Abstract

Emergence of antibiotics resistance (AR) represents a significant global health problem in today's society. Metal exposure makes not only bacteria resistant to heavy metals but also antibiotics. In this study, efforts were made to find the link between heavy metals pollution and AR in the different environment by estimating the abundance of different bacteria resistant to heavy metals and antibiotics as well as different resistant genes mediating resistance to metals and antibiotics and also the mobile genes, present in low and high metal polluted environments in U.K (Tyne River and Ouseburn River) and India (Ganga River, Yamuna River, and 2 STPs). Co-resistance studies were carried out by applying different combinations of heavy metals and antibiotics on the different pathogenic strains to estimate the role of heavy metals in the emergence and proliferation of AR. Genetic analysis was performed to find out the possible mechanism for the co-selection of heavy metals and AR in the different bacterial strains. High concentrations of heavy metals Pb, Cd, and Zn were observed in river Tyne at Featherstone and West Allen. In contrast, heavy metals such as Co, Ni, Cu, and Cr were detected in a very high concentration in the river Ganga at Kanpur and in river Yamuna. Heavy metals were detected in a low concentration in river Ouseburn and river Ganga at Rishikesh and Haridwar. The river Tyne at site Warks Burn has the lowest concentration of heavy metals as this site is relatively pristine with little or no human influences. The abundance of resistant bacteria was found higher in high polluted sites, Kanpur, at river Ganga and in river Yamuna compared to less polluted sites at river Ouseburn and river Ganga at Rishikesh and Haridwar and in high and low metal polluted sites of river Tyne. This was possibly due to a higher abundance of resistance genes in river Yamuna and river Ganga at Kanpur. The lower abundance of resistant bacteria and resistance genes in river Tyne might be due to a highly toxic environment in the river resulting from the high concentration of toxic heavy metals. The

abundance of heavy metals, resistant bacteria, as well as resistant genes, was observed higher in STPs. The higher abundance of resistant bacteria and resistance genes, along with a high concentration of heavy metals at Kanpur and in river Yamuna as well as in STPs, showed the association of heavy metals with the abundance of resistant bacteria and resistance genes. The network analysis indicates a significantly positive correlation between heavy metals concentration and abundance of resistant bacteria and resistance genes as well as between MRB and ARB, MRGs and ARGs, MRB and ARGs, and ARB and MRGs suggesting the co-occurrence of metal and AR in the environment. The abundance of pathogenic MRB, belonging to genera *Pseudomonas, Acinetobacter, Aeromonas, Bacillus,* and members of family *Enterobacteriaceae*, was observed higher in high polluted sites compared to low polluted sites. Co-resistance studies revealed that heavy metals tend to induce AR in different bacterial strains. Heavy metal Cu showed maximum tendency in inducing resistance against all the antibiotics with Zn inducing resistance to meropenem, erythromycin, ciprofloxacin, and ESBL; Pb to meropenem, ciprofloxacin, and ESBL; Ni to ciprofloxacin, erythromycin, and tetracycline; Co to ciprofloxacin and erythromycin; Cd to meropenem and ciprofloxacin and Cr to tetracycline. The genetic analysis indicates that the co-selection of heavy metals and AR in the different bacterial strains might be due to the close association of different MRGs and ARG on the plasmid DNA of bacterial strains (co-resistance) as well as due to the dominating efflux mechanism for resistance to both heavy metals and antibiotics.