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Occurrence and distribution of azithromycin in wastewater treatment plants, seawater, and sediments of the northern part of the Persian Gulf around Bushehr port: A comparison with Pre-COVID 19 pandemic

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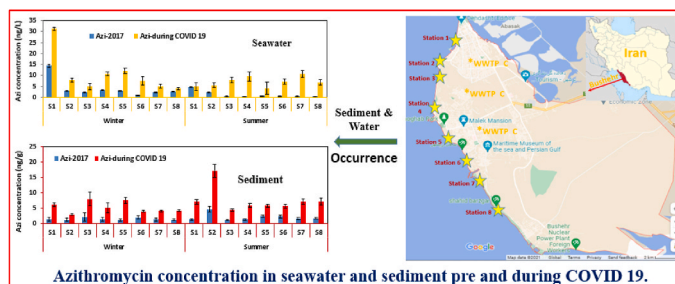
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HIGHLIGHTS

- Azithromycin in the seawater and sediments of the Persian Gulf coast was measured.
- Azithromycin (Azi) in wastewater treatment plants was studied as a possible source.
- Azi pollution in seawater and sediment was 3 and 4-fold higher than pre-COVID.
- Azi level in seawater was similar in winter and summer (7 ng/L).

GRAPHICAL ABSTRACT



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ABSTRACT

One of the environmental effects of COVID 19 is the contamination of ecosystems with antibiotics due to their high consumption to treat this disease. Many years ago, the distribution of antibiotics including azithromycin (Azi) in wastewater treatment plants in Bushehr city, seawater, and sediment of the Persian Gulf has been investigated. As Azi has been prescribed to COVID 19 patients, contamination of the environment with this drug can also be assumed. Thus, we decided to examine this hypothesis by repeating our previous study during COVID 19 period. We collected wastewater samples from influent, effluent, and different units of three wastewater

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Wastewater treatment plants
Seawater

treatment plants (WWTPs) including one municipal WWTP (Plant A) and two hospital-WWTPs (Plant B and C). Seawater and adjusted sediments were gathered from 8 stations located in the Persian Gulf in two seasons to evaluate the special and temporal variation. The results showed a huge growth of Azi pollution in all studied matrixes. The mean Azi values in the influent of Plant A, B, and C were 145 ng/L, 110 ng/L, and 896 ng/L, which represented an 9, 6, and 48-time increase compared with those obtained in 2017 (before COVID 19). The Azi removal efficiency had a different behavior compared to before COVID 19. The mean concentration of Azi in seawater and sediment samples was 9 ng/L and 6 ng/g, which was 3 and 4-fold higher than the previous study. Opposed to our former study, the Azi amount in the aqueous phase was less subjected to temporal seasonal variations. Our observations indicated the wide distribution of Azi in the environment and a future threat of intense growth of antibiotic resistance in ecosystems.

1. Introduction

Antibiotics are a widely used class of drugs that are effective in treating bacterial infections in humans and animals by killing bacteria or preventing them from growing and multiplying due to their functional group (Cano et al., 2020; Rodriguez-Mozaz et al., 2020; Murugesan et al., 2021). Today, over 250 chemical substances are classified as human and animal antibiotics (Rodriguez-Mozaz et al., 2020) and have become a group of daily consumed xenobiotics that enter to environment continuously, through residential, hospital, and clinical usage. They are complex molecules that their introduction of antibiotics into the environment as unmetabolized or incompletely metabolized forms poses a major health risk due to the emergence and selection of antibiotic-resistant genes and bacteria (Guo et al., 2020; Sabatino et al., 2020; Rathi et al., 2021). So, the World Health Organization has identified antimicrobial resistance as one of the top 10 global public health threats to humans (EclinicalMedicine, 2021).

The rate of antibiotic consumption has increased by 39% from 2000 to 2015 (Klein et al., 2018), whereas it is estimated that 700,000 people die each year from bacterial infections, and if left unamended, that number will rise to 10 million a year by 2050, and leaving a loss of 100 trillion USD (O'Neill, 2016).

Besides agricultural biosolids and aquaculture, wastewater treatment plants (WWTPs) are one of the main receptors for antibiotics. Wastewater treatment plants are usually not designed to remove micropollutants such as antibiotics (Prasannamedha et al., 2022; Saravanan et al., 2022). Therefore, the outlet of the treatment plant can be a hot spot for antibiotics to enter the environment. Different studies all over the world have surveyed the presence of antibiotics in effluents and their effect on the distribution of contamination in receiving environments such as rivers, seawater, sediments, and soil (Pan and Chu, 2017; Kairigo et al., 2020; Shi et al., 2020; Zafar et al., 2021).

While it seemed necessary to take any action to reduce the use of antibiotics, the emergence of a COVID 19 phenomenon messed up everything. Since December 2019, the world has been facing a pandemic called COVID 19 caused by the novel coronavirus SARS-CoV-2. Globally, as of July 15, 2022, the cumulative number of confirmed coronavirus cases and deaths were 557,917,904 and 6,358,899, respectively (Badvi and Javanbakht, 2021; WHO, 2022). As of July 11, 2022, a total of 12,130,881,147 vaccine doses have been administered (WHO, 2022). Counting three doses per person, a large population of the world has not yet been vaccinated. Although COVID is a viral disease, antibiotics are used to treat bacterial co-infections (Usman et al., 2020), and various studies have shown that even in the absence of a bacterial co-infection, antibiotics are prescribed to treat the disease (Chen et al., 2020a; Asmarawati et al., 2021). So, concerns about increasing antibiotic usage and associated resistance intensified. For example, a study by Abelenda-Alonso et al. in a 700-bed hospital in California reported a significant increase in antibiotic consumption during the COVID 19 period over the same time before the pandemic (Abelenda-Alonso et al., 2020).

Among the various antibiotics, azithromycin (Azi) from the class of macrolides, the third most widely consumed group of antibiotics (Klein et al., 2018), with antiviral and immunomodulatory effects, is known as

one of the most useful therapies for treating COVID 19 (Arshad et al., 2020; Echeverría-Esnal et al., 2021). Azi by acting against a wide range of microorganisms is used for curing respiratory diseases and sexually transmitted infections (Kagkellaris et al., 2018; Liu et al., 2018). So, by a continuous introduction to the environment, it is considered a pseudo-persistent pollutant (Zhang and Jiang, 2021). For example, in Guerra et al. study in 2014 on six treatment plants in Canada, Azi was detected in all influent and effluent samples (Guerra et al., 2014). Also, in Kulkarni et al. study in 2017 on four treatment plants in the United States, Azi showed the highest values (concentration range: 22–336 ng/L) in all influent samples compared to other studied antibiotics (Kulkarni et al., 2017). Azi is not biodegradable and some physico-chemical processes have been posed to the treatment of Azi (Talaie-khozani et al., 2020).

On the other hand, antibiotic resistance has been confirmed in Azi-receiving environments (Sivaranjane and Kumar, 2021). Bengtsson-Palme et al. and Milaković et al.'s studies on the effluent of Azi-producing plants reflected the high prevalence of Azi-resistant genes and bacteria in effluents with high concentrations of azithromycin (Bengtsson-Palme et al., 2019; Milaković et al., 2019). Therefore, the prevalence of COVID 19 and the intensification of Azi consumption may amplify concerns about increasing Azi resistance. Since the study of wastewater can monitor the process of drug use at a specific time and place, this period can also reflect the changes in antibiotic consumption (Reinstadler et al., 2021), especially Azi in this case. Among the studies conducted in this field is the study of Chakraborty et al. which in the period from August to September 2020 in 4 municipal WWTPs and one hospital WWTP in south India, Azi was found in 100% of the influent samples in the range of 54–360 ng/L (Chakraborty et al., 2021). However, there is still insufficient data to compare the levels of Azi in wastewater pre- and post-COVID 19.

In our previous study, in 2015 and 2016, we examined the concentration of six antibiotics in one municipal WWTP and two hospital WWTPs, as well as in receiving seawater and sediments on the northern shoreline of the Persian Gulf. The results showed that the highest value among the studied antibiotics in the influent samples from the municipal wastewater treatment plant belonged to Azi with an average concentration of 16 ng/L. Azi was also detectable in all influent, seawater, and sediment samples (Kafaei et al., 2018).

After COVID 19 pandemic, due to the importance of increasing the prescription of Azi on the distribution of this antibiotic in water bodies, we decided to repeat the study in the same previous places, in particular for azithromycin, and compare the results with previous findings and conclude whether the pandemic has increased the distribution of Azi in the environment? Therefore, the concentration of Azi was measured at the influent of one municipal WWTP and two hospital WWTPs and the effluent of each process in the evaluated WWTPs. Also, the prevalence of Azi in seawater and sediments of the northern coast of the Persian Gulf (around Bushehr port, Iran) was determined.

2. Material and methods

2.1. Description of the researched hospitals

The sewage of two main hospitals of Bushehr city (Bentolhoda Hospital and Shohaday-e-Khalij-e-Fars Hospital), which were heavily involved with corona patients, was investigated. The two researched hospitals used more than 60% of their capacity to treat corona patients during the years 2020 and 2021. It should be noted that in the second half of 2021, due to the severity of this disease in Iran, many patients were treated at home. One of the drugs prescribed by Iranian doctors for corona disease was the antibiotic azithromycin (Tarighi et al., 2021) (although this drug was not part of the treatment protocol announced by the Ministry of Health).

2.2. Sampling campaign

This study was conducted under the same protocol that was used for our previous study. Sampling points, gathering, preparing of samples, used materials and chemicals, and samples analysis were adjusted to before. Thus, more information about this section can be found in the previous study (Kafaei et al., 2018).

Three wastewater treatment plants located in Bushehr city (Iran) were subjected to sampling. Treatment plant A was a municipal treatment plant that utilized a stabilization pond as the treatment system. Sewage samples of this plant were gathered from the influent and effluent of the pond and the stream that passes through inline chlorination. Plant B was the treatment plant of a hospital (Bentolhoda Hospital) with a septic tank system and samples were collected before entering the system and after complete treatment by the septic tank. Plant C was another hospital treatment plant (Shohaday-e-Khalij-e-Fars Hospital) and samples were taken from raw influent wastewater, the effluent of the grit chamber, the effluent of the primary sedimentation unit, and the effluent of the secondary sedimentation unit. Other characteristics of treatment plants are summarized in Table 1. It is noteworthy that the operating conditions of the treatment plant have not changed before and during the coronavirus. Daily composite samples were gathered every 8 h, on 3 consecutive days for each unit. Fig. 1 shows the geographical location of wastewater treatment plants and stations on the north coast of the Persian Gulf around the Bushehr port.

To evaluate the special distribution of Azi in the receiving water and sediment, a series of samples were collected from the aqueous phase and sediment. To do this, 8 stations were chosen in the tidal zone of the Bushehr coastline located along the Persian Gulf. On the shores of Bushehr port, surface runoff along with (treated) sewage enters the sea. Treatment plant B discharges a part of the effluent between Station 1 and 2. The sewage treatment plant C discharges its output to the vicinity of Station 5. It should be noted that some old parts of Bushehr, such as the areas near stations 1 to 3, do not have a sewage collection network, and wells are used to discharge sewage from houses. Considering that the underground water level is high, it is likely that the improper disposal of sewage in these areas is also effective in the Azi pollution of seawater.

For studying temporal changes, sampling was conducted on August

Table 1
Characteristics of the treatment plants investigated in this study.

| Treatment plant | Type of treatment | Daily flow | Retention time | Use of effluent |
|-----------------|--------------------|------------|----------------|---|
| A | Stabilization pond | 35,250 | 6 h | Irrigation, dispose into the sea |
| B | Septic tank | 8 | 5 days | The output enters the inlet of treatment plant A with a tanker. |
| C | Activated sludge | 14.5 | 2 days | Irrigation, dispose into the sea |

2020 (dry season) and February 2020 (wet season) on 3 consecutive days. On each day, 1 composite sample was taken from each station at the 30-cm water depth at a radius of 5 m. Adjusted surface sediment (0–5 cm) samples were also gathered in the vicinity of the same places where water samples were taken at a surface area of 5 cm × 5 cm. Water and wastewater were collected in 500 mL pre-cleaned amber glass bottles and extracted by a 0.45 μm glass fiber filter. Sediment was taken through a shovel, after freeze-drying and sieving through an 80 μm filter, and kept at −20 °C until extraction.

2.3. Analytical method and azi distribution technique

The Azi antibiotic analysis in all samples (seawater, wastewater, and sediment) was performed by the instrument of high-performance liquid chromatography-electrospray ionization tandem mass spectrometry (HPLC–ESI-MS/MS). The details regarding the measurement of the Azi antibiotic including quality assurance-quality control (QA-QC), the recovery percentages, and limits of quantification (LOQ) are fully described in Table 2. Also, details regarding reagents and chemical used for the measurement of Azi is presented in the Supplementary Information.

ArcGIS 10.5 software and interpolation technique of inverse distance weighting (IDW) approach was employed to evaluate the spatial distribution of Azi antibiotic in the sediment and seawater. Details of this method are given in the Supplementary Information.

3. Results and discussion

3.1. Distribution of azi in the studied treatment plants

Fig. 2 shows the differences between the concentration of Azi in influent and effluent of 3 treatment plants. As we see, in all influents and effluents Azi was detected and had more concentration compared to previously detected ones. Since the operational conditions were the same as before in 3 studied plants, the most effective factor in AZI distribution was detected the consumption due to coronavirus prevalence.

The mean Azi value in the influent of the municipal treatment plant (145 ng/L) was 8.8-fold higher than doses before COVID 19 (16 ng/L). Before COVID 19 stabilization pond was able to degrade Azi completely, but during COVID 19 mean removal efficiency by the stabilization pond was 52% and Azi was present with a mean concentration of 70 ng/L in the effluent. In a study (Azanu et al., 2018), the concentration of macrolides was recorded at 96–1,931 ng/L, after stabilization pond decreased to 47–882 ng/L, and complete removal was not obtained. It seemed that stabilization pond is more effective for antibiotic removal in low concentration, with the respect that the only difference between this sampling campaign with former is the introduced concentration. Design and operational parameters mainly include sludge retention time, hydraulic retention time, and working capacity which were the most important factors in the various removal efficiency of 60–90% in 4 wastewater stabilization ponds studied by researchers (K'Oreje et al., 2018), were not affecting our study.

After the stabilization pond, wastewater was introduced to the chlorination line, and the mean concentration of Azi in the effluent of chlorination was measured at 17 ng/L. As in our previous study, any Azi did not enter to chlorination line, so we cannot compare it with that. In a study (Loganathan et al., 2009), chlorination cannot completely destruct Azi and reduced the concentration of Azi from 65 ng/L to 35 ng/L (remove to about half) showed less removal than our study (remove to about a quarter). It was also indicated that chlorination can be effective in antibiotic destruction but not completely (Batt et al., 2007). Studies have indicated that pH and initial free chlorine dosages are effective factors in the rate of macrolides destruction (Li and Zhang, 2012, 2013). Totally, the municipal treatment plant showed a mean removal efficiency of 88%. So, it can result in the effluent of the municipal WWTP is one of the distributors of Azi into the environment during COVID 19

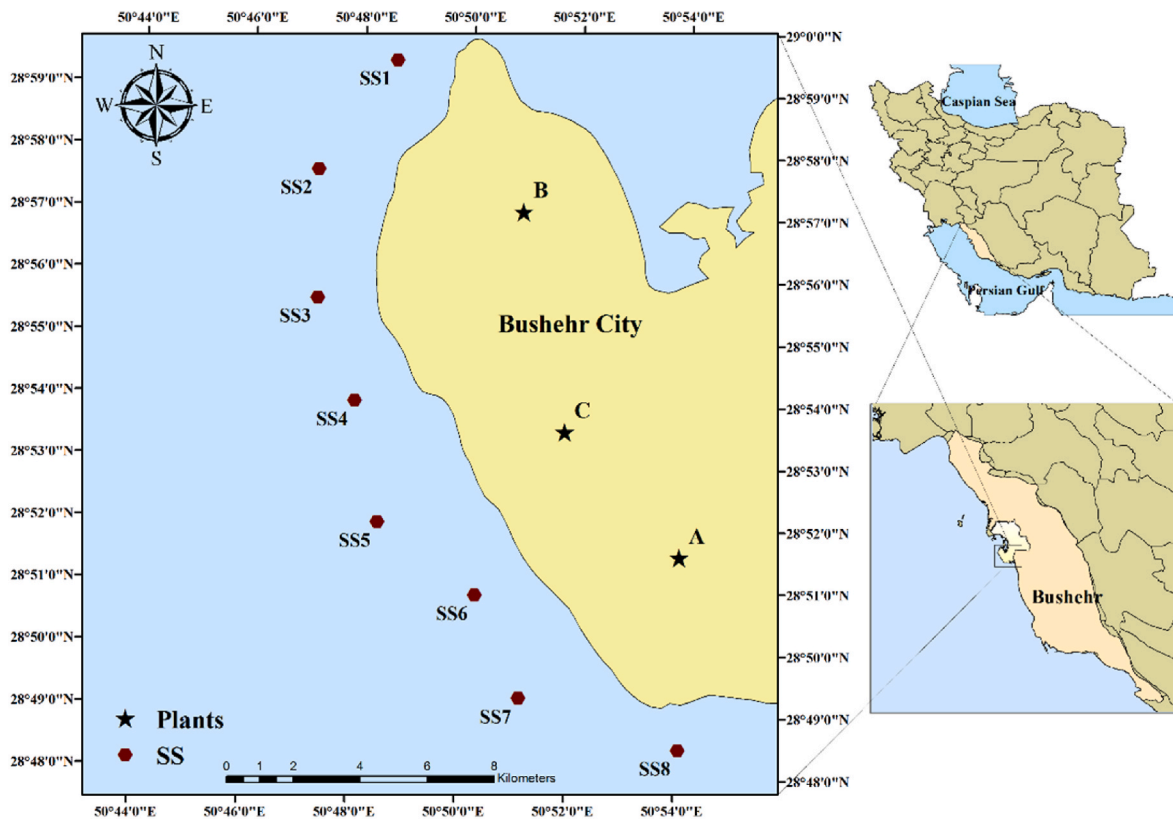


Fig. 1. Map of sampling stations (SS is the sampling stations. A, B, and C are WWTPs).

Table 2
The recovery percentage of Azi and LOQ of wastewater, seawater, and sediments sample.

| Wastewater sample | | | Seawater sample | | | | Sediment sample | | |
|-------------------------|------------|------------|-------------------------|------------|------------|-------------------------|-----------------|------------|--|
| Recovery percentage (%) | LOQ (ng/L) | | Recovery percentage (%) | LOQ (ng/L) | | Recovery percentage (%) | LOQ (ng/g) | | |
| 10 (ng/L) | 50 (ng/L) | 100 (ng/L) | 10 (ng/L) | 50 (ng/L) | 100 (ng/L) | 10 (ng/g) | 50 (ng/g) | 100 (ng/g) | |
| 81 | 86 | 82 | 81 | 81 | 90 | 94 | 82 | 83 | |
| | | | | 0.3 | 0.4 | | | 0.6 | |

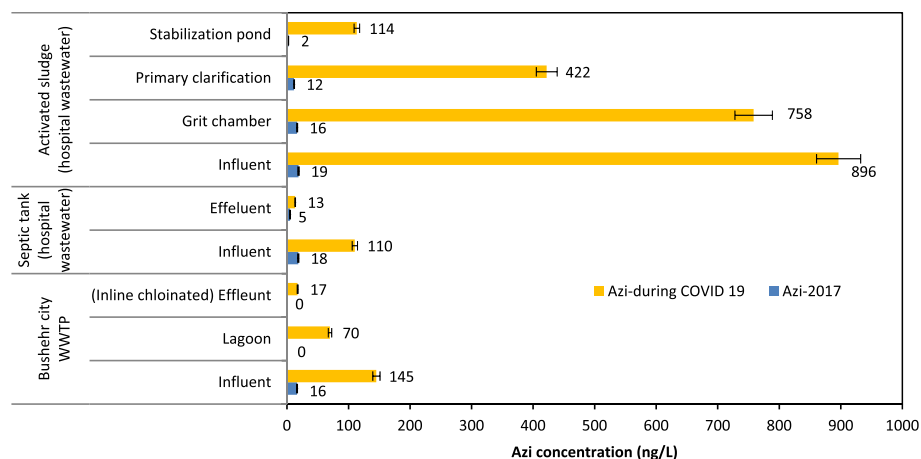


Fig. 2. Azi concentration in the studied wastewater treatment plants.

pandemic.

Before COVID 19, both hospital treatment plants had almost the same amounts of Azi in the influent (Plant B: 18 and Plant C: 19 mg/L). But during the pandemic, Plant C showed a much higher concentration of Azi, the mean Azi value in the plant influent was 47.8 times larger than before and detected in the mean value of 896 ng/L, while the mean

concentration of Azi in Plant B increased to 110 ng/L. The difference is related to this issue that COVID 19 patients' hospitalization mainly takes place in Plant C and Plant B just those positive corona patients had been hospitalized that had gone due to heart disease.

In Plant B the removal efficiency of Azi was about 87% and effluent concentration was detected at 13 ng/L, while the adjusted values before

COVID 19 were 73% and 5 ng/L. These results showed that the septic tank, however, is not able to remove Azi completely but is efficient in the removal of high values of Azi as much as low concentrations, even more. A study in Qatar in 2016 on a wastewater treatment plant (septic tank) showed 91% efficiency for macrolides removal (Al-Maadheed et al., 2019).

In Plant C which utilized the activated sludge process a huge increased amount of Azi was detected in influent and effluent of treatment process units. As we expected greatest mutation occurred in this plant, and the mean value of influent Azi was detected about 48 times higher than before. In comparison with before COVID 19, the mean values of Azi in influent, grit chamber effluent, primary clarifier effluent, and secondary sedimentation effluent increased from 19 to 896 ng/L, 16–758 ng/L, 12–422 ng/L, and 2–114 ng/L, respectively. The removal efficiency of Azi before and during COVID 19 for the great chamber, primary clarifier, and secondary sedimentation was measured at 12% and 15%, 30% and 44%, 79%, and 73%. In total, the efficiency of Plant C in removing azithromycin was the same (87%) for before and during the pandemic. This value showed that the activated sludge system had a similar trend to Azi removal with various ranges. In a study in China, the Azi concentration in the influent of 12 treatment plants that utilized a secondary treatment process was reported in a wide range (5–501 ng/L) and removal efficiency in the highest condition was very close to our results (Zhang et al., 2017). In another study (Yasojima et al., 2006), the mean concentration of Azi in the influent of 6 treatment plants in Japan was detected at 260 ng/L that decreased to 138 ng/L after the secondary treatment and total removal efficiency of Azi through activated sludge system was calculated 49%.

The activated sludge system is not designed for antibiotic removal. In this process, antibiotics are mainly removed through two mechanisms of adsorption and biodegradation (Oberoi et al., 2019; Zhu et al., 2021), while adsorption is dominant. Adsorption of antibiotics to primary and biological sludge depends on the sludge adsorption coefficient (K_d). Higher K_d values represent a greater affinity of antibiotics to adsorption to the sludge. Hydrophobic interactions are another factor that is effective for macrolide adsorption to sludge (Zhu et al., 2021).

The main removal mechanism in the grit chamber is the adsorption of antibiotics onto coarse particles and consequently sedimentation or degradation by photolysis or aeration (Liu et al., 2019). So, removal efficiency in the grit chamber is low for micropollutants including antibiotics. As we see lowest reduction level (12%) was recorded for the grit chamber and the Azi concentration was reduced from 896 ng/L to 758 ng/L. This finding is in accordance with a study (Pan and Yau, 2021) that reported a reduction of Azi through grit chamber in 2 treatment plants in China in the range of 1.7%–13.2%. Similar to our study, another study in China (Yuan et al., 2015) showed 17.5% removal efficiency for a horizontal grit chamber.

Similar to grit chamber, adsorption to primary sludge is the main way of antibiotic removal from wastewater, especially for a hydrophobic antibiotic such as Azi due to adsorption to lipid fraction of primary sludge (Park et al., 2017). The mean value of Azi was 758 ng/L in influent that reduced to 422 ng/L in the effluent (~30% removal), which showed a 15% lower reduction compared to before COVID 19. So, in this stage, it can be also concluded that better efficiency is happen for lower Azi content. The removal efficiency of primary treatment in WWTPs studied in Korea has been reported at 15% for most of the investigated antibiotics (Park et al., 2017). A study in the USA in 2017–2018 showed no significant reduction of antibiotics including Azi through primary treatment, while influent concentration was 22–639 ng/L (Angeles et al., 2020).

The effluent of the primary clarifier gets into secondary or biological treatment. Compared with before COVID 19, the removal efficiency of Azi in the biological treatment process did not show considerable variation and, in both studies, it was ~70–80%. Thus, in activated sludge systems the inlet concentration of Azi was not determining the removal efficiency. The removal efficiency might be depended on operational

conditions. As activated sludge includes negatively charged particles, and Azi carries a positively charged dimethylamino group, electrostatic interactions cause to accumulation of Azi in activated sludge (Hu et al., 2018). A study (Tran et al., 2016) has reported a moderate removal of macrolides by activated sludge process, as the median concentration of Azi in influent was 1,949 ng/L decreased to 470 ng/L in secondary effluent (the removal efficiency was 49–81%), which similar to our findings.

Removal efficiencies of different stages of treatment are plotted in Fig. 3. Based on data provided in Fig. 3, any process was not able to complete degrade or remove Azi. While before COVID 19 stabilization pond showed the most removal efficiency but during COVID 19 its efficiency decreased to about half. During COVID 19 most efficiencies were related to the septic tank unit, while its efficiency increased about 15% relative to before. Chlorination was the second effective unit during COVID 19 but we do not have data to compare with before. The next effective unit in both sampling campaign belonged to the activated sludge process. Primary clarification and grit chamber represented the lowest removal efficiency, respectively in both periods, however, their removal efficiency increased during COVID 19. As we expected primary treatment such as primary clarifier and great chamber did not have a bold role in Azi removal and the main task was on the secondary treatment including the septic tank, stabilization pond, and activated sludge process. It concluded that biological degradation and adsorption to secondary sludge are the most effective mechanisms for Azi reduction, while sedimentation along with coarse particles during primary treatment is not the main distributor of Azi removal.

Totally, 3 studied WWTPs showed a huge growth not only in the influent concentration of Azi, but in the effluents, and effluent values in Plant A and B were higher than influent samples belonged before COVID 19. It was detected that treatment processes were not ready for enough removal of Azi. Therefore, they have not been designed for micropollutant removal and in the critical condition, it would be worse. Accordingly, these systems might propose a larger threat to the environment compared before the prevalence of coronavirus. In the next step to evaluate this hypothesis, we would discuss the impact of this increase on receiving water and sediments.

3.2. Distribution of azi in seawater and sediments

In all 96 composite seawater and sediment samples, Azi was detected higher than the detection level, and we faced a considerable growth relative previous study (before COVID 19).

3.2.1. Azi in seawater

Azi concentration in seawater during COVID 19 compared to its concentration before COVID 19 in both winter and summer seasons has been depicted in Fig. 4. Generally, Azi concentration has increased by 3 and 6 times in seawater in winter and summer than the equivalent time of before COVID 19, respectively. This showed that COVID 19 pandemic has affected the marine environment and antibiotic pollution by Azi is more prevalent than pre-COVID. Ignoring Station 1, the average Azi concentration in winter and summer before COVID 19 was reported at 2 ng/L and 1 ng/L, respectively. This revealed that the mean concentration of Azi was impressed by temporal seasonal variation, and a lower concentration in summer was linked to more biodegradation, and photodegradation due to increasing summer sunlight, the temperature of seawater, and the activity of microorganisms. During COVID 19, mean values of Azi in winter and summer were close to each other (~7 ng/L). This indicated that the input concentration of Azi has overcome environmental degrading factors and large consumption and release of Azi due to COVID 19 have influenced both seasons in the same way. Although removal and degradation of antibiotics in water are rare, due to high stability (Xu et al., 2019) but generally sorption to sediment, biodegradation, photolysis, and hydrolysis are ways that may affect the removal of antibiotics in seawater (Desbiolles et al., 2018).

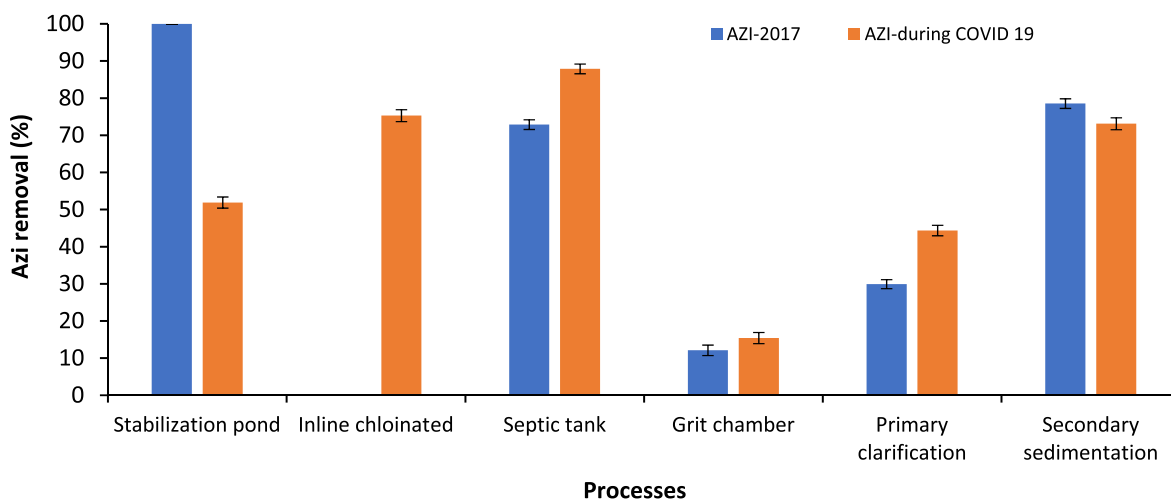


Fig. 3. Removal efficiency (%) of different processes in the AzI removal.

In winter a 1.5–3 fold increase in AzI values was experienced compared to before COVID 19 and mean values were measured in the span of 4–31 ng/L. Just like the previous study, the highest mean amount of AzI was detected in Station 1, as 31 ng/L during COVID 19 and 14 ng/L before COVID 19. The next values belonged to Station 5 and 4, as 12 and 11 ng/L showed 4 and 3 fold increases compared to before the pandemic, respectively. But highest increase degree is dedicated to Station 6, as the mean value of 1 ng/L before COVID 19, which increased to more than 7 ng/L during COVID 19 in the winter (increase rate: 7-time). The lowest mean amount belonged to Station 8 (4 ng/L), however, was higher than all detected values in all stations except Station 1 in our previous study.

We were faced with a wider range of enhancements for summer times samples. In Station 1 mean value before and during COVID 19 was around 5 ng/L. Before COVID 19 highest value was dedicated to Station 1 (~5 ng/L), but during COVID 19 s-lowest concentration after Station 5 (4 ng/L) was related to Station 1 (5 ng/L), which showed a smooth increase in AzI amount. But in Station 4 and 7, mean AzI values were obtained at 0.2 ng/L and 0.5 ng/L before COVID 19, which increased to 10 ng/L and 11 ng/L during COVID 19 showing an elevation rate of 50 and 22-fold, respectively. Station 7 was known as the most critical station for AzI release to seawater in summer.

Different studies have reported various ranges for AzI in seawater samples. The mean value of AzI (14 ng/L) in seawater samples adjust to a mariculture area in China in 2019 was about 2 times higher than our values (Du et al., 2019), while Du et al. in China reported the mean AzI concentration of 5 ng/L in coastal water, that was lower than our mean values in both seasons (Du et al., 2017). Physicochemical properties of seawater are a determining factor in the distribution of antibiotics. In our previous study, we demonstrated that the AzI content of seawater was directly correlated with the potassium level of seawater. But in this period, it seemed that the initial concentration of AzI is the most important factor in AzI distribution in the Persian Gulf water.

3.2.2. AzI in sediment

Fig. 5 represents the mean values of AzI in sediments during COVID 19 compared to amounts before COVID 19. Mean values of AzI in sediment samples in this study compared to before the pandemic raised from 1 ng/g to 5 ng/g in winter and 2 ng/g to 7 ng/g in summer showing a remarkable increasing rate in both seasons and indicated that AzI pollution similarly affected sediments in both seasons. Cation exchange has known as the most important mechanism of AzI adsorption to sediment (Hanamoto and Ogawa, 2019).

For winter samples, like before COVID 19, the highest mean AzI value belonged to Station 3, and the mean amount for this station was 2

ng/g and 8 ng/g for pre- and during COVID, respectively. The next biggest value was reported for Station 5 (7 ng/g), which showed the lowest amount in our previous study (1 ng/g), so the highest mean growth (7-fold) was recorded for this station. The pH level, TOC, and silt content of sediment have been detected as an important factor in the distribution of AzI in winter.

Such as the previous study, the mean AzI concentration in sediment samples in summer was greater than those in winter. For sediment samples taken in the summer before COVID 19, the lowest amounts of the evaluated antibiotic (1 ng/g) belonged to Station 1, 3 and 4. This trend was repeated in the COVID 19 period and the lowest AzI value was detected in Station 3 (4 ng/g) and Station 4 (6 ng/g). On the other hand, the highest concentration was detected in Station 2 for both the pre- and during the pandemic, with the mean value of 5 ng/g and 17 ng/g, respectively. The residential houses near Station 2 have an old texture and do not have a sewage collection network. Probably, the sewage wells in this area have caused more pollution to the beach near it. Compared to before COVID 19, the highest increase in summer samples was reported for Station 1 in which the mean calculated value raised from 1 ng/g to 7 ng/g, and minimum growth was seen in Station 5 and 6 (3-time increase). Based on Fig. 5, the highest detected amounts in winter and summer belonged to Station 3 and 2, respectively, which like the previous study indicated the ability of movement of antibiotics including AzI on the sediment. Fernandes et al. reported a higher concentration of AzI in bottom samples compared with the top zone, confirming the migration of AzI through sediment (Fernandes et al., 2020).

Among 6 antibiotics investigated in sediment samples in the north of Portugal in 2020, the highest values belonged to AzI (43 ng/g) which was much higher than our detected values in all stations (Fernandes et al., 2020). Our results were against Li et al. work that reported higher macrolides values in sediment in the wet season rather than the dry one (10 ng/g and 11 ng/g for the dry and wet seasons, respectively). They related this issue to the higher discharge of these antibiotics in the wet season as well as more antibiotic accumulation in sediment at higher flow rates (Li et al., 2018).

3.2.3. Relationship between seawater and sediments

The pseudo-partitioning coefficient ($k_{w,s}$) was used as a tool for quantitative description of the relationships of antibiotics (here, AzI) concentration between the sediment (C_s) and water phase (C_w) according to the following equation:

$$k_{w,s} = C_s/C_w \quad (1)$$

As we see in Table 3, during the COVID pandemic, $k_{w,s}$ values of AzI in Station 8 were close together, 1035 L/kg and 1025 L/kg in winter and

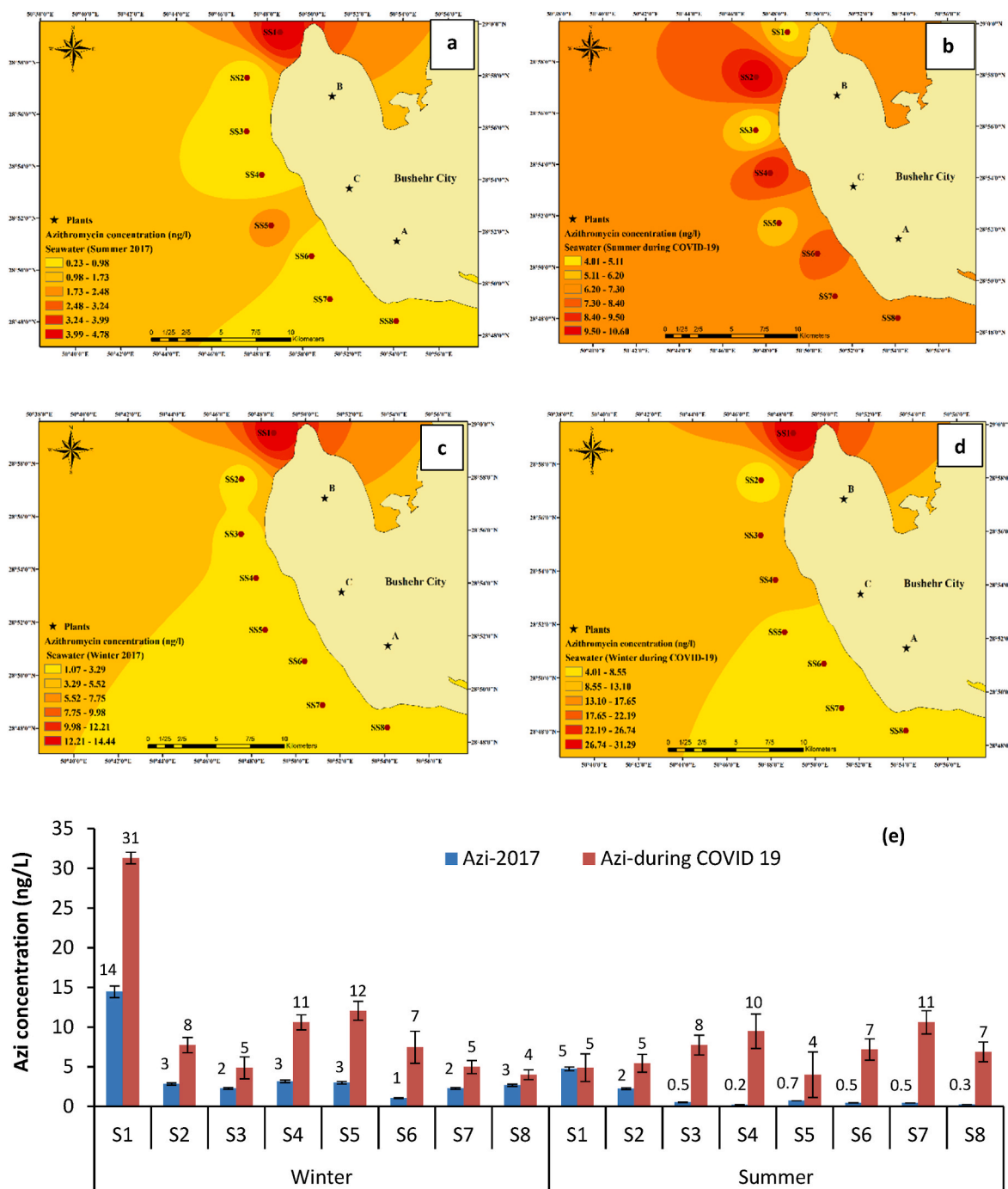


Fig. 4. (a–d) Distribution and (e) concentration of Azi in seawater samples of the Persian Gulf.

summer, respectively. These values for Station 3 and 5 were higher in winter than in summer, and for other stations were fewer in winter. Compared with before COVID 19 samples, in winter samples, except Station 2 and 6, $k_{w,s}$ has increased compared with before COVID, and even some stations (like 1 and 8) have faced more than two times increase. But in summer samples, except Station 1 and 2 reflected 6 and 2 times enhancement, other stations represented less $k_{w,s}$ amounts. This shows less accumulation of Azi in sediments than water in summer compared to before COVID 19, while we faced the opposite trend in winter. Guo et al. expressed that $k_{w,s}$ values related to macrolides had a negative relationship with dissolved organic matter in the water and total organic carbon in sediment (Guo et al., 2017). Chen et al. by analyzing the correlations between $k_{w,s}$ and physicochemical properties

of sediment and seawater, have indicated the complexity of partitioning behaviors of antibiotics between the seawater and sediment, and this equilibrium is affected by different physicochemical characteristics and hydrologic conditions (Chen et al., 2020b).

Coronavirus was a big shock for whole societies and the environment, and one of the most important outcomes of this phenomenon was the high consumption of water and medicines that strongly impressed wastewater treatment plants and water bodies consequently. Studied samples from seawater and sediment of the Persian Gulf indicated an increase in antibiotic burden in this area. Compared to the previous study (before COVID 19), distribution of a much higher level of Azi was observed in sediment and aqueous phase that can be received not only from wastewater treatment plants but from other resources such as

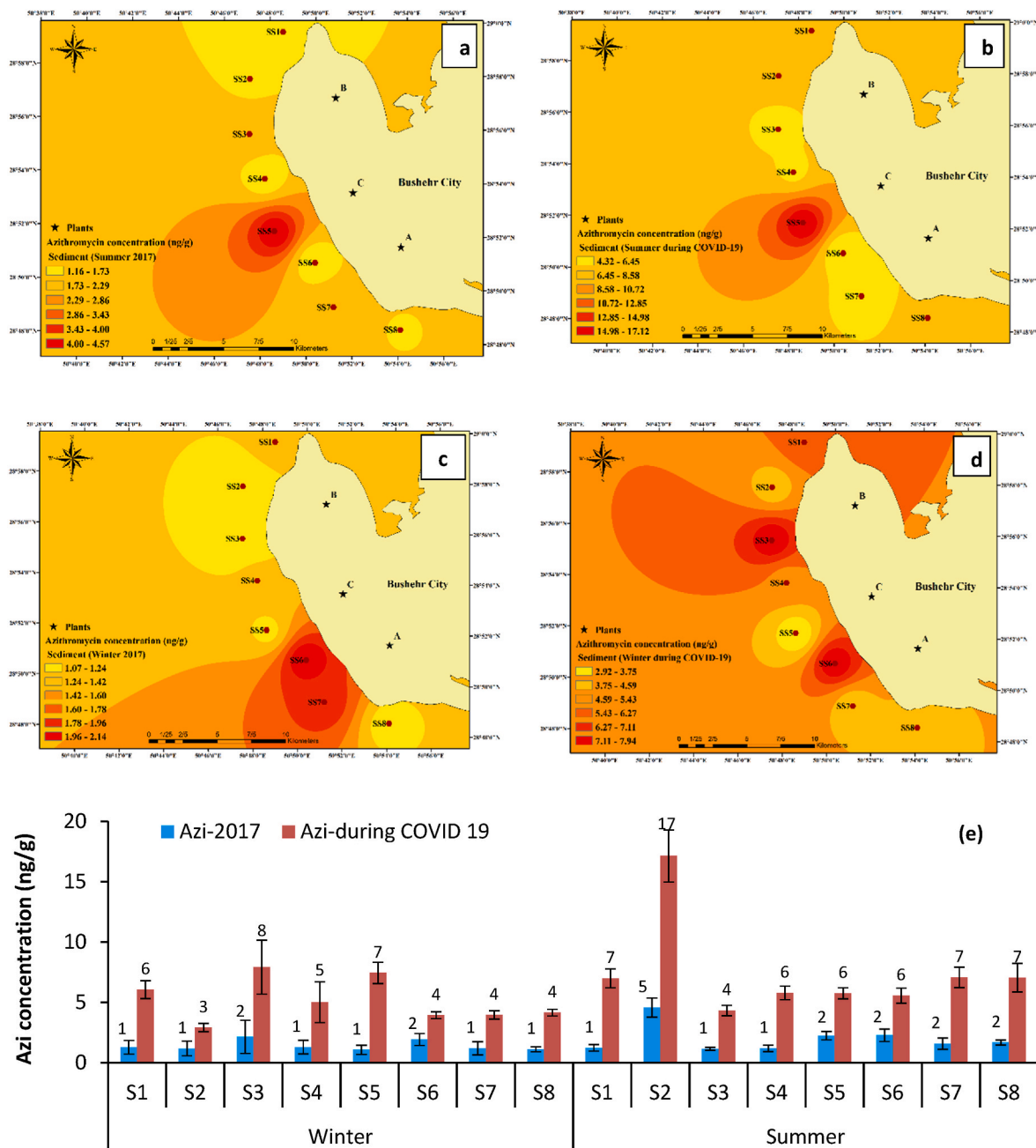


Fig. 5. (a–d) Distribution and (e) concentration of Azi in sediment samples of the Persian Gulf.

runoffs and illicit discharges. However, we should be aware of this massive growth in antibiotic resistance that has begun now and will continue in the post-COVID 19 eras.

4. Conclusions

The occurrence and distribution of azithromycin (Azi) in the influent and effluent of involved processes of the main wastewater treatment plant in Bushehr port as well as seawater and sediment of the Persian Gulf were investigated. The results of Azi concentration during the COVID 19 disease were compared with those before this period (i.e., 2017). Compared to before COVID 19, the concentration of Azi entering the treatment plants had increased by 6–48 times, while its elimination process did not follow a specific pattern. The stabilization pond worked less useful in higher Azi amounts but the efficacy rate of the septic tank was elevated. The concentration of azithromycin in seawater and

sediments samples increased during COVID 19 compared to before this disease. The Azi level in 8 stations along the Persian Gulf in the dry and wet season was measured in the range of 4–31 ng/L and 3–17 ng/g for seawater and sediment samples, respectively. The high level of Azi is an alarm to be careful about water bodies concerning antibiotic resistance promotion that may have been started now and is going to be a more serious problem in the post-COVID era.

Credit authorship contribution statement

F. Mirzaie: Formal analysis, Methodology. **F. Teymori:** Formal analysis, Writing-review & editing. **S. Shahcheragh:** Methodology. **S. Dobaradaran:** Conceptualization, Methodology. **H. Arfaeinia:** Methodology, Writing-review & editing. **R. Kafaei:** Supervision, Formal analysis, Methodology. **S. Sahebi:** Methodology, Funding acquisition. **S. Farjadfar:** Methodology. **B. Ramavandi:** Supervision, Methodology,

Table 3
The value of $k_{w,s}$ (L/kg) for Azi.

| Season | Sites | Azi-2017 | Azi-during COVID 19 |
|--------|-------|----------|---------------------|
| Winter | S1 | 89 | 194 |
| | S2 | 415 | 378 |
| | S3 | 949 | 1626 |
| | S4 | 408 | 473 |
| | S5 | 357 | 618 |
| | S6 | 1799 | 528 |
| | S7 | 529 | 795 |
| | S8 | 419 | 1035 |
| Summer | S1 | 259 | 1431 |
| | S2 | 2035 | 3143 |
| | S3 | 2183 | 558 |
| | S4 | 5270 | 610 |
| | S5 | 3082 | 1434 |
| | S6 | 4851 | 775 |
| | S7 | 3511 | 667 |
| | S8 | 6720 | 1025 |

Writing-review& editing.

Declaration of competing interest

The authors declare that they have no known conflict of interest that may obscure or affect their judgment to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.chemosphere.2022.135996>.

References

- Abelenda-Alonso, G., Padullés, A., Rombauts, A., Gudiol, C., Pujol, M., Alvarez-Pouso, C., Jodar, R., Carratalà, J., 2020. Antibiotic prescription during the COVID-19 pandemic: a biphasic pattern. *Infect. Control Hosp. Epidemiol.* 41, 1371–1372.
- Al-Maadheed, S., Goktepe, I., Latiff, A.B.A., Shomar, B., 2019. Antibiotics in hospital effluent and domestic wastewater treatment plants in Doha, Qatar. *J. Water Proc. Eng.* 28, 60–68.
- Angeles, L.F., Mullen, R.A., Huang, I.J., Wilson, C., Khunjar, W., Sirotkin, H.I., McElroy, A.E., Aga, D.S.J.E.S.W.R., Technology, 2020. Assessing pharmaceutical removal and reduction in toxicity provided by advanced wastewater treatment systems. *Environ. Sci. J. Integr. Environ. Res.: Water Research & Technology* 6, 62–77.
- Arshad, S., Kilgore, P., Chaudhry, Z.S., Jacobsen, G., Wang, D.D., Huitsing, K., Brar, I., Alangaden, G.J., Ramesh, M.S., McKinnon, J.E., O'Neill, W., Zervos, M., Nauriyal, V., Hamed, A.A., Nadeem, O., Swiderek, J., Godfrey, A., Jennings, J., Gardner-Gray, J., Ackerman, A.M., Lezotte, J., Ruhala, J., Fadel, R., Vahia, A., Gudipati, S., Parraga, T., Shallal, A., Maki, G., Tariq, Z., Suleyman, G., Yared, N., Herc, E., Williams, J., Lanfranco, O.A., Bhargava, P., Reyes, K., 2020. Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19. *Int. J. Infect. Dis.* 97, 396–403.
- Asmarawati, T.P., Rosyid, A.N., Suryantoro, S.D., Mahdi, B.A., Windradi, C., Wulaningrum, P.A., Arifianto, M.V., Bramantono, B., Triyono, E.A., Rusli, M., Rachman, B.E., Marfiani, E., Endraswari, P.D., Hadi, U., Kuntaman, K., Nasronudin, N., 2021. The clinical impact of bacterial co-infection among moderate, severe and critically ill COVID-19 patients in the second referral hospital in Surabaya. *F1000Res* 10, 113–113.
- Azanu, D., Styryshave, B., Darko, G., Weisser, J.J., Abaidoo, R.C., 2018. Occurrence and risk assessment of antibiotics in water and lettuce in Ghana. *Sci. Total Environ.* 622, 293–305.
- Badvi, K., Javanbakht, V., 2021. Enhanced photocatalytic degradation of dye contaminants with TiO₂ immobilized on ZSM-5 zeolite modified with nickel nanoparticles. *J. Clean. Prod.* 280, 124518.
- Batt, A.L., Kim, S., Aga, D.S., 2007. Comparison of the occurrence of antibiotics in four full-scale wastewater treatment plants with varying designs and operations. *Chemosphere* 68, 428–435.
- Bengtsson-Palme, J., Milakovic, M., Švecová, H., Ganjto, M., Jonsson, V., Grabic, R., Udikovic-Kolic, N., 2019. Industrial wastewater treatment plant enriches antibiotic resistance genes and alters the structure of microbial communities. *Water Res.* 162, 437–445.
- Cano, P.A., Jaramillo-Baquero, M., Zúñiga-Benítez, H., Londoño, Y.A., Peñuela, G.A., 2020. Use of simulated sunlight radiation and hydrogen peroxide in azithromycin removal from aqueous solutions: optimization & mineralization analysis. *Emerging Contaminants* 6, 53–61.
- Chakraborty, P., Pasupuleti, M., Jai Shankar, M.R., Bharat, G.K., Krishnasamy, S., Dasgupta, S.C., Sarkar, S.K., Jones, K.C., 2021. First surveillance of SARS-CoV-2 and organic tracers in community wastewater during post lockdown in Chennai, South India: methods, occurrence and concurrence. *Sci. Total Environ.* 778, 146252.
- Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y., Xia, J.a., Yu, T., Zhang, X., Zhang, L., 2020a. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 395, 507–513.
- Chen, Y., Cui, K., Huang, Q., Guo, Z., Huang, Y., Yu, K., He, Y., 2020b. Comprehensive insights into the occurrence, distribution, risk assessment and indicator screening of antibiotics in a large drinking reservoir system. *Sci. Total Environ.* 716, 137060.
- Desbiolles, F., Malleret, L., Tiliacos, C., Wong-Wah-Chung, P., Laffont-Schwob, I., 2018. Occurrence and ecotoxicological assessment of pharmaceuticals: is there a risk for the Mediterranean aquatic environment? *Sci. Total Environ.* 639, 1334–1348.
- Du, J., Zhao, H., Liu, S., Xie, H., Wang, Y., Chen, J., 2017. Antibiotics in the coastal water of the South Yellow Sea in China: occurrence, distribution and ecological risks. *Sci. Total Environ.* 595, 521–527.
- Du, J., Zhao, H., Wang, Y., Xie, H., Zhu, M., Chen, J., 2019. Presence and environmental risk assessment of selected antibiotics in coastal water adjacent to mariculture areas in the Bohai Sea. *Ecotoxicol. Environ. Saf.* 177, 117–123.
- Echeverría-Esnal, D., Martín-Ontiyuelo, C., Navarrete-Rouco, M.E., De-Antonio Cuscó, M., Ferrández, O., Horcajada, J.P., Grau, S., 2021. Azithromycin in the treatment of COVID-19: a review. *Expert Rev. Anti-infect. Ther.* 19, 147–163.
- EclinicalMedicine, 2021. Antimicrobial resistance: a top ten global public health threat. *eClinicalMedicine* 41, 101221.
- Fernandes, M.J., Paíga, P., Silva, A., Llaguno, C.P., Carvalho, M., Vázquez, F.M., Delerue-Matos, C., 2020. Antibiotics and antidepressants occurrence in surface waters and sediments collected in the north of Portugal. *Chemosphere* 239, 124729.
- Guerra, P., Kim, M., Shah, A., Alaei, M., Smyth, S.A., 2014. Occurrence and fate of antibiotic, analgesic/anti-inflammatory, and antifungal compounds in five wastewater treatment processes. *Sci. Total Environ.* 473–474, 235–243.
- Guo, X.-p., Zhao, S., Chen, Y.-r., Yang, J., Hou, L.-j., Liu, M., Yang, Y., 2020. Antibiotic resistance genes in sediments of the Yangtze Estuary: from 2007 to 2019. *Sci. Total Environ.* 744, 140713.
- Guo, X., Feng, C., Zhang, J., Tian, C., Liu, J., 2017. Role of dams in the phase transfer of antibiotics in an urban river receiving wastewater treatment plant effluent. *Sci. Total Environ.* 607–608, 1173–1179.
- Hanamoto, S., Ogawa, F., 2019. Predicting the sorption of azithromycin and levofloxacin to sediments from mineral and organic components. *Environ. Pollut.* 255, 113180.
- Hu, J., Zhou, J., Zhou, S., Wu, P., Tsang, Y.F., 2018. Occurrence and fate of antibiotics in a wastewater treatment plant and their biological effects on receiving waters in Guizhou. *Process Saf. Environ. Protect.* 113, 483–490.
- K'Oreije, K.O., Kandie, F.J., Vergeynst, L., Abira, M.A., Van Langenhove, H., Okoth, M., Demeestere, K., 2018. Occurrence, fate and removal of pharmaceuticals, personal care products and pesticides in wastewater stabilization ponds and receiving rivers in the Nzoia Basin, Kenya. *Sci. Total Environ.* 637–638, 336–348.
- Kafaei, R., Papari, F., Seyedabadi, M., Sahebi, S., Tahmasebi, R., Ahmadi, M., Sorial, G. A., Asgari, G., Ramavandi, B., 2018. Occurrence, distribution, and potential sources of antibiotics pollution in the water-sediment of the northern coastline of the Persian Gulf, Iran. *Sci. Total Environ.* 627, 703–712.
- Kagkellaris, K.A., Makri, O.E., Georgakopoulos, C.D., Panayiotakopoulos, G.D., 2018. An eye for azithromycin: review of the literature. *Therapeutic Advances in Ophthalmology* 10, 2515841418783622.
- Kairigo, P., Ngumba, E., Sundberg, L.-R., Gachanja, A., Tuhkanen, T., 2020. Occurrence of antibiotics and risk of antibiotic resistance evolution in selected Kenyan wastewaters, surface waters and sediments. *Sci. Total Environ.* 720, 137580.
- Klein, E.Y., Van Boeckel, T.P., Martinez, E.M., Pant, S., Gandra, S., Levin, S.A., Goossens, H., Laxminarayan, R., 2018. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc. Natl. Acad. Sci. USA* 115, E3463.
- Kulkarni, P., Olson, N.D., Raspanti, G.A., Rosenberg Goldstein, R.E., Gibbs, S.G., Sapkota, A., Sapkota, A.R., 2017. Antibiotic concentrations decrease during wastewater treatment but persist at low levels in reclaimed water. *Int. J. Environ. Res. Publ. Health* 14.
- Li, B., Zhang, T., 2012. pH significantly affects removal of trace antibiotics in chlorination of municipal wastewater. *Water Res.* 46, 3703–3713.
- Li, B., Zhang, T., 2013. Different removal behaviours of multiple trace antibiotics in municipal wastewater chlorination. *Water Res.* 47, 2970–2982.
- Li, S., Shi, W., Li, H., Xu, N., Zhang, R., Chen, X., Sun, W., Wen, D., He, S., Pan, J., He, Z., Fan, Y., 2018. Antibiotics in water and sediments of rivers and coastal area of Zhuhai City, Pearl River estuary, south China. *Sci. Total Environ.* 636, 1009–1019.
- Liu, H., Zhou, X., Huang, H., Zhang, J., 2019. Prevalence of antibiotic resistance genes and their association with antibiotics in a wastewater treatment plant. *Process Distribution and Analysis* 11, 2495.

- Liu, P.-y., Chen, J.-r., Shao, L., Tan, J., Chen, D.-j., 2018. Responses of flocculent and granular sludge in anaerobic sequencing batch reactors (ASBRs) to azithromycin wastewater and its impact on microbial communities. *J. Chem. Technol. Biotechnol.* 93, 2341–2350.
- Loganathan, B., Phillips, M., Mowery, H., Jones-Lepp, T.L., 2009. Contamination profiles and mass loadings of macrolide antibiotics and illicit drugs from a small urban wastewater treatment plant. *Chemosphere* 75, 70–77.
- Milaković, M., Vestergaard, G., González-Plaza, J.J., Petrić, I., Šimatović, A., Senta, I., Kublik, S., Schloter, M., Smalla, K., Udiković-Kolić, N., 2019. Pollution from azithromycin-manufacturing promotes macrolide-resistance gene propagation and induces spatial and seasonal bacterial community shifts in receiving river sediments. *Environ. Int.* 123, 501–511.
- Murugesan, A., Loganathan, M., Senthil Kumar, P., Vo, D.-V.N., 2021. Cobalt and nickel oxides supported activated carbon as an effective photocatalysts for the degradation Methylene Blue dye from aquatic environment. *Sustainable Chemistry and Pharmacy* 21, 100406.
- O'Neill, J., 2016. *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. Government of the United Kingdom.
- Oberoi, A.S., Jia, Y., Zhang, H., Khanal, S.K., Lu, H., 2019. Insights into the fate and removal of antibiotics in engineered biological treatment systems: a critical review. *Environ. Sci. Technol.* 53, 7234–7264.
- Pan, M., Chu, L.M., 2017. Fate of antibiotics in soil and their uptake by edible crops. *Sci. Total Environ.* 599–600, 500–512.
- Pan, M., Yau, P.C., 2021. Fate of macrolide antibiotics with different wastewater treatment technologies. *Water, Air, Soil Pollut.* 232, 103.
- Park, J., Yamashita, N., Park, C., Shimono, T., Takeuchi, D.M., Tanaka, H., 2017. Removal characteristics of pharmaceuticals and personal care products: comparison between membrane bioreactor and various biological treatment processes. *Chemosphere* 179, 347–358.
- Prasannamedha, G., Kumar, P.S., Shivaani, S., Kokila, M., 2022. Sodium alginate/magnetic hydrogel microspheres from sugarcane bagasse for removal of sulfamethoxazole from sewage water: batch and column modeling. *Environ. Pollut.* 307, 119523.
- Rathi, B.S., Kumar, P.S., Show, P.-L., 2021. A review on effective removal of emerging contaminants from aquatic systems: current trends and scope for further research. *J. Hazard Mater.* 409, 124413.
- Reinstadler, V., Ausweger, V., Grabher, A.-L., Kreidl, M., Huber, S., Grander, J., Haslacher, S., Singer, K., Schlapp-Hackl, M., Sorg, M., Erber, H., Oberacher, H., 2021. Monitoring drug consumption in Innsbruck during coronavirus disease 2019 (COVID-19) lockdown by wastewater analysis. *Sci. Total Environ.* 757, 144006.
- Rodriguez-Mozaz, S., Vaz-Moreira, I., Varela Della Giustina, S., Llorca, M., Barceló, D., Schubert, S., Berendonk, T.U., Michael-Kordatou, I., Fatta-Kassinos, D., Martinez, J. L., Elpers, C., Henriques, I., Jaeger, T., Schwartz, T., Paulshus, E., O'Sullivan, K., Pärnänen, K.M.M., Virta, M., Do, T.T., Walsh, F., Manaia, C.M., 2020. Antibiotic residues in final effluents of European wastewater treatment plants and their impact on the aquatic environment. *Environ. Int.* 140, 105733.
- Sabatino, R., Di Cesare, A., Dzhenbekova, N., Fontaneto, D., Eckert, E.M., Corno, G., Moncheva, S., Bertoni, R., Callieri, C., 2020. Spatial distribution of antibiotic and heavy metal resistance genes in the Black Sea. *Mar. Pollut. Bull.* 160, 111635.
- Saravanan, A., Kumar, P.S., Jeevanantham, S., Anubha, M., Jayashree, S., 2022. Degradation of toxic agrochemicals and pharmaceutical pollutants: effective and alternative approaches toward photocatalysis. *Environ. Pollut.* 298, 118844.
- Shi, Y., Liu, J., Zhuo, L., Yan, X., Cai, F., Luo, W., Ren, M., Liu, Q., Yu, Y., 2020. Antibiotics in wastewater from multiple sources and surface water of the Yangtze River in Chongqing in China. *Environ. Monit. Assess.* 192, 159.
- Sivaranjane, R., Kumar, P.S., 2021. The unfurl of the coronavirus and its thwack on humans and the environment: a review. *Current Opinion in Environmental Science & Health* 24, 100289.
- Talaiekhosani, A., Joudaki, S., Banisharif, F., Eskandari, Z., Cho, J., Moghadam, G., Rezania, S., 2020. Comparison of azithromycin removal from water using UV radiation, Fe (VI) oxidation process and ZnO nanoparticles. *Int. J. Environ. Res. Publ. Health* 17, 1758.
- Tarighi, P., Eftekhari, S., Chizari, M., Sabernavaei, M., Jafari, D., Mirzabeigi, P., 2021. A review of potential suggested drugs for coronavirus disease (COVID-19) treatment. *Eur. J. Pharmacol.* 895, 173890.
- Tran, N.H., Chen, H., Reinhard, M., Mao, F., Gin, K.Y.-H., 2016. Occurrence and removal of multiple classes of antibiotics and antimicrobial agents in biological wastewater treatment processes. *Water Res.* 104, 461–472.
- Usman, M., Farooq, M., Hanna, K., 2020. Environmental side effects of the injudicious use of antimicrobials in the era of COVID-19. *Sci. Total Environ.* 745, 141053.
- Who, 2022. WHO Coronavirus Disease (COVID-19) Dashboard. (Accessed 15 July 2022).
- Xu, K., Wang, J., Gong, H., Li, Y., Zhou, L., Yan, M., 2019. Occurrence of antibiotics and their associations with antibiotic resistance genes and bacterial communities in Guangdong coastal areas. *Ecotoxicol. Environ. Saf.* 186, 109796.
- Yasojima, M., Nakada, N., Komori, K., Suzuki, Y., Tanaka, H., 2006. Occurrence of levofloxacin, clarithromycin and azithromycin in wastewater treatment plant in Japan. *Water Sci. Technol.* 53, 227–233.
- Yuan, X., Qiang, Z., Ben, W., Zhu, B., Qu, J., 2015. Distribution, mass load and environmental impact of multiple-class pharmaceuticals in conventional and upgraded municipal wastewater treatment plants in East China. *Environ. Sci. J. Integr. Environ. Res.: Process. Impacts* 17, 596–605.
- Zafar, R., Bashir, S., Nabi, D., Arshad, M., 2021. Occurrence and quantification of prevalent antibiotics in wastewater samples from Rawalpindi and Islamabad, Pakistan. *Sci. Total Environ.* 764, 142596.
- Zhang, S., Jiang, J.Q., 2021. Comparative removal of imidacloprid, bisphenol-S, and azithromycin with ferrate and FeCl₃ and assessment of the resulting toxicity. *J. Chem. Technol. Biotechnol.* 96, 99–112. <https://doi.org/10.1002/jctb.6515>.
- Zhang, X., Zhao, H., Du, J., Qu, Y., Shen, C., Tan, F., Chen, J., Quan, X., 2017. Occurrence, removal, and risk assessment of antibiotics in 12 wastewater treatment plants from Dalian, China. *Environ. Sci. Pollut. Control Ser.* 24, 16478–16487.
- Zhu, T.-t., Su, Z.-x., Lai, W.-x., Zhang, Y.-b., Liu, Y.-w., 2021. Insights into the fate and removal of antibiotics and antibiotic resistance genes using biological wastewater treatment technology. *Sci. Total Environ.* 776, 145906.