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Emergence of Antibiotic Resistant Bacteria in Coastal Waters of India - A Looming Threat

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Abstract:

The antibiotic era started in the 1940's and it changed the profile of infectious diseases and human demography i.e. statistics of deaths, births, income etc. Antibiotic resistance (ABR) is the major issue posing a serious global health threat by which Low and middle income countries are likely to be most affected in terms of public health and economic burden. Many studies have highlighted the adverse effects of antibiotic resistant bacteria in humans and animals. Antibiotic resistant bacteria have been found in coastal waters being added through various sources shifting the natural biodiversity of coastal environment. Further it has also been found in sea food which directly affects human health by consuming the food. India has over 6000kms coastline. Antibiotics are utilized in large quantities for a few decades, until these substances in environment have received little attention. More complex investigation of antibiotic substances has been undertaken in order to permit an assessment of the environmental risks. Antibiotic input, occurrence, fate and effects increasing studies have been published within last decade. This article attempts to review the increasing numbers of antibiotic resistant bacteria in coastal waters of India. It also points towards sources, mechanism of antibiotic resistance in bacteria, risk on human health, antibiotic resistance in sea food and perspective. In this study, the main factors identified for prevalence of antibiotic resistance in coastal waters are anthropogenic activities, recreational activities and hospital effluents due to which there is seen increase in antibiotic resistant bacteria in wide amount in coastal waters of India bringing in the change in biodiversity of coastal waters.

Keywords: Antibiotics, Antibiotic resistant bacteria, Coastal waters, Sea food.5

Introduction:

Coastal environment plays a very important role as habitat to a number of microbes, plants and animals. They serve as shelters, breeding grounds, sources of food for marine life and also are home to number of species. Over 200 km of coastline is covered by the half of current global population. In future, the Centre for Climate Systems Research (CCSR) of the Earth Institute at Columbia University estimates a strong growth of coastal population by 2025. The coastal zone contains natural systems which provide more than half of the global ecosystems services such as natural protection from storms and tidal waves, recreation and goods such as fish, oil and minerals. From world's 17 largest megacities 14 are located along coasts and most of them are located in Asia's fastest growing economies. Large scale destruction of some of these habitats and has reduced their ability to adapt to drastic environmental changes is due to overcrowding of beaches. Development, climate change and commercialization have contributed a major part in increasing the pressure on beach ecosystems. Anthropogenic input of various pollutants especially antibiotics into the aquatic environment has increased the resistant capacity of the bacterial strains. Bacterial load is lower in overlying water body compared to sediments (Fouz *et al.*, 2020)

Sources Of Pollution In Oceans:

Ocean pollution i.e. marine pollution has harmful substances such as plastic, oil, agricultural waste, industrial waste and chemicals substances in the ocean. Anthropogenic activities have severely affected marine life. Occurrence of Antibiotics and antibiotic resistant genes on marine environments can have different mechanisms than the fresh water and waste water. Coastal runoff of ARB from terrestrial sources has been identified as one mechanism for antibiotic resistance occurrence in marine environments (Ben *et al.*, 2019). There are various **point and non-point sources of marine pollution** such as:

a) Sewage
b) Oil spills
c) Toxic chemicals from industries
d) Ocean mining
e) Littering
f) Radioactive waste

World's coastal lands are best places for habitation and industries. Coastal seas form a part of marine environment and are also very rich on fishes, crude oil, minerals (Varkey, 1999). Indian coastline is over 6000 kms. The coastline consists of lands like marshes, mangrove swamps, sandy coasts, rocky coasts, ports etc. These coastal environments are used for ports and shipping, industries waste dumping, salt pans, fishing, aquaculture etc. (Varkey 1999). The definition of coastal pollution by the world health organization is like "The introduction by man, directly or indirectly, of energy or substances into the marine environment, also including estuaries, which likely to result in such deleterious effects such as harm to marine life and living resources, hazards to human health, hindering factor to marine activities, including fishing and other uses of the sea, impairment of quality for the use of sea water and reduction of amenities" (Vikas and Dwarakish., 2015).

Figure 2 & 3 Coastal area's of India maxresdefault.jpg (1280×720) (ytimg.com)banjarmasinmarket.jpg (400×283) (bp.blogspot.com)

The increasing rise of Antibiotic resistant bacteria (ARB) is one of the greatest threats to human health in the 21st century. The presence of antibiotic resistance bacteria associated with coastal water has been a major public health concern (Servias and Passerat. 2009).

Antibiotic resistant bacteria are those bacteria which are not killed by antibiotic rather they continue to grow and even multiply. Antibiotics are used to treat infections in both humans and animals. Antibiotic resistance occurs when bacteria change in response to these antibiotics which leads in multiplication of bacteria. Bacteria become antibiotic resistant and these bacteria may infect animals as well as humans and the treatment for such resistant bacteria costs harder than of non - resistant bacteria (WHO).

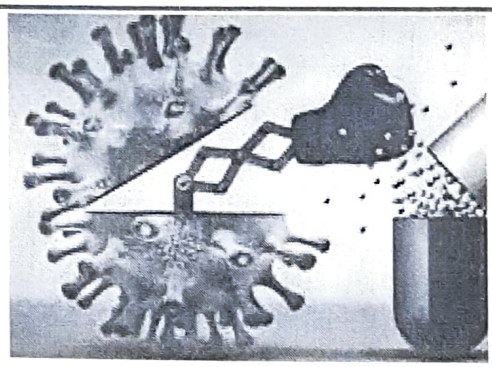

Figure 1: Antibiotic-resistant-bacteria-spread-through-the-environment too.jpg (1854×1165) (earth.com))

Antibiotics released into the aquatic environment are of great concern for three major reasons:

a) Contamination of water used for drinking, recreation and irrigation,

b) Occurrence of bacterial resistance to antibiotics and

c) Negative effect on microbes and life forms which play vital role in nutrient cycling (Costanzo *et al*, 2005).

Antibiotic residues in coastal waters have been recognized in recent years as emerging environmental contaminants (Ben *et al*, 2019). Higher use of antibiotics or overuse in animals and humans for treatment leads to release of antibiotic strains in the environment. After the use of antibiotics, they are partially metabolized and excreted by humans and animals (Diwan *et al*., 2018). Antibiotic resistant bacteria enter aquatic environment through various pathways such as hospital wastewater, municipal waste water, industrial effluent, agricultural sewage etc (Hanna *et al*., 2020) and have potential to be transferred to the aquatic species by horizontal gene transfer(Vernikos and Medini., 2014).

Antibiotic Resistance An Ecological Perspective :

Antibiotics have been used in immense quantities for some decades, until the time these substances in environment has received little attention. Antibiotic input, occurrence, fate and effects increasing studies have been published within last decade. For human medicine and veterinary medicine, antibiotic resistance is one of the major challenges. Despite the numerous studies performed, there is still lack of understanding and knowledge about presence, sources and significance of resistance in bacteria against antibiotics in the aquatic environment (Jalal *et al*., 2012).

Antibiotic resistance has potential of adversely affecting aquatic and terrestrial organisms which can reach to humans through drinking water and food chain. Due to the use of antibiotics, the history of resistance has recently been described more in details. The emergence of resistance is a complex process which is not yet understood with respect to the significance of the interaction of bacterial populations and antibiotics in medical environment as well. If plants are watered with sewage sludge or surface water, or if resistant bacteria are present in meat then the transfer of resistant bacteria to humans could occur via water or food. Transfer from animals to humans of antibiotic resistance is not yet fully understood. However to lower the unwanted intake of antibiotics, the monitoring of antibiotic resistance in sea products is done by many authorities in countries (Jalal *et al*., 2012).

The development of mutations that enable the species to survive in changing outer conditions is due to their ability to adapt to changes in the environment and survive unfavorable

conditions.

Antibiotics have qualitative as well as quantitative effects on the microbial communities in environment. Antibiotic concentrations in most soils are not at therapeutic levels to cause inhibitory effects on population of bacteria, it may still influence the selection of ARB. It has found an increased antibiotic resistance among *Pseudomonas* spp and *Bacillus cereus* after exposure to soil sediments. Many antibiotics have a good tendency to bind with particles of soil (Jalal *et al*., 2012)

Antibiotic Resistance In Sea Food

The antibiotics apart from being used in treating human and animal infection, have also been used in aquaculture and animal husbandry for growth promotion, improvement of feed efficiency and treatment of infections. The use in antibiotics in aquaculture is often arbitrary. Humans are exposed to antibiotic resistant pathogens through food and environment other than treatment of infections. The presence of resistant bacteria in food chain is due to use of antibiotics in food growing facilities. Food animals and birds are the natural reservoir of human pathogenic bacteria such as *Salmonella enterica, Escherichia coli* and *Campylobacter*. The use of antibiotics in animals food naturally leads to the development of resistance in these bacteria, which can be easily transmitted to humans through food. The direct impact on aquatic food such as fish or shellfish being carriers of such bacteria is due to contamination of aquatic environment with pathogenic, antibiotic resistant bacteria. Biomagnification of pathogenic bacteria can occur in filter feeding animals such as oysters and clams, which can accumulate pathogens to numbers several folds higher than the surrounding water. 42% of the isolates from shrimp were resistant to antimicrobial agents which includes human pathogens such as *E.coli*, *Enterococcus* spp, *Salmonella* spp, *Shigellaflexneri*, *Vibrio* spp and *Staphylococcus* spp (Sanathkumar *et al*., 2016).

Risk Of Antibiotic Resistance To Human Health:

Antibiotics are extensively used nowadays so the risk assessment to human exposure to antibiotic resistance in environment has attracted increasing attraction. Antibiotic resistance is the worldwide public health concern because the number of bacteria resistant to antibiotic is increasing. Once entering into human body, antibiotic residues might interact with human microbiome which contains great number of microorganisms inhabiting human body. Daily intake of antibiotic residues from environmental may largely enter the human gastrointestinal tract, where approximately 800-1000 different bacterial species and more than 7000 different strains inhabit. Of these microbes 95% are beneficial bacteria are harmful bacteria and opportunistic pathogens. Antibiotic therapy could lead to composition changes of intestinal microbiota and also induce the emergence of antibiotic resistant bacteria which could persist in human intestine for years. Once imbalance of intestinal microbiota occurs, it may lead to proliferation of harmful bacteria and opportunistic pathogens, and further lead to various diseases If intestinal bacteria have developed antibiotic resistance, multiplied in large numbers, and evolved into super-bugs, the diseases caused by these bacteria cause death thanks to incurability, This is not only a risk to human individuals, but to the global human population (Ben et al,. 2019).

During the course of antibiotic treatment, the taxa which were low in number and susceptible to antibiotics could also be lost, in contrast there upon the antibiotic resistant bacteria would be survived and accumulated. Both epidemiological studies have suggested that the

effects of antibiotics maybe cumulative in the human individuals, and thus it can expect that the effects of environmental antibiotic exposure on human microbiome may cumulate across generations (Ben *et al.* 2019).The most dangerous part of antibiotic resistance is that treatable illness such as pneumonia, tuberculosis and minor infections can become uncurable .

Impact Of Antibiotic Resistant Bacteria On Humans:

However, the resistance against different types of biocides including disinfectants, preservatives, antiseptics, sterilants has been studied and characterized. Only limited sound scientific evidence to correctly access the risks of antibiotic resistance induced by resistance to biocides is available. Although antibiotic usage has clearly benefited the animal industry and helped providing affordable animal protein to the growing human population, the use of antibiotics in food production has also contributed to the emergence and spread of antibiotic multiple resistance (AMR). Along with antibiotics used for human medicine, the use of antibiotics for animal treatment, prophylaxis and growth promotion exerts an inestimable amount of selective pressure toward the emergence and propagation of resistant bacterial strains. Animals can serve as reservoirs, mediators and disseminators of resistant bacterial strains and AMR genes. Antimicrobial resistance thanks to specific antibiotic utilized in food animals may end in reduced efficacy of most or all members of that very same antibiotic class, a number of which may be extremely important for human medicine. The current pharmaceutical era faces multi resistant infectious disease organisms that are difficult and impossible to treat successful (Jalal *et al.*, 2012).

When there is an increase in numbers of bacteria that are resistant to antibiotics, it will be more difficult and more expensive to treat human bacterial infections. According to the study published by the Centres for Disease Control and Prevention (CDC), there are more than 100 antibiotics approved by the US Food and drug administration for human use. As antibiotics fail to treat recurring infections, the consequences include frequent visits to the doctor, hospitalization or even a need for a more expensive medication as a replacement for the existing ineffective ones. Increase in healthcare costs are another important consequence of antimicrobial resistance. Increase in costs are due to the need for additional antibiotic treatments, diagnostic tests, long stay in hospitals, high professional costs and more pain management. In 1998, the Institute of Medicine estimated the annual cost of infections caused by ARB at US$ 4– 5 million per year. This occurrence of antibiotic resistance is found all over the world and has become a serious problem in the treatment of diseases (Jalal *et al*,. 2012)

Studies identify prevalence of antibiotic resistance microbes in coastal environment as well as the adverse effects of antibiotic resistant bacteria in humans and animals. In this study, we aimed to review the increase in the number of antibiotic resistant bacteria and in the coastal waters of India.

Antibiotic Resistant Bacteria In Indian Coasts:

Manjusha S *et al.*, (2005) in their study reported that out of total 119 vibrio isolates taken from Southwest coast of Kerala, 70.70 % were Multiple Antibiotics Resistance (MAR). Highest level of antibiotic resistance was found to be against Ampicillin, Amoxycillin, Carbenicillin, Cefuroxime and was evident in shrimp sample over water samples. Lower antibiotic resistance was seen against chloramphenicol, tetracycline, gentamycin, neomycin and amikacin. This sampling site was disease prone area where cholera outbreak was encountered and persistent use

of antibiotic against this disease might have resulted in antibiotic resistance.

The antibiotic resistance of *E.coli* and occurrence in seafood taken from fish market of southwest coast, Mangalore was studied from which highest s\antibiotic resistance was seen in vancomycin followed by cephalothin, penicillin and no resistance was observed to chloramphenicol, ciprofloxacin and gentamycin. The main reason was due to untreated or treated domestic sewage released into open estuaries and it contains hospital wastes(Kumar *et al.*, 2005).

In the southwest coast, the study was carried out from the samples such as shrimp, water and sediments and it reported that the vibrio parahaemolyticus strain was highly resistant to Ampicillin and polymyxin followed by furazolidone, Neomycin, chloramphenicol, streptomycin, kanamycin and gentamycin. In this study the sample were collected in 3 seasons and in pre monsoons highest antibiotic resistance was found maybe due to vibrios are more relevant in summers than winters (Rekhadevi *et al* .,2009).

In the study carried out by Diwan et al., 2010, in sea water sample of west coast, Ujjain the samples which were collected in afternoon showed higher number of antibiotic residues i.e. Amikacin followed by ciprofloxacin. The main source was hospital waste due to which antibiotic residues were found.

The study conducted on Digha coast of west Bengal showed higher antibiotic resistance to ampicillin which was examined from marine fish samples and high level of viable heterotrophic bacteria whereas Chloramphenicol and tetracycline resistant bacteria from these samples were found to be significantly low. High number of the antibiotic resistant bacteria in the fish may create ecological and public health implications (Ghosh and Mandal., 2010).

The water samples were collected from westcoast of keralafrom which vibrio strains were isolated. Highest antibiotic resistance was observed against amoxycillin followed by ampicillin, carbenicillin, cefuroxime, streptomycin, neomycin, amikacin, rifampicin andmeropenem. Lower resistance was against trimethoprim, gentamycin, sulphafurazole, ciprofloxacin. These antibioticas are mostly used to prevent diseases in human beings. It maybe anthropogenic activities which influenced in acquiring resistance in vibrio spp (Manuja S. and Bhat., 2011).

In the study carried out in southewestveraval coast, shoreline water sample was examined from which *E.coli*, fecal coliforms, *Klebsiella*spp, *Enterobacter*spp, *salmonella* spp were determined and were tested for antibiotic resistance. High antibiotic resistance was against bacitracin and penicillin G followed by oxacillin, ampicillin, vancomycin and no resistance was observed to polymyxin B, gentamycin. Multiple antibiotic resistance was noted in 100% *Enterobacter*spp, 86% fecal coliform, 85% *Klebsiella*. Main source causing marine environmental contamination were improper and unnecessary use of antimicrobial drugs by humans and animals (Maloo et al., 2014).

In this study, Fish samples were colleceted from Mumbai and Cochin coast, from which *Staphylococcus aureus* was isolated. The highest antibiotic resistance was seen against erythromycin followed by azithromycin, clarithromycin, ampicillin, penicillin G, amoxiclav and no resistance was observed in chloramphenicol. The main indication is the status of unhealthy handling of seafood by fisherman. S. aureus showed MDR to various antibiotic classes. In case of hospitals MDR level of S.aureus is upto 70% which shows that MDR percentage level of s.aureus of fish market origin is lesser resistant than of clinical origin (Visnuvinayagam S *et*

al.,2015).

Kumar *et al*., (2016) conducted a study on fresh sea food sample of north Mumbai and determined methicillin-resistant *Staphylococci*. Factors such as poor sanitation and hygiene during seafood handling and transportation, and cross-contamination by workers which are asymptomatic carriers of coagulase-positive s.aureus.

In this study, researcher collected samples of sediment from westcoast, Mumbai and determined halophilic and haloarchea. High antibiotic resistance was against ampicillin followed by trimethoprim and lower resistance was streptomycin. Antibiotic resistance may be due to presence of R-plasmids (Shinde and Thombre, 2016).

In the study conducted bySivaraman et al., 2017, the fish sample were collected from Veraval coast, Gujrat and E coli was isolated and tested for resistant level and EBSL production. High level of antibiotic resistance was against ampicillin followed by trimethoprim, cefeprim, sulfamethoxidole, ciprofloxacin, cefuroxime. The presence of antibiotic resistance bacteria in fish maybe due to post harvest contamination such as infected handlers, repeated use of contamination water and uncleaned vessel in the fishery outlets.

Study by Singh *et al*., (2020) showed *E coli* was isolated from sea food sample collected from markets of Mumbai, high antibiotic resistance was observed against cephalosporinscefotaxime followed by cefpodoxime, ceftazidime. The study highlights improper hygienic conditions of the coastal waters, retail market and the landing centres

In a study, by Stalin and Srinivasan., (2016) researcher collected sediment samples from black shrimp ponds and sea coast from which *vibrio harveyi* was isolated. High antibiotic resistance was observed for Amikacin, ampicillin, azithromycin, gentamycin, chloramphenicol, vancomycin, nalidixicacid, ciprofloxacin. As widespread use of antibiotic among humans, a global increase in number of antibiotics resistant bacteria caused resistant pathogens in aquatic environment.

Conclusion:

The coastal environment in its various niches i.e in water column, sediments on the surface of different life forms are found to harbour antibiotic resistant bacteria. Presence of virulence genes of Escherichia coli in the marine environment, Methicillin resistant strains in sea food and multiple drug resistant bacteria isolated sea food obtained from contaminatedcoastal environment indicates increasing health risk to public health in India who are either exposed to contaminated water during recreational activities or when consumesea food from such contaminated waters.

The routes and source of contamination is very hard to predict as an aquatic system receives bacterial population from diverse sources. There's a need to alert fishermans and fish handlers to take strict hygienic measures during storage, handling and harvest of fish. The resistant strain in sea food can form commensal flora via food chain. Raw or partially treated sewage which is released into fishing areas is the main concern that requires the attention of local regulatory bodies. Antibiotic resistance and Multiple drug resistance which occurs is not only limited to only pathogenic bacteria or organisms which involves hospital acquired infection but is also wide spread in marine halophilic bacteria isolated from their natural environment. It can be presumed that anthropogenic factors i.e. hospital effluents, recreational activities and sewage discharge can continue to pose major sources of contamination and alter the native biodiversity of marine environment.

From this study, we can understand that major factors responsible for emergence of antibiotic resistant bacteria in coastal waters of India are anthropogenic activities, recreational activities, unhygienic handling of fish and hospital effluents which indicates the increase in number of antibiotic resistance bacteria in coastal water can pose a serious threat of increased antibiotic resistance gene pool in the coastal environment.

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