

# Antibiotic Resistance (AR) Among Enteric Bacteria in Marine Environments of Marmara Sea



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## Abstract

Recently, antibiotic resistance has been identified as “the most important and the most urgent global danger” by United Nations. The subject of how and when the life-saver antibiotics have become the seven hundred thousand peoples’ cause of death has been on the United Nations’ agenda. Extraordinary meetings, political declarations and fast campaign decisions have shown the importance of the subject, the antibiotic resistance [1,2]. Each country had listed what they should do for their own and took action. The priority was the studies about determining the type of resistance and mechanisms about it. After that, the theme of raising awareness of community about rational usage of antibiotics became more important. The main topics aimed to be completed were also took shape for Turkey, an active attendee of the meetings. This mini review aims to address the need for a greater understanding of the role of the marine environment and host micro biome in influencing the evolution, acquisition and spread of antibacterial resistance, and acting as a reservoir for resistance, not only for Turkey but also for other countries.

**Keywords:** Antibiotic resistance; AR; Enteric bacteria; *Escherichia coli*; Marmara Sea; Turkey

## Introduction

Inappropriate and excessive consumption of one of the most important inventions in human history, antibiotics, with an increased rate, has resulted with the problem of antibiotic resistance (AR) [3]. Microorganisms are the oldest creatures of the Earth with a skill of fast adaptation for ever changing status of the environment. With that skill, sooner or later they develop an ability to combat with antimicrobial agents used for destroying them, the “resistance” [4]. This strategy, evolution of bacterial antibiotic resistances, had caused the resistance to become very important, life-threatening problem for all humanity [5]. Nowadays the rate of resistance is rapidly increasing not only for hospital-based cultures but also cultures taken from the environment, which enlarges the problem and makes it even more serious [6-8].

In International meetings, in order to solve the AR problem, the importance of supporting the projects is highlighted. Great deal of countries are supporting the cause and allocating the necessary budget in medical researches [7]. For this purpose, Research Councils like UCL, NERC, BBSRC and MRC, which help researchers willing to take part about the subject from other countries, are leading the projects with attendance of different countries with a budget of £6.5m. Four main topics have been defined to study about in these projects.

1. Understanding resistant bacteria.
2. Accelerating therapeutics and diagnostics development.
3. Understanding the real world interactions.
4. Behaviour within and beyond the health care setting.

As similar project calls, this programme also aims to address the need for a greater understanding of the role of the outdoor environment and host micro biome in influencing the evolution, acquisition and spread of antibacterial resistance and acting as a reservoir for resistance. The programme is restricted to antibacterial and resistant bacteria or bacterial resistance genes, of clinical and/or veterinary importance. Researches supported can be based in agriculture, aquaculture, wastewater and natural environments (and their interfaces), the human and animal host micro biome.

## Result and Discussion

Marine areas are special areas preferred for resting and recreational purposes. But unfortunately these special areas are also influenced by residential, industrial and ship wastes. Turkey is a rich country in marine areas, especially with Marmara Sea, which has a special attribute for being an inner-sea. However, in last 20 years, it gained a feature which itself feels and also shows

the pressure of increased infrastructure and intense pollution [9] 40-50 species that had been fished for commercial purposes have regressed to 20-25 species; annual fishing quotas have reduced with same rate, and most of the species can no longer be seen, yet hunted [10].

In addition, the Marmara Sea which suffered a lot in the subject of biodiversity has started to show changes in its micro flora, because of infrastructural problems and changes in coastal area usage awareness [11]. Even though in aquatic environments bacteria are also a natural part of the ecosystem [12] the enteric bacteria found in areas with residential wastes and heavy pollution represent dense fecal contamination. In recent years, just like the megacities of other countries, the most important city of Marmara Sea, İstanbul, is feeling the anthropogenic pressure amply. At the same time the other neighbours of Marmara Sea in İzmit and Bursa, which are the industrialization centres and in Yalova, which is the centre of shipyards are under a similar pressure. The reason for changes we face in flora of Marmara Sea can be explained with anthropogenic sourced wastewaters reaching the sea and excellent adaptation of bacteria to the environment. In Turkey, maximum and minimum limits for all the parameters necessary and recommended values for all water sources (excluding open sea water) are regulated in Surface Water Quality Regulation [13]. For "microbiologic water quality", accepted bacteriologic parameters are defined as "Total coliform" and "Fecal coliform", by Environmental Protection Agency (EPA) and World Health Organization (WHO). Maximum limits calculated by "Membrane Filtration (MF)" method are in limitations of >10000/100ml and >200/100ml respectively, in Turkey. But according to WHO, USEPA and WRC especially in aquatic areas used for recreational purposes, fecal coliform bacteria value should not exceed 200/100ml [14]. Unfortunately, in some coastal areas, particularly in ones without proper wastewater treatment systems and wastes reaching the sea, these values may reach up to 10<sup>6</sup>.

In the list of megacities of the world, İstanbul is in the 25<sup>th</sup> place with approximately 18% of Turkey population. In İstanbul, "problems based on environmental pollution and inadequacy of recreational areas and public social life areas" is the 5<sup>th</sup> most important problem being faced. To prevent the problems in place, the İstanbul coastal area is being monitored via testing the samples taken from at least 40 different stations monthly and for longer than 15 years [15,16]. Miniaturization is not being done only by universities, but also by authorized government units with care. In studies of determination of enteric bacteria in İstanbul's southwest shore surface water, it has been found that present bacterial pollution levels for last 8 years are exceeding aquaculture, fishing and recreational levels designated, frequently [17,18]. In molecular studies for determination of pathogenic existence, especially Gram negative pathogen species, *Escherichia coli*, *Enterobacter sp.*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa* had been found dominant in Marmara Sea [19,20]. This prominent situation threatening

both the ecosystem and public health may cause a different risk with addition of antibiotic resistant bacteria existence in place [21]. These bacteria with different antibiotic resistant genes are foreseen to spread on surface waters, deep waters, in sediment, in other words across all marine ecosystem [22,23].

In studies for molecular characterization and antibiotic resistance for same areas in residential wastes, bacteria from human intestinal flora with R-plasmid found present. R-plasmid in these bacteria, which makes them resistant to antibiotics, can easily spread to environment because of wastewaters mixing with environmental waters [24,25]. In studies of Marmara Sea coastal areas, 10 chosen antibiotics (ampicillin, amoxicillin, amikacin, streptomycin, nalidixic acid, trimethoprim-sulfamethoxazole, tetracycline, chloramphenicol, imipenem, ceftazidime) resistance percentages were investigated. The results point out the high density of especially beta-lactam type antibiotic resistant bacteria. With changes yearly, the highest resistance percentages were identified as, in order; ampicillin (%83.1), amoxicillin (%57.8), tetracycline (%50.7), trimethoprim-sulfamethoxazole (%42.2), nalidixic acid (%38), ceftazidime and streptomycin (%16.9), chloramphenicol (%14.1) [26,27]. In sea water samples of İzmit Gulf, these ratios were found as tetracycline %50, sulbactam/ampicillin %62.5, penicillin %62.5, gentamicin %50, amikacin %12.5, chloramphenicol %37.5, cephoperazone %25, kanamycin %37.5, trimethoprim/sulfamethoxazole %62.5 [28].

For studies accomplished in Turkish seas, it is possible to find similar percentages to Marmara Sea. In a study of sea water sourced coliform class 1 and class 2 integron gene cassettes and antibiotic resistance characterization in East Coast of Black Sea, resistance percentages were tetracycline (%23.2), ampicillin (%20), sulfamethoxazole (%11.6), streptomycin (%9.3), chloramphenicol (%4.6), trimethoprim (%2.3), respectively [29]. In a study of Iskenderun Gulf area, in isolated Gram negative bacteria strains, resistance percentages were, in order; ampicillin (%93.2), streptomycin (%90.2), cefazolin (%81.3), imipenem (%16.5), meropenem (%13.9), cefepime (%8), respectively [27].

Similar to seas of other countries, high resistance values and resistance genes which can be transferred by mobile elements like plasmid, transposon, integron have been detected in Turkey [28]. But intriguingly, in isolated bacteria strains coming from the samples of ship ballast tanks, cruising in most of our seas and going into and coming from Marmara Sea, high resistance to antibiotics were also identified [29,30]. This shows that the studies about the antibiotic resistance are necessary not only in medical practice but also in surface and sea waters and even in international transit ships.

### Conclusion

Apparently, common usage of antibiotics for human and animal health causes a specific pressure on bacteria, which

results with emergence and spread of antibiotic resistance. Antibiotic resistant bacteria, which are the food source for some of the organisms, can easily reach seas via rivers, streams and/or other kind of aquatic systems and spread their resistance genes to aquatic ecosystems.

Antibiotics indispensable for treatment, coming against us as “the most important and most urgent global danger: antibiotic resistance problem” in recent times. In order to solve this issue, preventing irrational use of medications, raising national awareness campaigns and creating “Rational Antibiotic Usage” educations are necessary. But in the same time, it should be known that antibiotic resistant bacteria may reach natural waters and seas, and can spread their resistance genes. In addition to successful national campaigns, inclusion of national and international environmental projects and studies are necessary for solution aims of this global problem. In this subject, Turkey continues on awareness campaigns and research projects as a strong leader in its region.

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