterium tuberculosis* as the major agent involved, followed by occurrence of Rickettsia spp. and *Coxiella burnetti* respectively (Baron and Miller, 2008).

Just as regulations differ in each area similarly, reporting requirements for LAIs also do vary depending on the country and the region. In case of notifiable diseases, it is the responsibility of the health care provider to report the infection (not the patient). These infections must be reported to the CDC. The patient who is seeking medical aid cannot report the infection himself so responsibility lies on the hands of a medical professional (Henkel et al., 2012).

Gillum et al. 2016 highlighted the importance of Laboratory Acquired Infections, emphasizing on the missing links and the difficulty in tracking and assessing underlying factors (Gillum, 2016).

Antibiotics:

Antibiotics are medicines that have critical role in attacking bacteria at various levels and by multiple means in the human body. Antibiotics also known as wonder drugs have significance that cannot be denied. Advancement in the treatment came with the introduction of first antibiotic; the treatment became easy and effective. During the course of time, changes and improvements have been made in treating out the infections. But with the introduction of wide range of antibiotics and their use, a global issue of antibiotic resistance has developed.

Beta-lactam antibiotics include; penicillin, cephalosporins, monoactums and carbapenems.

1. Penicillins:

Penicillins are a group of natural and semi-synthetic antibiotics that contain a β-lactam ring in the chemical nucleus, which is fused to a thio-zolidine ring. Penicillins are produced by a number of *Penicillium spp*. Difference in the type of Penicillin comes due to addition of different side chain, that modify the anti-microbial properties and pharma-kinetic activity (Waxman and Strominger, 1983).

Penicillin inhibits an enzyme, that are important in the of peptidoglycan synthesis, an essential part of the bacterial cell wall. By inhibiting trans-peptidases produced by bacterial cell wall, the antibiotics can effectively be used against Gram-positive bacteria. Other activities include, triggering ability of membrane associated autolytic enzymes, inhibition of endopeptidase and glycosidases. Damaged to RNA without causing cell lysis has also been suggested in the recent studies but more investigations still needs to be done to determine its significance.

This agent acts as a "suicide inhibitor". By forming an acyl enzyme complex (that is irreversible in nature) due to binding with β lactamases causes loss of functioning of the enzyme hence, halting cell wall synthesis (McDowell et al., 1989).

2. Cephalosporins:

Cephalosporins are derivatives *Cephalosporium acremonium* (also referred as *Acremonium chrysogenum*) as the fermentation products (Waxman and Strominger, 1983; Vidaillac and Rybak, 2009).

Cephalosporins are classified by well-accepted scheme of groupings by "generations" based on the general antibacterial activity and pharmo-kinetic properties. These first generation drugs are active against both the Gram-positive and Gram negative bacteria. Cephalothin and Cephazolin have higher activity against Gram positive bacteria, while these drugs display modest activity towards Gram negative bacteria (Jones, 1989; Wexler et al., 2005). Activity has been recorded against penicillin for both susceptible as well as resistant) *S. aureus* as well as *S. pneumoniae*, *S. pyogenes* and various other aerobic and anaerobic Streptococci. The second generation has prominent activity to combat infections caused by Gram negative bacteria as they are more stable against β-lactamases produced by these organisms (Zhanel et al., 2008).

3. Carbapenems:

These drugs also belong to the β-lactam antibiotics, having the broadest

spectrum of activity in comparison to currently available antibiotics. The carbapenems contain a hydroxyl ethyl side chain at position 6 (Trans-configuration). The bicyclic nucleus lacks a sulfur or oxygen atom. This structure confers stability against β-lactamases (Norrby et al., 1997).

The carbapenems binds to the PBP-1 and PBP-2 enzyme of Gram positive and Gram-negative bacteria, causing lysis and elongation of the cell. Bacterial resistance arises due to production of carbapenemases, such as produced by *Klebsiella pneumoniae*. Serine carapenemases (MSE, NMC-A, IMI AND GES) and metallo β-lactamases (IMI and VIM) hydrolyze the carbapenem nucleus with alteration of porin channel in the bacterial cell wall reducing it permeability (Spratt et al., 1977; Baldwin et al., 2008; Keam et al., 2008).

4. **B-lactamase Inhibitors:**

a) Tazobactum:

Tazobactum is a penicillanic acid, sulfone derived, structurally related to sulbactum. It acts as a suicidal β-lactamse inhibitor and binds to PBP-1 and PBP-2 (Moosdeen et al., 1988). The activity of tazobactum inhibits the β-lactamases of *Proteus spp*., the *B. fragillis* group, Staphylococci, *H. influenza, N. gonorrhoeae, E.coli*, *Prevotella spp* and *Porphyromonas spp.* (Appelbaum et al., 1986). Of all penicillin β-lactamase inhibitor combinations, piperacillin-tazobactum is the most active against β-lactamase producing aerobic and anaerobic Gram negative bacilli (Gutmann et al., 1986; Eliopoulas et al., 1989; Kuck et al., 1989).

b) Clavulanic acid:

Clavulanic acid is a debile antimicrobial agent, initially produced by *Streptomyces clavuligerus* (Neu and Fu, 1978; Bansal et al., 1985). The agent is capable of inhibiting β-lactamases from *Staphylococci* and many Gram-negative bacteria. The agent forms an irreversible acyl enzyme complex by binding to the β-lactamase, acting as "suicide inhibitor", leading to reduced activity of the enzyme (Finlay et al., 2003). The drug acts in synergism with penicillins and cephalosporins. These have effective activity against β-lactamase Staphylococci, Klebsiella, *Neisseria gonorrhoeae, Haemophilus influenza, Proteus spp*., the *Bacteroides fragilis* group, *Moraxella catarrhalis, Escherichia coli, Protella spp* and *Porphyromonas spp* (Finlay et al., 2003).

5. Aminoglycosides:

The aminoglycosides were first introduced in 1944, with the introduction of Streptomycin as antibiotic (Davies, 1983). These drugs have played a crucial role in the treatment of serious Gram negative infections. These drugs bind irreversibly to 30S ribosomal subunit, hence; stopping the bacterial protein synthesis. The bound ribosomes become unavailable for mRNA translation, leading to cell death (Galimand et al., 2003).

There are 3 known mechanisms of bacterial resistance, for aminoglycosides (Shaw et al., 1993):

a) The reduced accumulation of the drug intracellularly, and by alternating the outer membrane permeability, reducing active efflux.

b) The post transcriptional changes in 16S RNA (i.e., methylation).

c) Modification of the drug.

6. Quinolones:

These belong to a group of antibiotics related to nalidixic acid. The acid and its early analogs oxolinic acid and imoxacin have restricted clinical applications due to the emergence of bacterial resistance (Ball, 2000). Quinolones are now in use worldwide and are synthesized by modifying the original nephthyridone with different side chains as substituition (Hawkey, 2003). Quinolones target DNA gyrase for DNA replication recombination and repair (Morgan-Linnell et al., 2009; Strahilevitz et al., 2009).

Subunit A of DNA gyrase is the primary target of quinolones towards infections caused by Gram negative bacteria, while these drugs target topoisomerase 4 and Gram positive bacteria. Inhibition of these enzymes results in the relaxation and decantation of supercoiling of DNA causing a halting the chromosomal replication and interferes with cell division and cell expression (Ball, 2000). Hence by targeting the bacterial DNA synthesis these drugs clearly explicit bacteriosidal effect. The bacterial resistance to quinolones however may occur due to several reasons (Strahilevitz et al., 2009):

1) Single step chromosomal mutation.

2) Mutations in regulatory genes

3) Expression or over expression of energy dependent efflux pump

4) Acquisition of plasmid-mediated resistance genes encoding proteins

5) Acquisition of plasmid-containing the resistance gene

Quinolones may be categorized into groups with similar spectra of antibacterial activity. The narrow spectrum quinolones are inactive against Gram-positive cocci, and their clinical utility is limited by widespread prevalence and rapid emergence of bacterial resistance. Broad spectrum (second generation) fluoroquinolones are active against both Gram positive and Gram negative bacteria (Morgan-Linnell et al., 2009; Strahilevitz et al., 2009). Increased activity has been reported against Gram-positive cocci and favorable pharmaco-dynamic properties and major features of the new fluoroquinolones (third and fourth generation) (Ball, 2000).

7. Glycopeptides and lipopeptides:

Vancomycin a bacterial antibiotic obtained from *Streptomyces orientalis*, is the only glycopeptides marketed for commercial use (Somma et al., 1984). Initially introduced for its efficiency against penicillin resistant staphylococci, it has become effective useful against methicillin resistant staphylococci and in patients allergic to penicillins or cephalosporins (Courvalin, 2006).

Glycopeptides inhibits peptidoglycan synthesis, by complexing with the D- alanyl-D-alanine portion of the cell wall precursor. Resistance to vancomycin and teicoplanin can occur by the following mechanisms:

1) Presence of a complex series of bacterial cytoplasmic enzymes present in the vancomycin resistant enterococci synthesizing abnormal peptidoglycan precursors terminating in D-ananyl-D-lactate residues instead of D- alanyl-D-alanine. Thereby

moderately lowering the binding affinity with the glycopeptides.

2) Increased accumulations of peptidoglycan precursors (murein monomers) resulting in a thickened cell wall with trapping of drug molecules. Thereby preventing future diffusion of the drug into the inner pat of the cell wall layers of VISA (Jones, 2006).

3) Glycopeptides and lipopeptides are active mainly against aerobic and anaerobic Gram positive organisms, including methicillin susceptible and resistant staphylococci, streptococci, enterococci, corynebacterium spp., *Baccillus spp., Listeria monocytogenes*, Clostridium spp., and actinomyces spp. these agents are essentially bacteriostatic against enterococci and staphylococci. Vancomycin is useful in the prevention and handling of endocarditis caused by Gram positive bacteria particularly in patients, allergic to penicillin (Jones, 2006).

The glycopeptides and lipopeptides are not active against Gram-negative organisms or mycobacteria. They show no cross resistance with other unrelated antibiotics. They act as synergistically with aminoglycosides or rifampin against Staphylococci, Streptococci and enterococci (Courvalin, 2006) and they are bactericidal with aminoglycosides against *Listeria spp.*

Antibiotic resistance:

Antimicrobial resistance is one of the most serious global threats to human health in the 21st century and is responsible for raising the incidence of both devastatingly fatal and infectious diseases (Mckenna et al., 2013). World Health Organization (WHO) describes it as a global crisis and an imminent catastrophe leading us back to the pre-antibiotic era (WHO, 2015).The increasing trend of resistance is closely related with several factors involving the usage and utilization of the antibiotics in humans, animals and agriculture (Levy and Marshall, 2004). The antibiotic resistance is a public resistance is a public health issue, and is dominant in the developing countries. A number of factors are involved in causing the resistance of antibiotics. A few include;

1. Illiteracy
2. Lack of awareness among the general public
3. Compounded due to lack of concern of physician or pharmacist
4. Profit gaining goals of pharmaceutical industries and companies
5. Weak regulation of antibiotics in the market
6. Misuse of antibiotics
7. Overuse of antibiotics
8. Antibiotics not optimally prescribed
9. Incorrect dose and duration of use are also factors involved in the resistance of the antibiotics

Antibiotics, not only cause socio-economic loss but also weakens the health care system, making treatment of a simple infection difficult to cure day after day (Shaikh, 2017).

Mechanisms of action against resistance:

The resistance towards the antimicrobial agents has accelerated in the recent decade and need of new antimicrobials with the capability to control these pathogen is a major concern now-a-days. Drug resistant bacteria are very common in healthcare

institutions (Tenover, 2006), causing reduction in the workforce, failure in treatment along with the disturbance in the economy of a country. Bacterial infections are characterized into community-acquired and hospital acquired infections. The escalation reported for both community as well as hospital acquired antimicrobial resistant bacteria, is extremely alarming and the threat needs to be dealt effectively, with emphasis on treatment and control of prudent infections.

The resistance may develop due to spontaneous mutation, acquisition of plasmid/transposon, changes in the physiological state or reduced permeability of the cell wall. The mechanisms include (Davies, 1994; Webber and Piddock, 2003; Fabrega et al., 2009; Drapeau et al., 2010):

1. Enzymatic drug modification

2. Drug permeability reduction

3. Active efflux of Drugs

The resistance genes are borne on the chromosomal and extra-chromosomal elements. The selective pressure from the use of antibiotics provide a competitive advantage for the mutated strains and these resistant clones disseminate rapidly world widely.

1. **Modification of Antibiotic:**

In this type, the modifications are made in the drug to make it ineffective. Antibiotics that show resistance include; β-lactams and macrolides. B-lactams are employed worldwide and have significant applications against a large number of bacterial infections. However, the production of β-lactamases, an enzyme produced by multiple species of bacteria; has now created a major threatening resistance mechanism towards renowned antibiotics (Lin, 2015).

B-lactam antibiotics contain a central integral "β-lactam ring". The enzyme β-lactamase cleaves the β-lactam ring, inactivating the antibiotic and thus, confers antibiotic resistance towards the antibiotic; e.g., the penicillin resistance.

2. **Resistance by influx-efflux mechanism:**

Bacteria have well developed system of transportation for effective mobility of molecules across the cell membrane. For an antibiotic to be effective it is necessary to reach its target area within the cell. In case, it is not taken in the cell, it would not be able to have any effects. Some bacteria are capable of removing antibiotics via efflux pumps, developing resistance. Such resistance has been reported in Quinolones and Tetra-cyclines (Byarugaba, 2010).

3. **Modification of the target site:**

The bacteria harboring these drugs, resist, survive and can grow in the presence of antimicrobial agent. The various drug inactivation mechanisms involve the enzymatic hydrolysis of antibiotics, ribosome protection, by transfer of a group or biofilms formation (Walsh and Wrights, 2005; Roberts, 2011; Hoiby, 2010).

Antibiotic resistance in Laboratory Acquired Infections:

Emergence of resistance in bacterial pathogenesis is recognized as a major threat for the public health, affecting humans worldwide. Bacteria from nosocomial and non-nosocomial settings are rapidly becoming resistant to conventional antibiotics, uprising a

socio-economic concern round the globe. At first, concern and focus regarding bacterial resistance involved Gram-positive bacteria e.g., involving Methicillin resistant *Staphylococcus aureus*, Vancomycin resistant Enterococcus. But, resistance of Gram negative bacteria has also been introduced at community level posing a "global health problem".

The decreasing effectiveness of antibiotics has quickened recently against commonly occurring infections and with the arrival of untreatable strains and with this ineffectiveness, we are at the edge of the post antibiotic era. While mentioning the resistance, the infections are largely responsible infections in occupational health hazards e.g. laboratory-acquired skin infection of Staphylococcus aureus (Duman et al., 2017).

Workers employed in health care facilities have been reported to be at high risk for acquisition of pathogen. Therefore, strict adherence to infection control measures during their work while processing an infective/clinical material is recommended by the CDC. During survey studies, it has been observed that thousands of laboratory staff has acquired occupational infections while hundreds have died as a result of the acquisition. Antibiotic resistance has become a global public health issue and its pace is escalating with the development of new drugs, therefore it is imperative that new antibiotics continue to be manufactured.

The antibiotic resistant bacteria are recognized confounding factor in the selection of therapeutic agents. Among antibiotic resistant bacteria the multidrug resistant category of microbes has in the recurrent era rapidly spread causing infection in the health setting such as bacteremia, pneumonia, meningitis, infections of the urinary tract and wound infections.

The survival capacity of these multidrug resistance microorganisms makes them special and important to thrive for longer period on the surface, causing outbreaks and making them health-care settings associated pathogen. e.g., the outbreak of multi drug resistant bacteria was reported in many publications, due to environmental contamination caused by the bacteria. The contamination traces of the contaminated bacteria were found on curtains, laryngoscope blades, door handles, patient lifting, keyboards equipments and mop etc.,. Their spread can be due to the contamination of respiratory care equipment, humidifiers, wound care procedures and patient care items. Therefore, emphasis on the disinfection of materials and shared items is essential along with caution with respiratory and wound care procedures, was suggested in the literature several times. There are several bacteria reported to cause important infections e.g. Shigella species, *Vibrio cholerae*, Entero-pathogenic *E. coli*, *Salmonella typhii* and *Salmonella enteritis*. Others include *Staphylococcus aureus* and species from genus Acinetobacter. This progressive antimicrobial resistance in these bacterial species makes them world-wide importance gaining bacteria especially with reference to developing countries. Proper surveillance data is required so that updates and modification sin the guidelines can be done in order to have empirical treatment and drugs for specific infection causing pathogen.

Among all LAIs, the bacterial pathogens are the most common (Baron and Miller, 2008). The elevated incidence of LAIs in the developing countries including, Pakistan mainly depend upon a number of

socioeconomic and political factors. A few of the factors include:

1. Poor quality of antibiotics (due to improper or lack of monitoring and Quality Compliance).

2. Use of expired, counterfeit drugs having low amount of active substance or availability of the degraded antibiotics.

3. Poor patient compliance also causes the inappropriate use of antibiotics leading to resistance.

4. The misuse of antibiotics by unskilled practitioners, physicians, clinicians and publically without any prescription has also contributed to acquire resistance in bacteria to antibiotics in developing countries.

CONCLUSION

Occupational illness or laboratory-associated infections are not new and have been affecting the economic and health status of many countries since several decades. Proper surveillance and risk assessment may help in controlling and managing the spread of these infections into the community. Although it is not highlighted that much, but is a concern worth pondering on. Many steps have been taken by organizations such as WHO and CDC to bring awareness and to provide better guidance at managing such infections but much efforts are still needed to be taken to resolve this issue.

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