**ANTIMICROBIAL RESISTANCE GLOBALLY AND IN PAKISTAN**

**INTRODUCTION:** Antimicrobial Resistance (AMR) is a complex global public health challenge, and no single or simple strategy will success to fully contain the emergence and spread of infectious organisms that become resistant to the available antimicrobial drugs. The development of AMR is a natural phenomenon in microorganisms, and is accelerated by the selective pressure exerted by use and misuse of antimicrobial agents in humans and animals. The ability of microorganisms to become resistant to the major therapies used against them has long been recognized and is becoming increasingly apparent .*(Ashley D, 1960 )*. Resistance rates for many isolates are rising but are highly variable. For example, the proportion of isolates of Staphylococcus aureus resistant to methicillin increased from close to zero 10.15 years ago to approximately 70% in Japan and the Republic of Korea, 40% in Belgium, 30% in the United Kingdom, and 28% in the USA by 1998 *.* Recent rates of resistance to Streptococcus pneumonia were less than 2% in Belgium, Italy, and Finland, but 7% in Germany, 9.5% in Iceland, 25% in Romania, 44% in Spain and 58% in Hungary *(Appelbaum P, 1992).*

Increasing antimicrobial resistance (AMR) presents a major threat to public health because it reduces the effectiveness of antimicrobial treatment, leading to increased morbidity, mortality, and health care expenditure (4). For example, the mortality rate in outbreaks involving resistant strains of Salmonella spp. was found to be 3.4%, whereas it was only 0.2% in those involving sensitive strains. *(Holmberg S, 1987 )*. In 1995 the cost of containing an outbreak of infection caused by methicillin-resistant S. aureus in a district general hospital in the United Kingdom was estimated to exceed US$ 560 000, while the annual health care cost associated with the treatment of resistant infections in the USA was estimated at over US$ 4 billion , an amount recently revised to more than US$ 7 billion . AMR is the cause of professional, governmental, and public concern and has been classified as a national security risk in the USA *.(Kaldec R, 1997).*

AMR is a global problem. Globalization increases the vulnerability of countries to imported diseases, and infectious diseases travel faster and further than ever before. During the 1990s, for example, a resistant Pneumococcus sp. first identified in Spain was rapidly found in Argentina, Brazil, Chile, China (Province of Taiwan), Columbia, Malaysia, Mexico, the Philippines, Republic of Korea, South Africa, Thailand, USA, and Uruguay *(WHO , 2000).* No country acting on its own can adequately protect the health of its population against AMR. International collective action is essential, yet responsibility for health remains predominantly national. *(Fidler D, 1998).* Consequently, there is a potentially significant disparity between the problems and solutions associated with AMR and the institutions and mechanisms available to deal with them .(*Jamison D, 1999).*

Bacterial resistance has been well documented in several studies and surveys conducted over a decade in Pakistan. Resistance in Gram-negative organisms was increasingly recognized with extended spectrum beta lactamases (ESBLs) being a major concern. A study conducted by Aga Khan University, Karachi from 2001-2006 indicated an increase in ESBL and multidrug-resistant organisms (MDR) producing K. pneumoniae to >30% and 0.4% Carbapenem resistance. A study of blood stream infections (BSIs) from Lahore revealed an alarmingly high resistance in Enterobacteriaceae against 3rd generation Cephalosporins (93.7%); and 6.5% carbapenem resistance among Pseudomonas and Acinetobacter isolates. Infection with pan-drug resistant Acinetobacter is also increasing in many hospital settings across Pakistan with reported high mortality among patients. Different studies conducted during 2004 – 2013 also indicate increasing resistance of E. coli to 3rd generation Cepaholosporins ranging from 12.6% to 94% among clinical isolates. Similarly, high resistance i against 3rd generation Cephalosporins has been reported among Klebsiella spp isolates with increasing frequency. Typhoid continues to be an important public health threat across the country due to drug resistance and associated treatment failure. A study conducted by Aga Khan University on sample size of over 5,000 isolates of Salmonella typhi and S. paratyphi A between 2001-2006 indicated that MDR rate has increased significantly from 34.2% to 48.5% among S. typhi isolates, while quinolone resistance has increased from 1.6% to 64.1 % among S. typhi and from 0% to 47% among S. paratyphi A isolates. Methicillin-resistant S. aureus (MRSA) commonly associated with soft tissue and skin infections (SSTIs), bone and joint infections, blood stream infections (BSIs) and hospital acquired infections (HAIs) has reportedly revealed high rates of resistance. . High prevalence (35%-40%) of MRSA isolates in different hospitalized patients has increasingly led to the use of second line costly drugs. Various studies published between 2004 – 2013 reports Methicillin resistance between 1.2% - >72 % among clinical isolates of S. aureus. Anecdotal evidence suggests that MRSA infections within the community may also be on the rise. Tuberculosis and malaria are also major public health problems in Pakistan. Resistance has emerged with potential negative fallout on the National Programs and grave implications for the public at large. Antimalarial drug resistance has been closely monitored since the early 60s when the honeymoon period of Chloroquine and other aminoquinolines had just begun. However, the first ever report about Chloroquine resistant falciparum was first documented in 1980 and since then the level of resistance has reached >80% (2004)..