Journal of Environmental Management 308 (2022) 114609

Contents lists available at ScienceDirect

Journal of Environmental Management

journal homepage: www.elsevier.com/locate/jenvman

An assessment of hospital wastewater and biomedical waste generation, existing legislations, risk assessment, treatment processes, and scenario during COVID-19

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ARTICLE INFO

Keywords:
Advanced oxidation processes
Biodegradation
Biomedical waste management
Emerging contaminants
Hospital wastewater treatment
Legislations

ABSTRACT

Hospitals release significant quantities of wastewater (HWW) and biomedical waste (BMW), which hosts a wide range of contaminants that can adversely affect the environment if left untreated. The COVID-19 outbreak has further increased hospital waste generation over the past two years. In this context, a thorough literature study was carried out to reveal the negative implications of untreated hospital waste and delineate the proper ways to handle them. Conventional treatment methods can remove only 50%–70% of the emerging contaminants (ECs) present in the HWW. Still, many countries have not implemented suitable treatment methods to treat the HWW in-situ. This review presents an overview of worldwide HWW generation, regulations, and guidelines on HWW management and highlights the various treatment techniques for efficiently removing ECs from HWW. When combined with advanced oxidation processes, biological or physical treatment processes could remove around 90% of ECs. Analgesics were found to be more easily removed than antibiotics, β-blockers, and X-ray contrast media. The different environmental implications of BMW have also been highlighted. Mishandling of BMW can spread infections, deadly diseases, and hazardous waste into the environment. Hence, the different steps associated with collection to final disposal of BMW have been delineated to minimize the associated health risks. The paper circumscribes the multiple aspects of efficient hospital waste management and may be instrumental during the COVID-19 pandemic when the waste generation from all hospitals worldwide has increased significantly.

1. Introduction

Hospitals play an essential role in the welfare of mankind and assist in the advancement of medical science and research. They contribute to health services by offering continual services to address complicated health scenarios (Kumari et al., 2020). However, these activities are associated with the generation of large quantities of wastewater (Boillot et al., 2008; Patel et al., 2019). Furthermore, hospitals also generate a large quantity of biomedical waste (BMW) (Ansari et al., 2019). The size of the hospital highly influences the characteristics, and the quantity of HWW and BMW generated, services and facilities offered and the waste management practices followed.

Abbreviations: **AOP**, Advanced oxidation process; **ASP**, Activated sludge process; **ARGs**, Antibiotic-resistance genes; **ARB**, Antibiotic-resistance bacteria; **BAT**, Best available techniques; **BEP**, Best environmental practises; **BWMHR**, Biomedical waste management and handling rules; **BMW**, Biomedical waste; **BOD**, Biochemical oxygen demand; **CBMW**, Common biomedical waste management; **COD**, Chemical oxygen demand; **CPF**, Carcinogenic potency factor; **CWs**, Constructed wetlands; **CWA**, Clean water act; **CWAO**, Catalytic wet air oxidation; **DWEL**, Drinking water equivalent limit; **ECs**, Emerging contaminants; **EU**, European Union; **FBR**, Fluidized bed reactors; **GNI**, Gross national income; **HAdV**, Human adenoviruses; **HRT**, Hydraulic retention time; **HQ**, Hazard quotient; **HWW**, Hospital wastewater; **ICRP**, International commission on radiological protection; **ISWA**, International Solid Waste Association; **K_{ow}**, Octanol-water partition coefficient; **MBBR**, Moving bed biofilm reactor; **MBR**, Membrane bioreactor; **MERS-CoV**, Middle east respiratory syndrome coronavirus; **MWW**, Municipal wastewater; **NF**, Nanofiltration; **NSAIDs**, Non-steroidal anti-inflammatory drugs; **ORMs**, Ozone-reactive moieties; **PAC**, Powder activated carbon; **PhACs**, Pharmaceutically active compounds; **pKa**, Acid dissociation constant; **PNEC**, Predicted no-effect concentration; **POPs**, Persistent organic pollutants; **PPE**, Personal protective equipment; **RQ**, Risk quotient; **RO**, Reverse osmosis; **SARS-CoV**, Severe acute respiratory syndrome coronavirus; **SRT**, Sludge retention time; **TOC**, Total organic carbon; **TFs**, Trickling filters; **US EPA**, United States environmental protection agency; **UV**, Ultraviolet; **WHO**, World health organisation; **WWTP**, Wastewater treatment plant.

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https://doi.org/10.1016/j.jenvman.2022.114609
Received 5 December 2021; Received in revised form 23 January 2022; Accepted 24 January 2022
Available online 26 January 2022

HWW is generally characterized by a high concentration of biochemical oxygen demand (BOD), chemical oxygen demand (COD) and total organic carbon (TOC)), ammonia nitrogen, organic nitrogen, nitrites, nitrates, total phosphorus, and total solids (Emmanuel et al., 2005; Majumder et al., 2021a; Verlicchi et al., 2010b). Additionally, HWW also hosts a significant concentration of pathogens (bacteria, viruses, protozoa, and fungi), antibiotic-resistance genes (ARGs), and antibiotic-resistance bacteria (ARB) (Emmanuel et al., 2005; Hocquet et al., 2016; Majumder et al., 2021a). Several studies have found that the concentration of these parameters in HWW is higher than municipal wastewater (MWW) (Carraro et al., 2016; Emmanuel et al., 2005; Verlicchi et al., 2010b). Furthermore, studies show that the average biodegradability index (BOD/COD) of HWW is generally lower than that of MWW, indicating that HWW is difficult to treat using conventional biological treatment systems (Carraro et al., 2016; Majumder et al., 2021a; Meo et al., 2014; Verlicchi et al., 2010b). The low BOD/COD ratio of HWW is mainly due to the presence of toxic and non-biodegradable pollutants, such as pharmaceutically active compounds (PhACs), X-ray contrast media, surfactants, and disinfectants, which are highly persistent compounds (Emmanuel et al., 2005; Verlicchi et al., 2010b). Most of these contaminants, emerging contaminants (ECs) can be toxic to human beings and other aquatic organisms at low concentrations (μg/L to ng/L) (M. T. Khan et al., 2021; N. A. Khan et al., 2021; Tran et al., 2018). ECs have come to common knowledge only in recent times because of the advancement of analytical techniques. Furthermore, their effect on the environment can only be speculated upon since there is not enough data on their toxicity assessment, and this may be the reason only a few countries have established standards related to HWW (Carraro et al., 2016; N. A. Khan et al., 2021; Parida et al., 2021).

Conventional WWTPs are often not able to completely degrade ECs as they are generally not designed to handle such compounds with high hydrophilic nature and complex structures (Patel et al., 2019; Tran et al., 2018). Many WWTPs also fail to meet the general quality standards as well (Mirra et al., 2020). Many studies have reported the use of advanced oxidation processes (AOPs) to enhance the removal of these recalcitrant pollutants (Kovalova et al., 2013; Segura et al., 2021; Yadav et al., 2021). Although these treatment methods have proven effective in degrading different ECs, the high operation cost and complexity of the process prevent them from being used in full-scale treatment plants (Ahmed et al., 2021). Hence, alternative green sustainable technologies should be opted to tackle different types of wastewater (Ali et al., 2016; Hashem et al., 2021; Majumder et al., 2019b). Therefore, various biological treatment processes, such as membrane bioreactors (MBR), moving bed biofilm reactors (MBBR), constructed wetlands (CWs), activated sludge process (ASP), trickling filters (TF), fluidized bed reactors (FBR), can be combined with adsorption-based processes, filtration-based processes, and various AOPs to form a hybrid system that can remove ECs from HWW with high efficiency (Kovalova et al., 2013; Nguyen et al., 2013; Parida et al., 2021).

The generation of a large quantity of solid waste has also increased significantly over the past two years due to the COVID-19 outbreak (Agamuthu and Barasarathi, 2021; Das et al., 2021). According to Kalantary et al. (2021), the COVID-19 pandemic resulted in a 102.2% increase in BMW generation in hospitals of Iran (Kalantary et al., 2021). Many studies have reported that improper disposal or mishandling of BMW can significantly affect human beings and the environment as well (Ansari et al., 2019; Askarian et al., 2004; Windfeld and Brooks, 2015). Therefore, solid waste generated by hospitals must be appropriately managed to avoid associated health risks.

Previously, researchers have focused only on the source and pathway of HWW generation, HWW characterization, and treatment (Carraro et al., 2017; M. T. Khan et al., 2021; Suárez et al., 2008). The removal of different pharmaceuticals from aqueous environments has also been studied (Majumder et al., 2019a; Parida et al., 2021). Furthermore, a lot of the studies on this topic are only limited to lab-scale. Also, many countries are still not treating the HWW separately and neglect the negative implications of hospital waste (Al Aukidy et al., 2018; Verlicchi et al., 2015). As a result, sufficient studies on the guidelines and regulations for HWW management and the performance of pilot-based units in removing ECs are lacking. Additionally, a crucial factor in hospital waste management is the handling of BMW, which often gets ignored. Previously, many studies have only focused on the liquid waste aspect of hospitals, but the solid waste is not sufficiently addressed (Al Aukidy et al., 2018; N. A. Khan et al., 2021; Majumder et al., 2021a). Hence, it is necessary to bring forth the various negative implications of untreated hospital waste and the proper ways to handle them. In this perspective, the main objective of the paper is to provide a fresh perspective on generation, management, and legislation on HWW and BMW. The study highlights the HWW generation from different countries segregated based on gross national income (GNI). The review discusses the characteristics of HWW, the existence and concentration levels of various ECs in HWW, and the existing regulations and guidelines that must be followed to manage HWW effectively. Subsequently, the study primarily focuses on various pilot-scale and full-scale treatment techniques to remove contaminants from HWW. The present review also emphasizes different hybrid technologies comprised of various biological treatment methods integrated with tertiary treatment techniques to achieve complete removal of ECs. The later section of the review focuses on the worldwide generation of BMW, its categories, health and environmental risks, effective BMW management (BMWM) techniques, and the measures taken by different countries to manage BMW in the context of COVID-19 appropriately. This study also throws light on different computational methods used in the different aspects of hospital waste management. The review discusses and updates the various aspects of HWW and BMW, the current treatment scenario, and the way forward. Hence it may be helpful for the researchers, environmental engineers, and scientists dealing with the management of hospital wastes.

2. Methodology

A systematic review has been carried out by going through various studies and a statistical analysis using the Scopus database to get an overview of the research trends on HWW and BMW. The data from Scopus was accessed on September 19, 2021. This platform was chosen because of the quality and reliable database of peer-reviewed research material relevant to the study area. The publications related to HWW were searched using the keywords, such as “hospital wastewater”, “hospital effluents”, “hospital liquid waste”, “health care effluents”, “nursing home effluents”, and “medical center effluents”. Review articles and other documents were excluded, whereas research publications during the last two and a half decades (1996–2020) were considered for this study. The search returned 945 research articles for HWW. Similarly, the research publications related to BMW were searched using the keywords, such as “biomedical waste”, “hospital solid waste”, “health care solid waste”, “nursing home solid waste”,” medical center solid waste”, and “health clinic solid waste”. The search returned 3725 research articles for BMW. Review articles were not considered in this study because these articles do not report any new findings or results pertaining to our study. The keywords were carefully chosen to cover almost all research articles related to this topic. A manual screening was carried out to filter out the documents, which were not related to our topic. The trend analysis was carried out using this methodology.

The information on water demand and generation of wastewater from hospitals, the characteristics of the HWW, the pathways for the different contaminants into the HWW, the legislation pertaining to HWW management, and its treatment were assembled, compiled, and presented carefully in this study by going through ample literature in the past few years. The data was extracted from different literature, and a thorough analysis of the data was carried out before reporting our findings. Similarly, in the case of BMW, the information on the generation of BMW, the existing legislation, and the management of BMW were gathered by carrying out an intensive literature survey.

Since, during the COVID-19 pandemic, most hospitals are facing severe crisis due to an overload of patients, special emphasis has been provided on the implications of COVID-19 on hospital waste generation and how to handle the waste generated. The information on hospital waste generation during COVID-19 and protocols followed by different countries to fight the pandemic were collected by going through various published work in the last 2 years.

3. Current publication scenario on hospital wastewater and biomedical waste

The trends in the publication of different types of contaminants, such as PhACs, personal care products, X-ray contrast media, disinfectants, pathogens, detergents, stimulants, ARGs, and ARB found in HWW is represented in Fig. 1a. Even though research on this topic began in the late 1970s, the major increase in publications regarding the characterization and removal of ECs from HWW was recognized after 2012. It was observed that approximately 82% of research articles were published between 2012 and 2020. The advancement in medical science and availability of modern analytical instruments in recent times has facilitated the detection of these contaminants with low concentrations, which has significantly improved research on this topic. Similarly, the trends in the publication of various classes of BMW, such as infectious waste, pathological waste, pharmaceutical waste, chemical waste, radioactive waste, sharps, and other general waste, are represented in Fig. 1b. In the case of BMW, the research began in the late 1950s. However, after 2008 there was a significant increase in publications relevant to the generation, identification, and management of BMW. It can be observed that approximately 73% of research articles were published between 2008 and 2020.

In the present study, to better understand the research trend and the future of research in HWW and BMW, a logistic model was employed for making an S-curve simulation using the following Eq. (1) (Bengisu and Nekhili, 2006; Du et al., 2019; Mao et al., 2020).

$$X_t = \frac{P_s}{1 + e^{-a(t-b)}} \tag{1}$$

where “X_t” represents annual cumulative publications (dependent variable in the logistic curve), “a” and “b” are model parameters, “P_S” represents the publication saturation value, and “t” represents the time, in this study. Fig. 1c and d represent the cumulative number of articles published annually for both the literature research. The S- curve or the predicted publication trend is also shown in Fig. 1c and d, which also depicts the several phases such as birth phase, growth phase, maturation phase, and saturation phase of the trend. It can be noted that, at present, the research on this topic is currently in its early stages of the growth phase and will most likely continue until the late 2040s and 2050s for HWW and BMW, respectively. Moreover, it can be predicted that the research on HWW and BMW would reach saturation by the late 2060s and 2070s, with a P_s value of 3861 and 5970, respectively.

4. Hospital wastewater

4.1. Water demand, consumption, and wastewater generation from hospitals

As discussed earlier, various services and facilities in the hospitals demand a large quantity of water. According to a report published by the Massachusetts Water Resources Authority, a case study was conducted

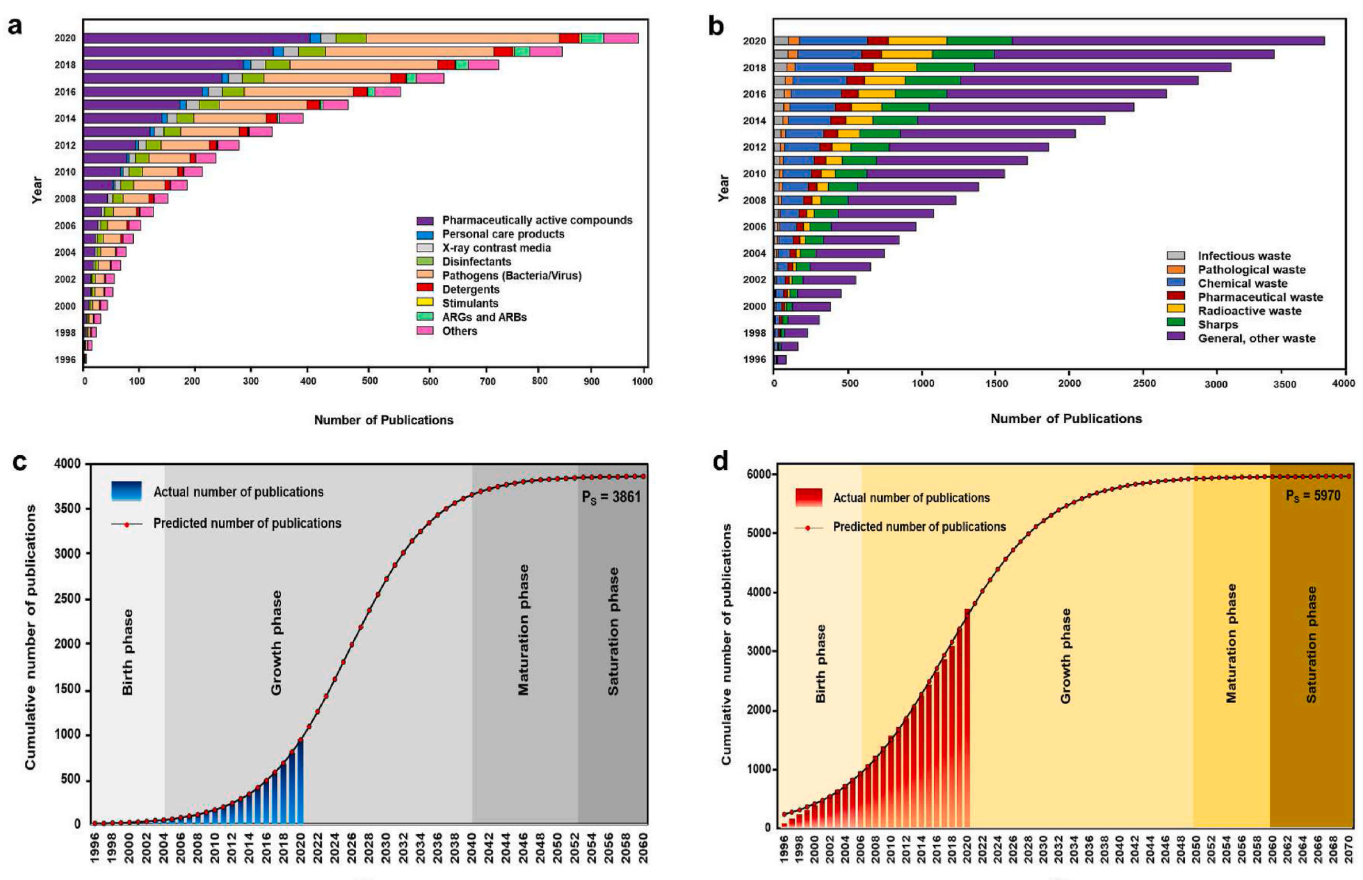

Fig. 1. Year-wise publications of research articles on different (a) ECs found in HWW and (b) various categories of BMW, respectively. The cumulative number of publications and corresponding S-curve for (c) HWW and (d) BMW, respectively.

in seven hospitals in the United States, with facilities ranging from 138 to 550 beds with daily water usage ranging from 156 to 697 m^3 (MWRA, 2020). According to the Bureau of Indian Standards (BIS), the average water required per patient is approximately 340 L/bed/day when the number of beds is less than 100, and 450 L/bed/day when the number of beds exceeds 100, including laundry activities (BIS, 1993). Jehle et al. (2008) found that approximately 18.5 L of water are required for performing one surgery in OT for disinfection purposes (Jehle et al., 2008). According to the World Health Organization (WHO) guidelines for the proper functioning of healthcare facilities, 100 L of water is needed per intervention in the midwife obstetric units, and approximately 15–20 L of water is required per consultation for supplementary feeding system (Adams et al., 2008). Several studies have reported that patients suffering from polydipsia, dehydration, diarrhoea, vomiting, or running with fever also require a significant quantity of water (Gotfried, 2020; Hickman, 2021; Majumder et al., 2021a).

Verlicchi et al. (2010b) reported that the average water consumption per bed ranged from 200 to 1200 L/bed/day, with the highest values were reported from high-income countries, and the lowest values were reported from lower-middle-income countries (Verlicchi et al., 2010b). The average HWW generated by different countries based on their income groups was calculated using the data from various literature (Table 1), and it was found that the high-income countries discharged maximum HWW with an average value of 466 m^3/day, while the upper and lower-middle-income countries discharged 297 m^3/day and 95 m^3/day of HWW, respectively as shown in Fig. S1. It can also be observed that the average wastewater generated by individual patients in high-income countries is comparatively high, with an average per capita discharge of 0.791 m^3/bed/day, compared to hospitals in upper and lower-middle-income countries, with an average discharge of 0.642 m^3/bed/day and 0.269 m^3/bed/day, respectively.

4.2. Pathway of hospital wastewater contaminants into the aquatic ecosystem

The pathways involved in transporting HWW contaminants to aquatic bodies have been depicted in Fig. 2. Unmetabolized fractions of ECs and other contaminants from hospitals are discharged along with the hospital effluent (N. A. Khan et al., 2021; Verlicchi et al., 2010b). These contaminants contribute to the total organic components and solids content present in HWW. Most of the lower-middle-income countries discharge hospital effluents directly into freshwater streams without treatment (Akter et al., 2012; Ashfaq et al., 2016; Beyene and Redaie, 2011; Duong et al., 2008; Lin et al., 2010; Messrouk et al., 2014; Mubedi et al., 2013; Shrestha et al., 2001). Disposal of wastewater directly into the environment leads to high concentrations of organic

Table 1
The number of in-patients beds and the quantity of wastewater generated by different hospitals and health care facilities worldwide based on global national income (GNI), World Bank.

Class	Country	No. of beds	Wastewater generated (m^3/d)	Reference
High Income	Australia	190	138	Ort et al. (2010)
	Belgium	641	250	(De Gusseme et al., 2011; EAHM, 2019)
	Belgium	1048	600	("Erasmus Hospital," 2021; Guillaume et al., 2000)
	Denmark	691	360–500	Rodriguez-Mozaz et al. (2018)
	France	750	450	Emmanuel et al. (2005)
	France	–	651.6	Boillot et al. (2008)
	Japan	477	460	Azuma et al. (2016)
	Netherlands	1076	240	Rodriguez-Mozaz et al. (2018)
	Portugal	1120	1000	Varela et al. (2014)
	Spain	750	429	Carraro et al. (2016)
	Spain	850	400	Isidori et al. (2016)
	Germany	1274	617	Sib et al. (2020)
	Germany	580	200	Rodriguez-Mozaz et al. (2018)
	Germany	340	768	Rodriguez-Mozaz et al. (2018)
	Italy	900	630	Verlicchi et al. (2010a)
	Italy	300–900	382	Verlicchi et al. (2012a)
	Italy	300	180	Carraro et al. (2016)
	Saudi Arabia	215–300	763	Al Qarni et al. (2016)
	Switzerland	1781	640	Daouk et al. (2016)
	Switzerland	346	187	Kovalova et al. (2012)
	Switzerland	415	380	Weissbrodt et al. (2009)
Upper middle income	Brazil	180	150	Kern et al. (2013)
	Brazil	–	432	Carraro et al. (2016)
	Brazil	328	190	(De Abreu Rodrigues et al., 2015; De Almeida et al., 2013)
	Brazil	322	220	Santoro et al. (2015)
	Brazil	–	326	Prado et al. (2011)
	China	–	575	Huang et al. (2021)
	Costa Rica	100	84.5	(Ramírez-morales et al., 2020)
	Mauritius	556	500	Mohee (2005)
	Turkey	780	300	Top et al. (2020)
	Turkey	750	344	Arslan et al. (2014)
	Turkey	201	92	Hocaoglu et al. (2021)
	Thailand	–	350	Kajitvichyanukul and Suntronvipart (2006)
Lower middle income	Ethiopia	305	143	Beyene and Redaie (2011)
	Ghana	413	8.3	Wiafe et al. (2016)
	India	310	50	Sharma et al. (2015)
	India	–	50	Akiba et al. (2015)
	India	200	50	Prabhakaranunni Prabhasankar et al. (2016)
	Iran	130	47	Sarafraz et al. (2007)
	Iran	85	14.5	Kafaei et al. (2018)
	Morocco	400	367	Tahiri et al. (2012)
	Nigeria	600	100	Ogwugwa et al. (2021)
	Pakistan	–	0.5535 m^3/bed/day	Rashid et al. (2021)
	Sri Lanka	1453	200	Young et al. (2021)

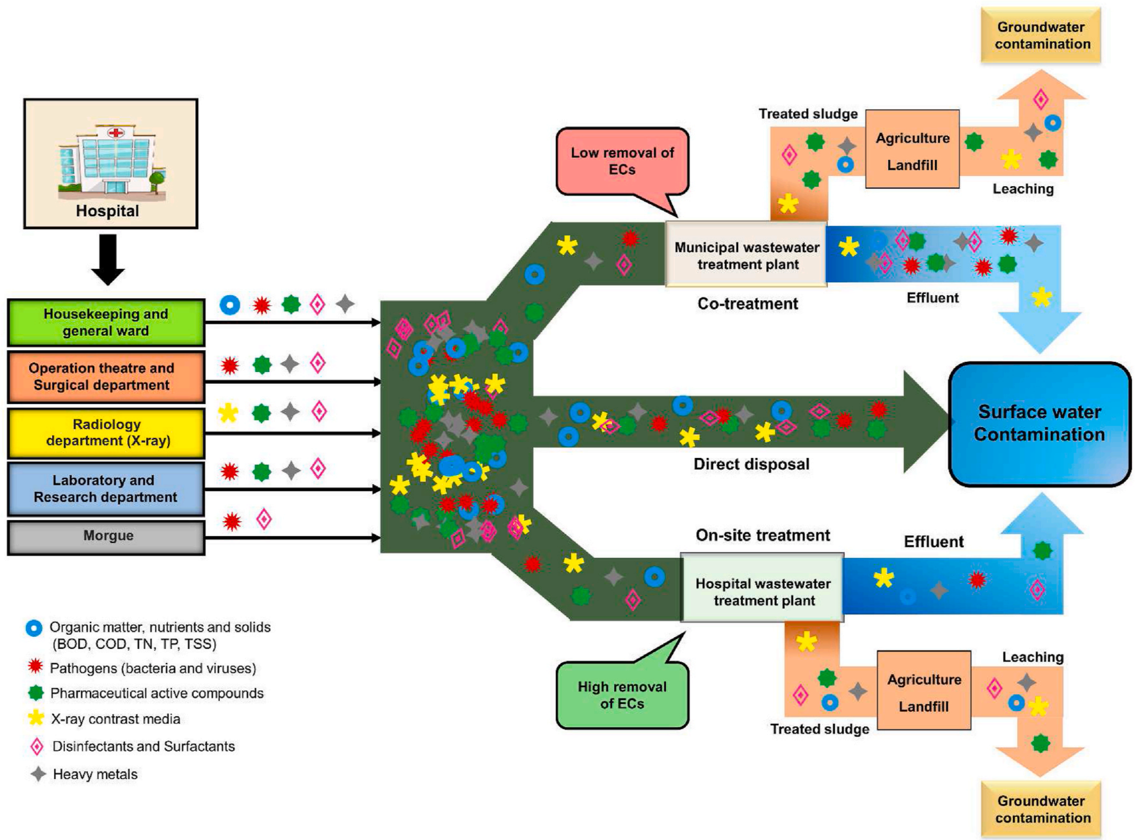

Fig. 2. Generation of different contaminants from the hospital and healthcare facilities and their subsequent pathway into different aqueous environments.

matter, pathogens, ECs in the aquatic ecosystems (Akter et al., 2012; Gupta and Gupta, 2021).

Many countries, such as Iran, Japan, Egypt, Australia, South Africa, India, and Thailand practice co-treatment, where the HWW flows into domestic sewers reaching to the municipal WWTPs, where they are treated along with MWW (Akiba et al., 2015; Azuma et al., 2016;

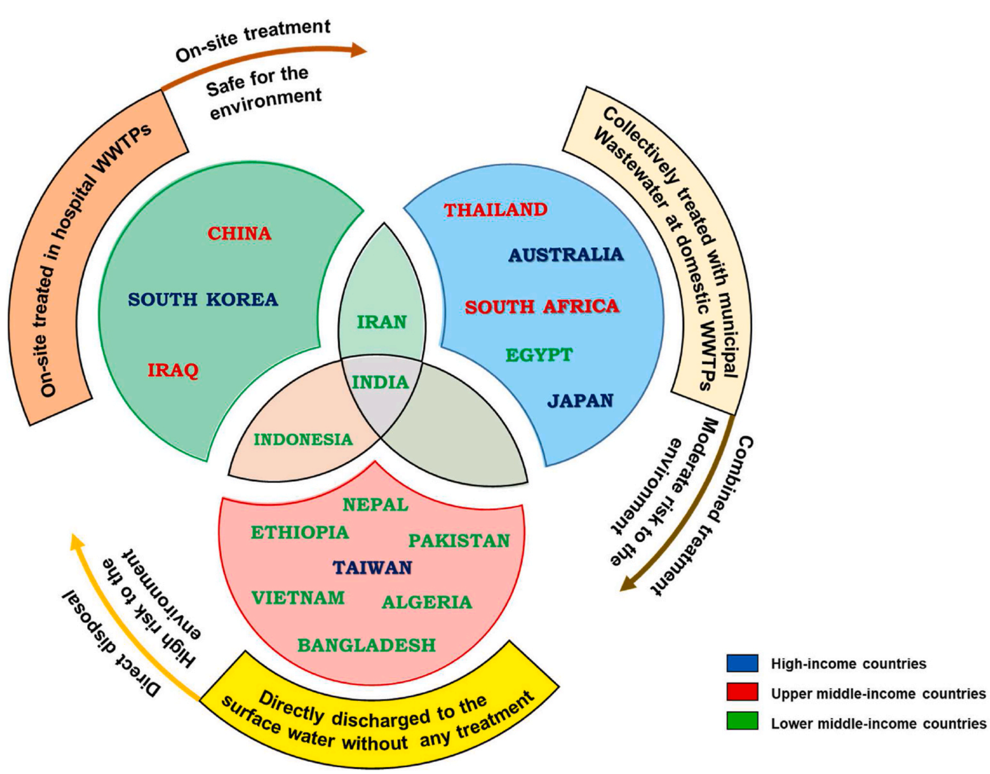

Fig. 3. Various treatment approaches for HWW management in different countries. [Adapted from (Akiba et al., 2015; Akter et al., 2012; Ali et al., 2013; Ashfaq et al., 2016; Azuma et al., 2016; Beyene and Redaie, 2011; Duong et al., 2008; El-gawad et al., 2011; Iweriebor et al., 2015; Kajitvichyanukul and Suntronvipart, 2006; Lin et al., 2010; Messrouk et al., 2014; Mubedi et al., 2013; Nasr and Yazdanbakhsh, 2008; Prabhakaranunni Prabhasankar et al., 2016; Prayitno et al., 2012; Shrestha et al., 2001; Sim et al., 2013; Thompson et al., 2013; Verlicchi, 2018):].

El-gawad et al., 2011; Iweriebor et al., 2015; Kajitvichyanukul and Suntronvipart, 2006; Nasr and Yazdanbakhsh, 2008; Thompson et al., 2013). Most of the municipal WWTPs are not designed to deal with such complex organic compounds (Parida et al., 2021; Patel et al., 2019). As a result, the majority of ECs are only partially removed by the municipal WWTPs. Therefore, municipal WWTPs often become a primary source for discharging these ECs into different water matrices (Patel et al., 2019; Wilson and Aqeel Ashraf, 2018). Further, the treated sludge from these municipal WWTPs is often applied to the soil as fertilizer in agriculture. Hence, a fraction of ECs may escape from the soil to the groundwater via leaching (Ebele et al., 2017; M. T. Khan et al., 2021; Suárez et al., 2008). Stuart et al. (2012) have reported the presence of various ECs in groundwater samples (Stuart et al., 2012).

In contrast, most high-income countries have on-site hospital WWTPs that pre-treat HWW before releasing it to municipal sewers (Ali et al., 2013; Prayitno et al., 2012; Sim et al., 2013; Verlicchi, 2018). Since this treatment is targeted to HWW specific contaminants, much higher removal of organics, pathogens, and ECs can be attained. However, on-site treatment of HWW is expensive and requires a high amount of energy for operation and maintenance. The approaches to HWW management adopted by different countries have been shown in Fig. 3.

4.3. Characteristics of hospital wastewater

The discharge from hospitals can be primarily divided into two major categories, i.e., domestic discharges and specific discharges (Carraro et al., 2016). Domestic discharges contain a wide range of pathogens and ECs, such as PhACs, contrast media, disinfectants, detergents, and other cytotoxic or mutagenic agents have been detected in such discharges (Carraro et al., 2016; Verlicchi et al., 2012a; WHO, 2014). On the other hand, the *specific discharges* of hospitals are the wastewater generated from analysis, research activities, diagnosis, and radiology departments. These discharges mainly contain disinfectants, contagious feces, body fluids, drug residues, radioactive elements. It also includes hazardous compounds such as acids, solvents, alkalis, benzenes, hydrocarbons, dyes, and other chemicals (Carraro et al., 2016; Majumder et al., 2021a; WHO, 2014). These compounds are largely responsible for the low BOD/COD ratio in HWW.

4.3.1. Physicochemical characteristics

Many studies have reported that the concentration of physicochemical parameters in HWW is generally higher than MWW (Carraro et al., 2016; Emmanuel et al., 2005; Verlicchi et al., 2010b). Verlicchi et al. (2010b) compared HWW with the MWW of different countries to check whether there is a correlation between the wastewater quality parameters, and it was observed that the parameters including BOD, COD, TSS in the hospital effluents were 2–3 times higher than MWW (Verlicchi et al., 2010b).

In the present study, an attempt has been made to show the variation in the concentration of different HWW parameters among the high,

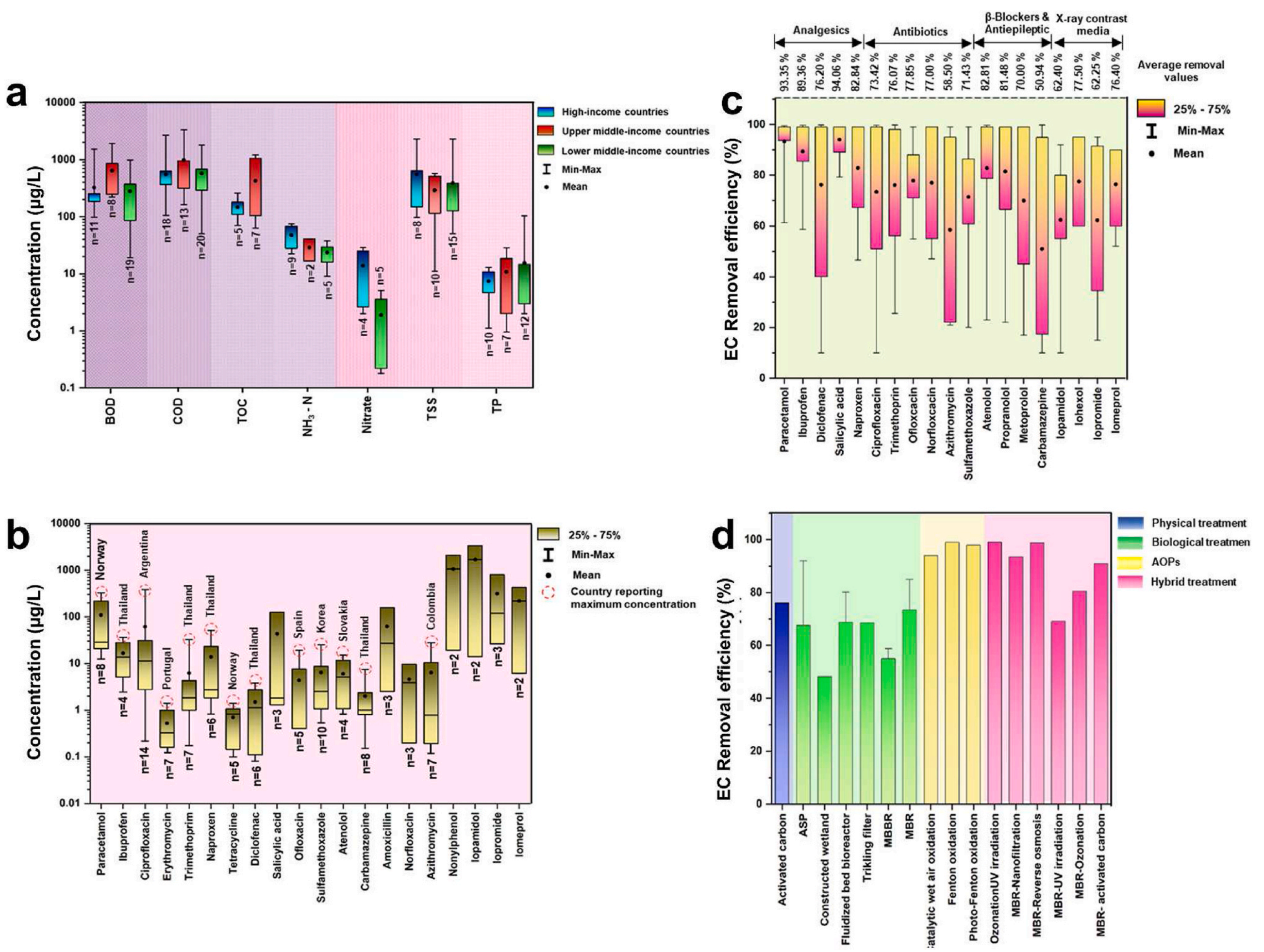

Fig. 4. Box and whisker plots showing variation in the worldwide concentration of (a) different HWW physicochemical parameters and (b) selected ECs in HWW effluents/hospital WWTPs influents (where n represents sample size). (c) Box and whisker plots showing variation in the removal of selected ECs in HWW by different treatment methods and (d) performance of various treatment methods in terms of removal of ECs from HWW [Data source: Table S1 for (a) Table S2 for (b), Table S3 for (c) and (d) in Supplementary Material].

upper, and lower-middle-income countries (Fig. 4a). The average BOD concentration of HWW from upper-middle-income countries was found to be 528 mg/L, which was higher than the average BOD values found in high and lower-middle-income countries, which were 324 mg/L and 280 mg/L, respectively (Fig. 4a). The average COD concentration in the HWW of upper-middle-income countries was found to be 986 mg/L, which was again higher compared to the high and lower-middle-income countries with average values of 574 mg/L and 551 mg/L, respectively (Fig. 4a). The average BOD/COD ratio for HWW in lower-middle-income countries was 0.49, which is lower than the average BOD/COD values for HWW in upper-middle-income and high-income countries, which were 0.53 and 0.59, respectively. The average BOD/COD ratio of HWW in lower-middle-income countries was lower than the standard biodegradable component for MWW, thereby making it more challenging to biodegrade (Tchobanoglous et al., 2004).

The average pH of HWW across the world was found to be 7.55 (Table S1). The average TOC concentration in hospital effluents of upper-middle-income countries was observed to be 427 mg/L, which was more than the average value of 147 mg/L in high income-countries. The average ammonia nitrogen and nitrate concentration of 47.5 mg/L and 13.8 mg/L, respectively, in high-income countries, was higher than that of the lower-middle-income countries (Fig. 4a). The average concentration of TSS was found to be 554 mg/L in high-income countries, which is higher than lower and upper-middle-income countries with average values of 390 and 292 mg/L, respectively (Fig. 4a).

4.3.2. Microbiological characteristics

HWW includes a wide range of microorganisms, such as fungi and numerous bacteria, including *Escherichia coliform* (*E. coli*), total *coliform*, *thermotolerant coliform*, *Streptococcus*, *Mycobacterium, Pseudomonas aeruginosa*, etc. (Hocquet et al., 2016; Khan et al., 2020; Majumder et al., 2021a). Many studies have reported the presence of a high concentration of coliform species and other bacteria species from HWW in different countries across the world (Table S1) (Majumder et al., 2021a; Tulashie et al., 2018; Vo et al., 2016). García-Muñoz et al. (2017) reported the total *coliform* concentration of around 3.8×10^6 MPN/100 mL in HWW of Madrid, Spain (García-Muñoz et al., 2017). Periasamy and Sundaram (2013) reported the concentration of total heterotrophic bacterial count and total *coliform* ranging from 1.9×10^7 CFU/mL to 8.3×10^{12} CFU/mL and 1.2×10^3 MPN/100 mL to 1.6×10^3 MPN/100 mL, respectively in hospital effluents collected from several locations in India. Furthermore, antibiotic-resistant *E. coli*, *Streptococcus* species, *Pseudomonas* species, and *Bacillus* species were also detected in all of the locations with concentrations ranging from 1.2×10^3 CFU/mL to 1.74×10^4 CFU/mL, 2×10^2 CFU/mL to 3.2×10^3 CFU/mL, 2×10^2 CFU/mL to 4×10^2 CFU/mL, and 2.8×10^3 CFU/mL to 1.07×10^4 CFU/mL, respectively, (Periasamy and Sundaram, 2013).

Although hospital effluents contain significant concentrations of microorganisms, such as *E. coli* and total *coliform*, they should not be seen as harmless indicators of faecal contaminations but rather as pathogens that propagate antibiotic resistance due to their exposure to high concentrations of drugs and antibiotics (Carraro et al., 2016; Hocquet et al., 2016). Many studies have reported about the presence of resistant bacteria, such as *Pseudomonas aeruginosa, vancomycin-resistant enterococci, Proteus Vulgaris*, *mycobacteria*, etc. and resistant strains, such as *Methicillin-resistant staphylococcus aureus*, *Enterobacter sakazakii, Extended-spectrum beta-lactamase*-producing-strains, etc., in various HWW samples (Boillot et al., 2008; Hocquet et al., 2016; Majumder et al., 2021a). The bacteria present in the wastewater can develop antibiotic resistance by their intrinsic ability to evolve quickly through mutations or by the transfer of DNA (via horizontal gene transfer) (Gupta et al., 2019). Hence, hospitals are one of the primary sources for the release of high concentrations of pathogens in various environmental matrices.

HWW also contains a wide range of viruses in addition to bacteria and other microorganisms. The most common human transmitting infectious viruses transmitted through water, particularly HWW includes enveloped and non-enveloped viruses. Enveloped viruses, such as Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Ebola, and avian influenza (Achak et al., 2020; Assiri et al., 2013; Haas et al., 2017; Wong et al., 2017) and non-enveloped enteric viruses, such as hepatitis A, adenoviruses, enteroviruses, noroviruses, and rotaviruses are known to cause severe infections (Majumder et al., 2021a; Prado et al., 2011; Sibanda and Okoh, 2012). These viruses often pose a serious threat to the whole community, resulting in an epidemic or pandemic (Bishop and Kirkwood, 2008; Itagaki et al., 2018; Thongprachum et al., 2018). The most recent example of the severity of viruses is the SARS-coronavirus 2 (SARS-CoV-2) outbreak (Achak et al., 2020; Gonçalves et al., 2021; Zhang et al., 2021). Prado et al. (2011) detected rotavirus A, human adenoviruses (HAdV), norovirus genogroup I and II, and hepatitis A viruses from two hospital WWTPs located in Rio de Janeiro, Brazil (Prado et al., 2011). Zhang et al. (2021) reported a virus count of SARS-CoV-2 ranging between 255 copies/L and 18,744 copies/L detected in the wastewater samples collected from a hospital located in Wuhan, China (Zhang et al., 2021). Likewise, Sibanda and Okoh (2012) reported an average virus count of HAdV ranging between 6.54×10^3 (genome copies/L) and 8.49×10^4 (genome copies/L), detected in the wastewater collected from a sampling site located near sewage outfall points of Victoria Hospital, South Africa (Sibanda and Okoh, 2012). These studies indicate that HWW is a host to numerous dangerous viruses, which may give rise to another dangerous epidemic or pandemic if not efficiently dealt with.

4.3.3. Heavy metals characteristics

A wide range of heavy metals are also present in HWW (Khan et al., 2020; Verlicchi et al., 2010b). Amongst, Hg has been continuously detected in HWW because of its use in diagnostic agents, diuretic agents in treatment, and as an active ingredient of disinfectants (Khan et al., 2020; Verlicchi et al., 2010b). Also, Pt has been found in hospital effluents resulting from excretions by oncological patients treated with cis-platinum and carbo-platinum (Kümmerer, 2001). Ba and Gd are commonly used in hospitals for several purposes, such as computed tomography sensitivity, organ functioning effect, and biochemical data. It was reported that approximately 98% of unmetabolized Ba and Gd are discharged in HWW within 24 h of usage (Khan et al., 2020; Kümmerer, 2001). In Iran, Hg, Pb, Cd, Cr, Zn, and Ni were detected in the HWW with an average concentration of 7.5 μg/L, 26.5 μg/L, 2 μg/L, 34 μg/L, 429 μg/L, and 30 μg/L, respectively (Amouei et al., 2015). The presence of heavy metals in HWW may constitute a serious threat to aquatic species and humans if HWW is discharged directly into freshwater.

4.3.4. Emerging contaminants

Over the past few decades, advancements in medical science and excessive medicine usage have resulted in the existence of ECs in various water matrices. As a result, hospitals are regarded as one of the primary sources for the release of such contaminants (Frédéric and Yves, 2014; M. T. Khan et al., 2021; Langford and Thomas, 2009; Thomas et al., 2007). The occurrence of various ECs detected in the HWW of different countries has been presented in Fig. 4b.

Among the different ECs, PhACs have been most frequently detected in different water matrices due to their excessive use in medical facilities (Majumder et al., 2021a). More than 300 PhACs, including their metabolites and transformed products, have been identified in various HWW (M. T. Khan et al., 2021). The PhACs detected in such a concentration that may pose a threat to aquatic life and humans have been considered in the present study. It has been found that PhACs like antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) have been more frequently detected in HWW. The average concentration of antibiotics detected from HWW of high-income countries was more than in upper and lower-middle-income countries. Ciprofloxacin, sulfamethoxazole, trimethoprim, erythromycin, and tetracycline were the most commonly reported antibiotics in HWW ranging from 0.1 μg/L to 382 μg/L (Table S2). Whereas, the most commonly detected NSAIDs in hospital effluents were acetaminophen, diclofenac, ibuprofen, and naproxen ranging from 0.08 μg/L to 330 μg/L (Table S2). The average concentration of NSAIDs in high income-countries was in the same range compared to upper and lower-middle-income countries. Among the β-blockers, atenolol and metoprolol were detected in hospital effluent of a few high-income countries. Other PhACs such as carbamazepine, an antiepileptic drug was found in the range of 0.151 μg/L to 7.5 μg/L in hospital effluents of different countries (Table S2). Furthermore, few studies have reported that X-ray contrast media such as iopamidol, iopromide, and iomeprol have been detected in hospital effluents of different countries (Gönder et al., 2021; Kovalova et al., 2013; Santos et al., 2013). High concentrations of iopamidol (3353 μg/L), iopromide (118 μg/L), and iomeprol (430 μg/L) were detected from HWW of Switzerland (Table S2) (Kovalova et al., 2013).

Apart from PhACs and contrast media, hospital effluents also carry numerous chemical contaminants like surfactants and disinfectants that can pose high toxicity to biotic components (Henriques et al., 2012; Prayitno et al., 2012; Torres Trajano et al., 2021). Surfactants, such as nonylphenol, didecyl dimethyl ammonium chloride, chlorhexidine digluconate, and others have been detected in HWW of different countries, with nonylphenol being the most frequently detected (Foster, 2007; Torres Trajano et al., 2021). Henriques et al. (2012) reported a high concentration of nonylphenol ethoxylate in one of the hospital effluents of Brazil with an average concentration of 2097.5 μg/L (Henriques et al., 2012). In an Argentinian study, the disinfectant residues such as sodium hypochlorite, povidone-iodine, and glutaraldehyde have been detected in hospital effluents (Magdaleno et al., 2014). Most of the ECs detected in hospital effluent had a concentration greater than the predicted no-effect concentration values, indicating that they may be a threat to the aquatic environment (Parida et al., 2021).

4.4. Regulations and guidelines for hospital wastewater

WHO and statutory agencies of only a few high and upper-middle-income countries have set their HWW treatment guidelines (Carraro et al., 2016; N. A. Khan et al., 2021; WHO, 2014). The WHO guidelines suggest that HWW should only be discharged into municipal WWTPs if it fulfills local regulatory standards. For example, the municipal treatment plant must meet minimum requirements, i.e., the treatment plant should either be able to remove at least 95% of bacteria from wastewater, or the plant should employ primary, secondary, and tertiary treatment. If these conditions cannot be fulfilled, the hospital effluents should be treated on-site in HWW treatment plants. The guidelines describe the protocols regarding the disinfection of wastewater, proper disposal of sludge, and possible reuse of the treated wastewater using modern treatment technologies for HWW treatment (WHO, 2014). Furthermore, the guideline also emphasizes the importance of providing proper sanitation in all hospitals and health care facilities by providing enough bathrooms and toilets. It also describes procedures for safe handling of hazardous liquid waste such as vomit, mucus, blood, and feces from highly infectious patients, which should be collected separately and thermally treated before disposal (WHO, 2014).

The International Commission on Radiological Protection (ICRP) has issued guidelines for the safe release of HWW generated by patients who have been exposed to unsealed radionuclides. Since patients who have received radioactive treatment may have radioactive compounds in their excretory fluids, the ICRP advises the staff operating such patients should be specially trained to identify and deal with unsealed radionuclides that they may release. The ICRP also warns the sewage workers and general public regarding the radionuclides released into sewage systems which may cause radiation (ICRP, 2004). The guidelines and regulations, including the discharge standards related to HWW treatment in different countries, are presented in Table 2.

Most of the high income-countries and European countries have set guidelines and regulations for HWW generation and treatment. In the United States, the Environmental Protection Agency (US EPA) issues effluent limitation guidelines and standards for new and existing sources that discharge wastewater directly into surface waters. According to the guidelines, the average daily BOD and TSS concentration for 30 successive days shall not exceed 33.6 g/bed and 33.8 g/bed, respectively, in the wastewater discharged from the hospital point source (US EPA, 1976). The US EPA also established the Clean Water Act (CWA), which recommends the point sources of water pollution like hospitals to follow specific regulations and discharge permits. According to the CWA, wastewater generated by healthcare facilities is divided into two categories: indirect discharge (wastewater discharged directly to local municipal sewers) and direct discharge (wastewater discharged directly to streams or rivers). Hospitals that release wastewater indirectly should be regulated by the local sewer authority, which the CWA governs. In contrast, the hospitals that discharge wastewater directly to surface water should follow national discharge standards set by the US EPA. These standards are even more difficult to meet than the restrictions imposed on indirect dischargers (CWA, 1972). Several harmful ECs detected in HWW of the United States, such as erythromycin, perfluorooctane sulfonic acid, perfluorooctanoic acid, etc., have been listed in the contaminant candidate list (US-EPA, 2008).

According to European Directive no. 532 of May 3, 2000 (EU, 2000/532/EC), hospital waste, such as pharmaceutical products, medicines, solvents, and soap residues, iodine-based contrast media, and others must not be directly discharged into local sewers but should be treated as a waste product before disposal (Carraro et al., 2016). Furthermore, in some countries such as Spain, China, India, HWW is considered as industrial discharges. Hence, discharge into municipal WWTPs requires specific permission issued by competent authorities (WWTPs). However, in Brazil and Germany, HWW falls into the category of MWW and does not require specified limits for discharge into domestic WWTPs, but requires limits for discharge in surface water (Carraro et al., 2016; Yan et al., 2020).

Although few countries have guidelines pertaining to some of the ECs, many countries still do not have any legislative protocols regarding the presence of ECs in the aqueous environment and their removal (Khan et al., 2021). In this context, the drinking water equivalent limit (DWEL) for different ECs based on the body weight of different individuals has been provided using Eq. (2) (de Jesus Gaffney et al., 2015; Sharma et al., 2019).

$$\mathrm{DWEL} = \frac{\mathrm{ADI} \times \mathrm{BW}}{\mathrm{GA} \times \mathrm{ADWI} \times \mathrm{E_f}} \tag{2}$$

where ADI represents the acceptable daily intake (mg/kg/day), BW is the body weight of adults in kg, GA is the gastrointestinal absorption rate, taken as 1 for all compounds, ADWI is average daily water intake (L/day), and E_f is the frequency of exposure which is assumed to be 1. The ADI values and predicted no-effect concentration (PNEC) values have been provided in Table 3. The ADWI values as prescribed by WHO are 2.9 L/day for males and 2.2 L/day for females (WHO, 2003). Furthermore, the ADWI varies significantly with the change in the climate. The people from colder countries consume lesser water as compared to people from warmer countries. Hence, in this work, the average daily water intake for males and females has been taken (2.55 L/day). The calculated DWEL values of all target ECs for different ranges of body weights have been presented in Table 3. These values represent the lifetime average daily dose or lifelong exposure to ECs at which severe health effects are unlikely to occur. The DWEL values can be used as reference values by different countries for framing their legislative policies pertaining to the ECs.

4.5. Health and environmental hazard associated with hospital wastewater

Most of the toxic contaminants released by hospitals can

Table 2
The guidelines and regulations including the discharge standards related to HWW treatment in different countries.

Guidelines/Regulation	Organization/ country	Type of disposal/ discharge<	pH	BOD (mg/ L)	COD (mg/L)	Suspended Solids (mg/L)	Oil and Grease (mg/L)	Ammonia nitrogen (as N) (mg/L)	Total phosphorous (mg/L)	Bio-assay test/ *E. coli*/bacteria count	References
The Bio-Medical Waste (Management and Handling) Rules, 1998	India	On-site treated HWW before discharge to surface water	Not-indicated								(Carraro et al., 2016; CPCB, 1986; MOEFCC, 2016)
		For HWW before discharged into municipal WWTP	5.5–9.0	350	–	600	20	50	–	90% survival of fish after 96 h in 100% effluent	
		Direct discharge to surface water after pre-treatment	6.5–9.5	30	250	100	10	–	–	90% survival of fish after 96 h in 100% effluent	
DRP No. 227/2011 on simplification on environmental law, 2011 Legislative Decree No. 152/2006 on environmental protection, 2006	Italy	On-site treated HWW before discharge to surface water	Not-indicated								Carraro et al. (2016)
		For HWW before discharged into municipal WWTP[a]	5.5–9.5	≤300	≤700	≤700	≤ 40	≤50	≤30	<5000 UFC/ 100 mL	
		Direct discharge to surface water after pre-treatment[b]	5.5–9.5	≤40	≤160	≤80	≤20	≤15	≤10	<5000 UFC/ 100 mL	
National Standard of the People's Republic of China Integrated Wastewater Discharge Standard GB 8978, 1996	China	On-site treated HWW before discharge to surface water	Not-indicated								(Carraro et al., 2016; NSPRCIW, 1996)
		For HWW before discharged into municipal WWTP	6–9	≤300	≤500	≤400	–	–	≤0.3	Bacteria count: ≤ 1000–5000 pieces/L	
		Direct discharge to surface water after pre-treatment	6–9	100–150	100–150	70–150	–	15–25	≤0.1	Bacteria count: ≤ 100–500 pieces/L	
National Council for the Environment-CONAMA. Resolution No.430, 2011	Brazil	On-site treated HWW before discharge to surface water	5–9	≤120	–	Sediment materials: up to 1 mL/L in a 1-h cone test (Imhoff)	≤100	–	–	–	(Carraro et al., 2016; NEC-CONAMA, 2011)
		HWW before discharged into municipal WWTP	Not-indicated								
			5–9		–			≤20	–	–	

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Table 2 (*continued*)

Guidelines/Regulation	Organization/ country	Type of disposal/ discharge<	pH	BOD (mg/ L)	COD (mg/L)	Suspended Solids (mg/L)	Oil and Grease (mg/L)	Ammonia nitrogen (as N) (mg/L)	Total phosphorous (mg/L)	Bio-assay test/ *E. coli*/bacteria count	References
		Direct discharge to surface water after pre-treatment		60% of untreated sewage		Sediment materials: up to 1 mL/L in a 1-h cone test (Imhoff)	Mineral oil: ≤ 20 Vegetable oil: ≤ 50				
Decreto n.26,042-S- MINAE on management of discharges and reuses of effluents, 1997	Spain	On-site treated HWW before discharge to surface water	Not-indicated								Carraro et al. (2016)
		For HWW before discharged into municipal WWTP	6–9	≤300	≤1000	≤500	≤100		≤0.1	–	
		Direct discharge to surface water after pre-treatment	5–9	–	–	≤1	–	–	≤0.1	≤1000 CFC/ 100 mL	
Effluent Guidelines and Standards (CFR 40) (Part – 460, Hospital point source) (US EPA), 1976	USA	On-site treated HWW before discharge to surface water	Not-indicated								US EPA (1976)
		For HWW before discharged into municipal WWTP	Not-indicated								
		Direct discharge to surface water after pre-treatment	6–9	41 kg/1000 occupied beds/day	–	55.6 kg/1000 occupied beds/ day	–	–	–	–	
Wastewater Ordinance (AbwV), 2004	Germany	On-site treated HWW before discharge to surface water	–	15–40	75–150	≤35	–	≤10	1–2	–	(Carraro et al., 2016; WWO, 2004)
		For HWW before discharged into municipal WWTP	Not-indicated								
		Direct discharge to surface water after pre-treatment	Not-indicated								
The Urban Waste Water Treatment (England and Wales) Regulations (SI-2841), 1994	England and Wales	On-site treated HWW before discharge to surface water	–	25	125	–	–	Total N: 15 mg/L (population 10,000–100,000), 10 mg/L (population >100,000),	2 mg/L (population 10,000–100,000), 1 mg/L (population >100,000),	–	(Carraro et al., 2016; UWWTR, 1994)
			Not-indicated								

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Table 2 (*continued*)

Guidelines/Regulation	Organization/ country	Type of disposal/ discharge<	pH	BOD (mg/ L)	COD (mg/L)	Suspended Solids (mg/L)	Oil and Grease (mg/L)	Ammonia nitrogen (as N) (mg/L)	Total phosphorous (mg/L)	Bio-assay test/ *E. coli*/bacteria count	References
		For HWW before discharged into municipal WWTP									
		Direct discharge to surface water after pre-treatment								Not-indicated	
National technical regulations QCVN 28:2010/BTNTM on Healthcare wastewater effluent quality, Environmental and Social Management Framework, 2010	Vietnam	On-site treated HWW before discharge to surface water	Not-indicated								ESMF (2012)
		For HWW before discharged into municipal WWTP	6.5–8.5	≤50	≤100	≤100	≤20	≤10	≤10	Total coliform: 5000 (MPN/ 100 mL)	
		Direct discharge to surface water after pre-treatment	6.5–8.5	≤30	≤50	≤50	≤10	≤5	≤6	Total coliform: 3000 (MPN/ 100 mL)	
Safe Management of Wastes from Healthcare Activities (2014	WHO	On-site treated HWW before discharge to surface water	Yes, if municipal WWTP failed to remove 95% bacteria load from HWW								WHO (2014)
		For HWW before discharged into municipal WWTP	Yes, if municipal WWTP achieve to remove 95% bacteria load from HWW								
		Direct discharge to surface water after pre-treatment	Not indicated								
European Union Directive 91/271/EEC on urban wastewater treatment, 1991	EU	On-site treated HWW before discharge to surface water	Not indicated								Carraro et al. (2016)
		For HWW before discharged into municipal WWTP	Requires pre-authorization before discharging MWW into urban sewers (as in certain country is considered the hospital effluent)								
		Direct discharge to surface water after pre-treatment	Not indicated								
European Union Directive 2008/98/EC on waste, 2008	EU	On-site treated HWW before discharge to surface water	Not indicated								Carraro et al. (2016)
			HWW containing PhACs and PPCPs must not be discharged to municipal sewers								

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Table 2 (*continued*)

Guidelines/Regulation	Organization/country	Type of disposal/discharge<	pH	BOD (mg/L)	COD (mg/L)	Suspended Solids (mg/L)	Oil and Grease (mg/L)	Ammonia nitrogen (as N) (mg/L)	Total phosphorous (mg/L)	Bio-assay test/*E. coli*/bacteria count	References
		For HWW before discharged into municipal WWTP									
		Direct discharge to surface water after pre-treatment								Not indicated	

[a] DRP No. 227/2011 on simplification on environmental law, 2011(Italy).
[b] Legislative Decree No. 152/2006 on environmental protection, 2006 (Italy).

contaminate entire water supply systems in towns, causing various types of skin and kidney diseases (Gautam et al., 2007; X. Zhang et al., 2020). Some of these compounds are carcinogenic and mutagenic and can cause or promote cancers and genetic mutations (Gautam et al., 2007; Weissbrodt et al., 2009; X. Zhang et al., 2020). Studies have found that their residues can easily leach into the soil and contaminate groundwater, thus increasing the risk of their exposure by ingestion (Ebele et al., 2017; M. T. Khan et al., 2021). Similarly, various types of pathogens and microorganisms have been reported to cause different types of waterborne diseases like cholera, diarrhoea, typhoid, amoebic dysentery, hepatitis, and others (Gautam et al., 2007; WHO, 2014).

PhACs, such as ciprofloxacin, tetracycline, acetaminophen, and others that contain nitrogen atoms, can decompose during biodegradation processes, releasing toxic fumes of nitrogen oxides which may be harmful to humans (PubChem, 2022). Similarly, fluoride-containing drugs like norfloxacin, ciprofloxacin, and others release hydrogen fluoride gas during decomposition, which irritates the eyes, nose, and respiratory tract (PubChem, 2022). Further, PhACs such as carbamazepine and atenolol can inhibit the growth of embryonic stem cells in humans (Majumder et al., 2019a). Among the contrast media, iohexol, iopamidol, and iopromide have been reported to show toxic effects on humans and animals (Parida et al., 2021). Iohexol, a benzene group compound, has adverse effects on the bone marrow, resulting in a decrease in red blood cells, leading to anemia. Iopromide and iopamidol have renal toxicity to laboratory-tested rats and other rodents (PubChem, 2022). Some studies have also found that these contrast media compounds are nephrotoxic and may cause kidney damage (PubChem, 2022; Schriks et al., 2010; Weissbrodt et al., 2009). Moreover, linear alkyl benzene sulfonic acid, sodium lauryl sulfate, alkyl ethoxy sulfates, and other anionic surfactants can attach to bioactive macromolecules, such as peptides, enzymes, and DNA to alter their biological function via changes in polypeptide chain folding and molecular surface charge (Pereira et al., 2015). Furthermore, phosphate-based detergents promote algae growth, reducing dissolved oxygen in the water, making the survival of aquatic life. In animal studies, they have been linked to osteoporosis and cardiovascular illness among different laboratory-tested animals (Effendi et al., 2017).

The ecotoxic potential of various ECs detected in surface waters of different countries can be estimated from their respective PNEC values. This type of PNEC is generally calculated by dividing half-maximal effective concentration (EC_{50}) or lowest observed effective concentration (LOEC) by an assessment factor of 1000 (Nika et al., 2020). The risk quotient (RQ) can be derived from the measured environmental concentrations (MEC) of the ECs. The RQ can be used as an effective parameter to assess the environmental risks associated with chronic toxicity of ECs on aquatic organisms. RQ is the ratio between MEC and PNEC (Nika et al., 2020; Rout et al., 2021). Based on different studies, it was suggested that if $RQ < 0.1$, the target pollutant has a low probability of causing ecotoxic effects on aquatic species. Whereas, an $RQ \geq 1$ indicates that the particular compound could pose severe ecotoxicity effects (Gani et al., 2020).

HWW is a potential site for horizontal gene transfer and a reservoir for ARGs and ARB (Gupta et al., 2019). The resistance genes are then introduced into natural bacterial ecosystems, where the non-pathogenic bacteria can serve as a platform for resistance genes (Hu et al., 2021; Jiang et al., 2021). They reduce the curative potential of antibiotics to fight against pathogens causing disease in humans and animals (Hocquet et al., 2016; Hu et al., 2021). In Pakistan, ceftriaxone-resistant *Salmonella enterica* was responsible for typhoid fever. Azithromycin and nalidixic acid-resistant *Shigella isolates* were responsible for the outbreak of Shigella in China. In Tajikistan, multi-drug resistant *Salmonella Typhi* in water was found to be responsible for around 100 deaths (Amarasiri et al., 2020; Sanganyado and Gwenzi, 2019). Apart from these resistant ARB and ARGs have also been reported to be responsible for the outbreak of various diseases. They have been known to cause a wide range of anomalies among human beings including gastroenteritis,

Table 3
Predicted no-effect concentrations (PNECs) values for ecotoxicity to aquatic organisms and calculated drinking water equivalent limit (DWEL) values of selected ECs.

ECs	PNEC (µg/L)	References	ADI (mg/kg/day)	References	DWEL (mg/L)					
					Body weight (kg)					
					41–50	51–60	61–70	71–80	81–90	91–100
Paracetamol	1.4	You et al. (2015)	0.34	Schwab et al. (2005)	5.46–6.67	6.80–8.00	8.13–9.33	9.47–10.67	10.80–12.00	12.13–13.33
Ibuprofen	1.65	Verlicchi et al. (2012b)	0.11	Schwab et al. (2005)	1.77–2.16	2.20–2.59	2.63–3.02	3.06–3.45	3.49–3.88	3.92–4.31
Diclofenac	0.05	Tran et al. (2018)	0.0016	Snyder (2008)	0.026–0.031	0.032–0.037	0.038–0.044	0.045–0.050	0.051–0.056	0.057–0.063
Salicylic acid	1.28	Tran et al. (2018)	0.75[b]	EU (2002)	12.06–14.71	15.00–17.65	17.94–20.59	20.88–23.53	23.82–26.47	26.76–29.41
Naproxen	0.33	Tran et al. (2018)	0.046	Snyder (2008)	0.74–0.90	0.92–1.08	1.10–1.26	1.28–1.44	1.46–1.62	1.64–1.80
Ciprofloxacin	1.2	Tran et al. (2018)	0.0016	Schwab et al. (2005)	0.026–0.031	0.032–0.037	0.038–0.044	0.045–0.050	0.051–0.056	0.057–0.063
Erythromycin	0.02	Tran et al. (2018)	0.04	Schwab et al. (2005)	0.64–0.78	0.80–0.94	0.96–1.10	1.11–1.25	1.27–1.41	1.43–1.57
Norfloxacin	0.16	Zhou et al. (2019)	0.19	Schwab et al. (2005)	3.05–3.72	3.80–4.47	4.54–5.21	5.29–5.96	6.04–6.71	6.78–7.45
Trimethoprim	0.16	Tran et al. (2018)	0.0042	Schwab et al. (2005)	0.067–0.082	0.084–0.099	0.100–0.115	0.117–0.132	0.133–0.148	0.150–0.165
Ofloxacin	0.016	Verlicchi et al. (2012b)	2[b]	PubChem (2022)	32.16–39.21	40.00–47.06	47.84–54.90	55.69–62.75	63.53–70.59	71.37–78.43
Tetracycline	–	–	0.03	Schwab et al. (2005)	0.48–0.59	0.60–0.71	0.72–0.82	0.84–0.94	0.95–1.06	1.07–1.18
Azithromycin	–	–	0.011	NWQMS (2008)	0.18–0.21	0.22–0.25	0.26–0.30	0.31–0.34	0.35–0.38	0.39–0.43
Sulfamethoxazole	0.027	Verlicchi et al. (2012b)	0.13	Schwab et al. (2005)	2.09–2.55	2.60–3.06	3.11–3.57	3.62–4.08	4.13–4.59	4.64–5.10
Carbamazepine	0.025	Tran et al. (2018)	0.00034	Snyder (2008)	0.0055–0.0067	0.0068–0.0080	0.0081–0.0093	0.0095–0.0107	0.0108–0.0120	0.0121–0.0133
Atenolol	20	Tran et al. (2018)	0.0027	Snyder (2008)	0.0434–0.0529	0.0540–0.0635	0.0646–0.0741	0.0752–0.0847	0.0858–0.0953	0.0964–0.1059
17 β -Estradiol	0.002	Caldwell et al. (2012)	0.00005	NWQMS (2008)	0.0008–0.0009	0.0010–0.0011	0.0012–0.0013	0.0014–0.0015	0.0016–0.0017	0.0018–0.0019
Iohexol	10,000	Tran et al. (2018)	125[a]	Baken et al. (2018)	2009.8–2451.0	2500.0–2941.2	2990.2–3431.4	3480.4–3921.6	3970.6–4411.8	4460.8–4902.0
Iopromide	370,000	Tran et al. (2018)	83.333[a]	Baken et al. (2018)	1339.9–1634.0	1666.7–1960.8	1993.5–2287.6	2320.3–2614.4	2647.0–2941.2	2973.8–3268.0
Iopamidol	–	–	118.6[a]	Baken et al. (2018)	1906.9–2325.5	2372.0–2790.6	2837.1–3255.7	3302.2–3720.8	3767.3–4185.9	4232.4–4651.0

[a] Tolerable daily intake (TDI).
[b] Calculation provided in Supplementary Material.

urinary tract, lower respiratory tract, bloodstream infections, and others (Amarasiri et al., 2020; Sanganyado and Gwenzi, 2019).

During the biodegradation processes, the PhACs and other ECs may undergo several stages of transformation. In many cases, it has been found that the parent compounds are partially degraded and may be transformed into another product that is equally toxic and, in some cases, has a greater negative effect than the parent compounds (Majumder et al., 2019a; Sharma et al., 2018). These transformed products are typically found in mixtures with their parent compound, and when they enter the environment, they bioaccumulate and pose greater ecological risks. Many studies have also reported that these transformation products are genotoxic and may cause cancer (Majumder et al., 2019a; Parida et al., 2021; Sharma et al., 2018). Thus, the presence of such harmful disease-causing agents necessitates the need to treat HWW before being discharged.

4.6. *Treatment technologies for hospital wastewater*

Conventional primary and secondary treatment units are often incapable of completely removing ECs and other micropollutants (Parida et al., 2021; Patel et al., 2019; Rout et al., 2021). Therefore, tertiary treatment is required for the complete removal of these ECs from HWW. In this study, we have discussed various types of primary, secondary, and tertiary treatment techniques currently being used to treat HWW (Fig. 4c and d) along with their advantages and disadvantages, as shown in Fig. 5. The following section provides an overview of the removal capacity of some of the treatment methods.

4.6.1. *Primary treatment of hospital effluents*

Chemical flocculation was applied as a primary treatment in a dedicated full-scale hospital WWTP in Korea to remove suspended particles and colloids from HWW that do not settle easily (Sim et al., 2013). In another study, the removal of organic matter, solids, and some portion of ECs was achieved using coagulation and flocculation as a primary treatment followed by FBR in Barcelona (Spain). Coagulants and flocculants, with average doses of 95 mg/L and 10 mg/L, respectively were used (Mir-Tutusaus et al., 2016, 2017). The main mechanism involved in the removal of micropollutants during primary treatment is sorption (Suárez et al., 2008). Therefore, only those contaminants with higher sorption properties were removed. Hydrophobic compounds having an octanol-water partition coefficient (log $K_{ow} > 1$) can quickly bind to particles and thereby be eliminated along with the sludge, whereas hydrophilic compounds only partially adsorb on these particles and are thus partially eliminated (Parida et al., 2021; Suárez et al., 2008). From the above studies, it can be concluded that primary treatment can be considered an effective treatment for removing solids and oily matter from HWW and also favors BOD and COD removal to some extent. However, in most cases, the primary treatment processes do not effectively remove ECs from wastewater (Parida et al., 2021).

4.6.2. *Secondary treatment of hospital effluents*

4.6.2.1. Conventional suspended and attached growth processes. The performance of secondary treatment methods in terms of removal of ECs has been presented in Fig. 4d. Kosma et al. (2010) discussed the performance of a conventional full-scale ASP with chlorination as a post-treatment for removal of targeted PhACs from one of the hospital effluent of Greece. The study exhibited high removal of BOD and COD with removal efficiencies of 95.7% and 94.9%, respectively (Table S3). The average PhACs removal was found to be 75%, with high removal of 92.3% achieved for ibuprofen. However, when chlorination is applied as a post-treatment for ASP, the combination has shown high removal of PhACs. This may be due to the presence of chlorine in water, which releases free chlorine radicals that are strong oxidants that can degrade the complex organic PhACs (Kosma et al., 2010). Likewise, Prayitno

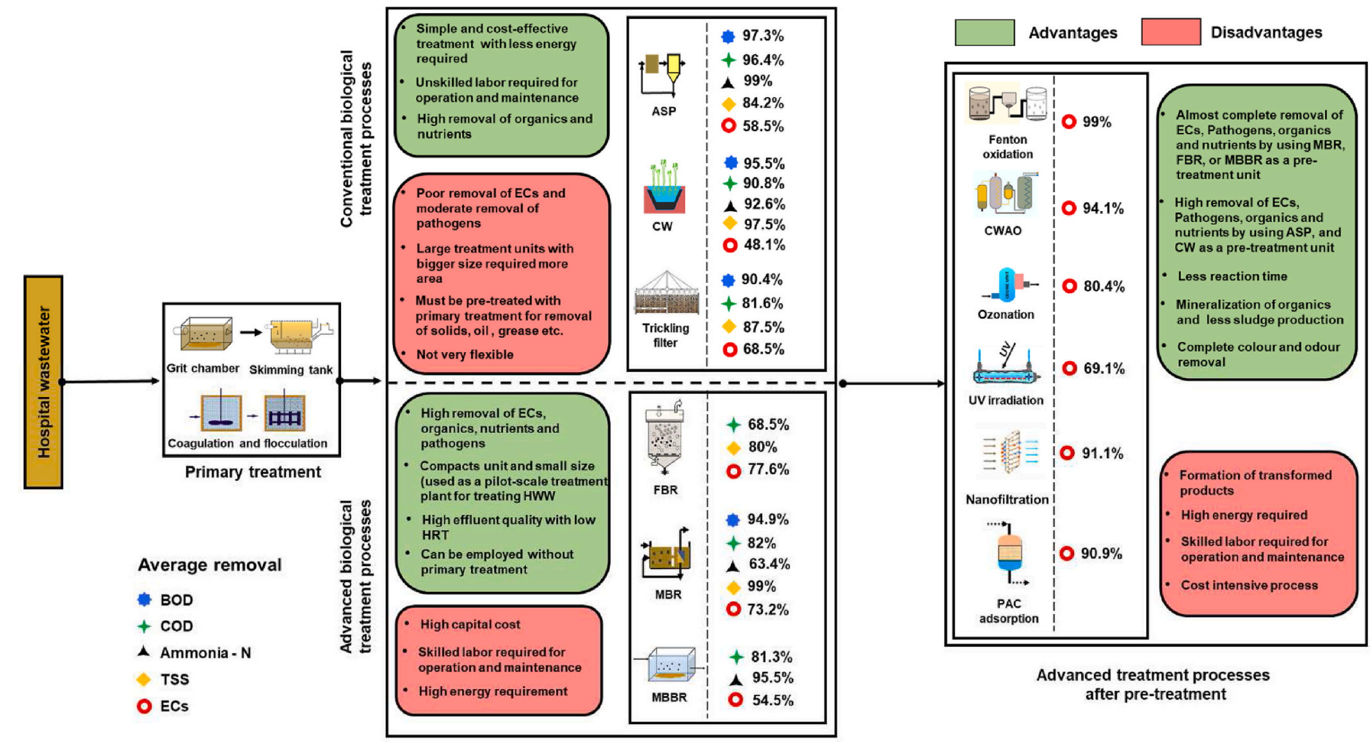

Fig. 5. Recommended treatment methods for HWW remediation based on existing pilot/full-scale units along with their advantages and disadvantages. [Data source: Table S4 in Supplementary Material].

et al. (2012) examined the effectiveness of ASP and extended aeration in removing organic matter, surfactants, and bacterial contamination from the HWW of two Indonesian hospitals. The extended aeration showed better results in terms of COD, BOD, ammonia nitrogen, surfactants, and fecal coliform removal with efficiencies of 74.9%, 80.9%, 84.3%, 60.5%, and 77.4%, respectively, while removal efficiencies of 73.4%, 73.8%, 74.2%, 60.4%, and 75.4%, respectively were achieved by ASP. Low food to microorganism ratio (F/M) and long hydraulic retention time (HRT) may be possible reasons for extended aeration having better performance than the conventional ASP (Prayitno et al., 2012). Santos et al. (2013) used four TFs, each having a volume of 3030 m^3 for the removal of selected ECs from four hospital effluents in Coimbra (Portugal). The TFs exhibited good removal efficiencies of around 91%, 82%, and 87% for BOD, COD, and TSS, respectively (Table S3). The average PhACs removal was found to be 68%. However, diclofenac, carbamazepine, and iopromide showed low removal of 38.4%, 18.6%, and 38%, respectively (Santos et al., 2013).

From the studies above, it can be concluded that conventional WWTPs employing ASP, extended aeration, and trickling filters can achieve on an average PhACs removal of 70–80% from HWW. Biodegradation and sorption are the two significant mechanisms occurring in biological reactors. Hence, the physicochemical properties of PhACs, and the operational parameters of WWTP, such as pH, temperature, biomass concentration, sludge retention time (SRT), HRT, and configuration type (aerobic or anaerobic), are key determinants for the removal of PhACs in WWTPs (Rout et al., 2021; Tran et al., 2018). Therefore, it is recommended that such techniques can be combined with other advanced treatment processes for more effective results (Fig. 5).

4.6.2.2. Constructed wetlands. In the field of wastewater treatment, CWs are increasingly gaining recognition due to their adaptability and durability in removing pollutants. Apart from efficiently removing organic matter from wastewater, a few studies have shown that CWs can degrade recalcitrant organic pollutants (Auvinen et al., 2017; Casierra-Martinez et al., 2020). Auvinen et al. (2017) evaluated the performance of a transportable pilot-scale aerated subsurface flow constructed wetland to treat a hospital effluent in Belgium. The operating conditions of this CW are listed in Table S3. High removal efficiencies of 95.7% and 83% were achieved for ammonia nitrogen and COD, respectively. Whereas, the system showed mixed results for PhACs removal with atenolol showing high removal of 94.6%, while diclofenac, carbamazepine, and sulfamethoxazole showed poor removal with efficiencies of 36%, 12%, and 50%, respectively (Auvinen et al., 2017) (Table S3). In another study, the performance of a full-scale two-staged CW for treating HWW in Nepal was evaluated. The system could effectively remove TSS, BOD, COD, ammonia nitrogen, and bacterial contamination (Shrestha et al., 2001). In terms of organic matter, nutrients, and bacteria removal, CWs performed efficiently compared to other treatment methods, possibly due to altered aeration regimes and the effective nitrification-denitrification process that can occur in CWs (Auvinen et al., 2017). However, in treating PhACs and other micropollutants CWs have shown average results. This variability in the results for the removal of PhACs may be due to various reasons such as the daily fluctuations of influent concentration, retransformation of TPs to their parent compound during treatment processes, low DO concentration, and low HRT (Auvinen et al., 2017; Conkle et al., 2012). Applying a longer HRT, providing sufficient aeration, and the combination of CWs with other treatment techniques can be a vital solution for the economic treatment of HWW.

4.6.2.3. Membrane bioreactors. Advanced biological processes like MBR have received much attention in treating HWW due to their high removal efficiency of organics and ECs (Majumder et al., 2021a; Vo et al., 2019). For instance, Kovalova et al. (2012) have discussed the performance of a pilot-scale MBR (effective volume of 1.2 m^3) installed at a hospital in Switzerland for treating the wastewater discharged from the hospital. The system showed satisfactory results with an average removal of more than 80% for PhACs, while, X-ray contrast media, such as iopromide, iomeprol, etc., showed poor removal (Kovalova et al., 2012). Similarly, Prasertkulsak et al. (2016) had set up a pilot-scale MBR (effective volume of 1.3 m^3) for treating the hospital effluent in Bangkok, Thailand. The system showed effective results for the removal of solids and organic matter with removal efficiencies of 99%, 94.9%, 67%, and 78.6% for TSS, BOD, COD, and TOC, respectively. PhACs like ibuprofen, naproxen, trimethoprim, and sulfamethoxazole were removed with an average removal efficiency of 85%, with ibuprofen showing high removal of more than 99% (Prasertkulsak et al., 2016). Vo et al. (2019) studied the performance of a lab-scale sponge-MBR for treating raw HWW collected from a hospital in Vietnam (Table S3). The system achieved a removal efficiency of 97% for COD, 94% for ammonia nitrogen, and 47% for TP. The system achieved an average PhACs removal of 70%, with norfloxacin showing high removal of 93% (Vo et al., 2019). MBR systems have also shown promising results for the removal of most of the hydrophobic PhACs from HWW, which may be due to significant adsorption of these micropollutants onto the sludge and colloidal particles in the supernatant (Prasertkulsak et al., 2016; Vo et al., 2019). The performance of MBRs can be improved by integrating them with AOPs, adsorption, and filtration-based treatment techniques (Fig. 5). The major disadvantage of using MBR-based treatments systems is that they are subjected to membrane clogging and fouling and require frequent cleaning. This could bring down their performance and increase the overall treatment cost. However, periodic backwashing, aeration, or gas scrubbing can address these problems.

4.6.2.4. Moving bed biofilm reactors. Ooi et al. (2018) employed a six-stage MBBR operated with a filling ratio of 50% to treat HWW collected from a hospital in Denmark. The results were promising, with 91.3% and 88.4% ammonia nitrogen and TOC removal. The system achieved an average removal of more than 80% for ECs, with high removal of more than 95% for atenolol, iohexol, and iopromide (Table S3) (Ooi et al., 2018). In a similar study, Casas et al. (2015) installed a three-stage MBBR at Aarhus university hospital in Denmark to treat the wastewater generated by the hospital. The system achieved very high nutrient removal with almost complete removal of ammonia nitrogen from effluent, while COD and TOC were removed with efficiencies of 81.3% and 79.1%, respectively. The system achieved average PhACs removal of more than 70%, with high removal (95%) occurring for propranolol (Casas et al., 2015). The above studies showed that MBBR-based processes efficiently remove organics and nutrients from HWW. However, when it came to PhACs, complete removal could not be achieved. This may be because the continuous presence of such toxic organic contaminants can kill the microorganisms responsible for degradation. Combining MBBRs with AOPs, filtration, and adsorption-based techniques can improve their performance, allowing for the complete removal of ECs (Fig. 5).

4.6.3. Tertiary treatment of hospital effluents

4.6.3.1. Advanced oxidation processes. In the last two decades, a significant amount of research has been conducted for the removal of ECs and other micro contaminants from HWW by various tertiary treatment techniques such as Ultraviolet (UV) treatment, ozonation, catalytic wet air oxidation (CWAO), adsorption, nanofiltration (NF), reverse osmosis (RO) and others (Segura et al., 2021; Souza et al., 2018; Yadav et al., 2021). Segura et al. (2021) evaluated the performance of three AOPs, including CWAO, Fenton, and photo-Fenton treatment for treating wastewater of a hospital sewer in Madrid, Spain (Table S3). The AOPs showed very promising results in removing the PhACs from HWW (Segura et al., 2021). In another study, Kovalova et al. (2013) integrated the MBR process with ozonation (effective dose of 1.08 g O_3/g DOC) and UV treatment (effective fluence rate of 7200 J/m^2) to form a hybrid treatment system for high removal of ECs from a hospital effluent in Switzerland. The results were promising, with an average removal of ECs of 85.6% and 82.4% achieved with ozonation and UV treatment, respectively (Kovalova et al., 2013). Performance of tertiary treatment methods in terms of removal of ECs has been presented in Fig. 4d. Similarly, Souza et al. (2018) combined ozonation and UV irradiation (working at 96 W power with a UV-C source) for treating HWW collected from a hospital in Porto Alegre, Brazil. The integrated system performed efficiently and obtained almost complete removal of ciprofloxacin, trimethoprim, atenolol, propranolol, and metoprolol. Surfactants were also efficiently removed with an efficiency of more than 94.9% (Souza et al., 2018). From the above studies, it can be concluded that ozonation has shown effective removal for most of these ECs which could be due to the reactivity of ozone-reactive moieties (ORMs) of these ECs. The compounds without ORMs are easily oxidized by hydroxyl radicals (•OH) that are formed during ozonation as oxidants, while molecules with ORMs are partially oxidized (Kovalova et al., 2013). However, AOPs also possess some drawbacks, such as high operational and maintenance costs due to the use of expensive chemicals and equipment, high energy requirements, and complex design (Karimi Estahbanati et al., 2020; Kovalova et al., 2013; Parida et al., 2021). In addition, the dissolved organic matter, solids, and nutrients present in wastewater can react with the oxidizing radicals and thereby reduce the system's reaction rate by consuming the radicals needed to oxidize the target pollutants (Majumder and Gupta, 2021; Nicholas, 2019). Therefore, it is recommended that AOPs be used in conjunction with secondary biological processes to effectively remove these ECs (Fig. 5).

4.6.3.2. Adsorption-based processes. Several research studies have also reported the use of activated carbon (AC) as an adsorbent for the removal of ECs from HWW (Kovalova et al., 2013; Sim et al., 2013). Sim et al. (2013) assessed the performance of AC as an adsorbent for the removal of targeted PhACs from HWW in Ulsan and Busan, Korea. The process obtained high removal of PhACs, such as naproxen, acetaminophen, and atenolol, with high adsorption capacities of 94.4%, 88%, and 90.4%, respectively. However, carbamazepine and metoprolol exhibited poor adsorption with adsorption capacities of 55.1% and 50%, respectively (Table S3) (Sim et al., 2013). Similarly, Kovalova et al. (2013) have studied the performance of powdered AC (PAC) adsorbents for the removal of specific ECs. The results of the study were promising, with ECs, such as ciprofloxacin, carbamazepine, azithromycin, norfloxacin, and metoprolol being almost completely removed from the HWW, with 43 mg/L of PAC dose. However, overall ECs removal was 90.9% (Kovalova et al., 2013). This variation in the removal of ECs by adsorption-based systems could be due to several reasons, such as the compounds which are non-polar, hydrophobic (log $K_{ow} > 1$), and uncharged, have no electrostatic interactions with functional groups, and are thereby effectively adsorbed on the surface of AC (Kovalova et al., 2013; Majumder et al., 2021b; Parida et al., 2021). Other reasons that could influence the removal of these ECs are the molecular size of adsorbate, aromatic and aliphatic compounds, presence of typical functional groups, the surface area, pore size, and texture of adsorbents, etc. (Kovalova et al., 2013). The adsorption process cannot be used alone as they will result in poor removal of ECs as the natural organic matter, solids, and nutrients present in wastewater may occupy the active sites of the AC which are responsible for adsorption processes (Nicholas, 2019). Therefore, they must be combined with biological treatment processes to form hybrid adsorption systems to achieve higher removal of these recalcitrant pollutants (Fig. 5).

4.6.3.3. Membrane filtration-based processes. A few filtration-based processes such as NF and RO have also been studied for the removal of PhACs from HWW (Beier et al., 2010; Jadhao and Dawande, 2012). The effectiveness of these membranes for the removal of ECs depends upon various factors, including the molecular weight of these compounds. The compounds with molar weight more than the molecular weight cut-off (molecular weight at which 60–90% of substances are retained) are easily adsorbed by these membranes (Beier et al., 2010).

Aside from molecular size, adsorption effects and charge also play important influencing factors for the removal performance of membrane (Beier et al., 2010). The sorption mechanism removes the non-polar compounds and suspended solids, whereas the charged particles are rejected in the NF and RO process due to electrostatic interaction (Beier et al., 2010; Bellona et al., 2004). In a pilot-scale study, NF and RO membrane module was employed to treat MBR filtrate generated by a hospital WWTP in Germany. The hybrid system removed PhACs efficiently, with an average removal efficiency of 98.7% for the RO and 93.5% for the NF. However, ibuprofen had shown moderate removal by NF. Due to the low acid dissociation constant (pK_a), ibuprofen was only partially rejected by the charged membranes (Beier et al., 2010). The performance of various filtration-based treatment methods in terms of removal of ECs is presented in Fig. 4d. Furthermore, these systems have several advantages over other treatment techniques, including the ability to produce high-quality effluent with minimal sludge generation, low energy use, and operation in a wide range of pH and temperature ranges (Fu and Wang, 2011; Hocaoglu et al., 2021). However, filtration-based systems are quite expensive, and they are susceptible to membrane fouling, resulting in a decrease in permeate flux. Expensive cleaning and regeneration techniques may be required (Dhangar and Kumar, 2020).

The variation in the removal of selected ECs in HWW by different treatment systems is presented in Fig. 4c and d. According to this figure, most NSAIDs or analgesics have shown less variation in their removal by different treatment systems as compared to antibiotics, β-blockers, and X-ray contrast media. Also, the average removal efficiency of the analgesics was higher as compared to the other ECs (Fig. 4c). This could be because when compared to NSAIDs most of the antibiotics, β-blockers, and X-ray contrast media have lower sorption coefficients ($K_d < 500$ L/kg MLSS) and lower degradation kinetic constant ($k_{bio} < 0.01$ L/gMLSS d) (Majumder et al., 2021b; Parida et al., 2021). These ECs have a lower affinity for sorption and remain persistent during biodegradation processes, resulting in high removal efficiency in some treatment methods and low removal efficiency in others.

5. Biomedical waste

Over the last few decades, the increasing generation of BMW has also posed a significant threat to public health and the environment (Ansari et al., 2019; Windfeld and Brooks, 2015). In addition, the impact of the COVID-19 pandemic has also increased the worldwide BMW generation quantity (Das et al., 2021; Sarkodie and Owusu, 2021). Due to the increased consumption and panic buying of single-use products, such as masks, gloves, hazmat, and personal protective equipment (PPE) suits, etc., there has been an increase in the production of these items, resulting in the generation of a large quantity of BMW (Islam et al., 2021; Sarkodie and Owusu, 2021).

Several studies have recently focused on the generation and management of BMW (Ansari et al., 2019; Tsakona et al., 2007; Windfeld and Brooks, 2015). The publication trend related to the generation and management of BMW in selected high, upper, and lower-middle-income countries during 2012–2020 is shown in Fig. S2 of supplementary material. According to the figure, the majority of the studies are reported from upper and lower-middle-income countries such as India, China, Brazil, Iran, Turkey, Pakistan, Taiwan, and Nigeria. These findings indicate that more research has been conducted in these countries on BMW generation rate (BMWGR), BMW composition, BMWM, public health, and environmental issues. On the other hand, on average, high-income countries generate less BMW than upper and lower-middle-income countries (Fig. S2).

Previous studies have reported that improper disposal and mishandling of BMW could result in the spread of infections, rodent-borne diseases, and others. Hazardous waste, such as toxic chemicals, nuclear or radioactive substances, may significantly affect the environment and harm all living organisms exposed to it (Ansari et al., 2019; Tsakona et al., 2007). Consequently, several studies, particularly from upper and lower-middle-income countries, have also reported the adverse effect of BMW on humans and the environment (Ansari et al., 2019; Gao et al., 2009; WHO, 2014).

5.1. Worldwide generation of biomedical waste

In the last few decades, several studies have been published that have reported about the worldwide BMWGR (Askarian et al., 2004; Farzadkia et al., 2015; Thirumala, 2013). Among the upper and lower-middle-income countries, a high BMWGR of 14.8 kg/bed/day has been reported from a hospital in Shiraz, Iran (Table S4) (Askarian et al., 2004). Whereas, amongst the high-income countries, a high BMWGR of 10.7 kg/bed/day is reported from a city hospital in Florida, United States (WHO, 2014). This high generation rate of BMW could be due to many reasons, such as types of health services offered in hospitals, modern facilities provided to patients, their social and cultural status, and poor management policies. Fig. 6a represents the BMWGR among different countries covered in this study.

On average, the BMWGR in high-income countries generally ranges between 2 and 4 kg/bed/day, which is lower compared to upper and lower-middle-income countries ranging between 4 and 6 kg/bed/day, which could be due to various reasons, such as high-income countries have better management policies, more advanced disposal technologies, competent regulatory authority, and trained HSW workers compared to upper and lower-middle-income countries. From Table S4, it can be observed that there are several variations in the BMWGR among the same country. For example, in Iran, the average BMWGR of private specialized hospitals (8.6 kg/bed/day) is higher than the average BMWGR of public hospitals (3.1 kg/bed/day). This may be because, in private hospitals, more modern facilities are offered to patients, and a wide range of specialized treatments are accessible, resulting in a higher BMWGR than public hospitals. In Pakistan, a total of 38,978 kg of solid waste is generated daily from 17 hospitals, among which 10,789 kg has been estimated to be infectious wastes (Arub et al., 2020).

The hazardous and non-hazardous component of the BMW generated in different countries covered in the study is represented in Fig. 6b. From this figure, it can be observed that the highest proportion of hazardous BMW (70.7%) and non-hazardous BMW (98.7%) has been reported from a hospital in Pakistan and Serbia, respectively (Table S4) (Stanković et al., 2008; WHO, 2014). According to WHO guidelines, approximately 85% of total BMW generated is considered general or non-hazardous waste, while the remaining 15% is classified as hazardous waste, including all kinds of infectious and radioactive waste (WHO, 2014).

5.2. Categories of biomedical waste

The BMW includes all types of waste generated from different departments of hospitals, such as general wards, OT and surgical departments, radiology departments, laboratory and research departments, morgue, and others (Ansari et al., 2019; Tiwari et al., 2013; WHO, 2014). According to WHO guidelines, BMW is generally classified into two categories (non-hazardous waste and hazardous waste). General wastes or domestic wastes that do not create any nuisance to the environment are generally termed non-hazardous waste. These wastes are mostly generated from general wards and housekeeping facilities provided in hospitals like food waste, paper, plastics, and others. On the other hand, hazardous waste can pose a severe threat to human health and the environment (WHO, 2014). A wide range of hazardous waste generated by hospitals has been classified into several sub-categories, such as infectious waste, pathological waste, sharps, pharmaceutical waste, genotoxic and cytotoxic waste, chemical waste, and radioactive waste to facilitate BMWM by different international organizations and regulatory bodies as shown in (Fig. 6c) (MOEFCC, 2016; SANS, 2008; US EPA, 1992; WHO, 2014). These sub-categories of hazardous waste are discussed briefly in section 2.1 of supplementary

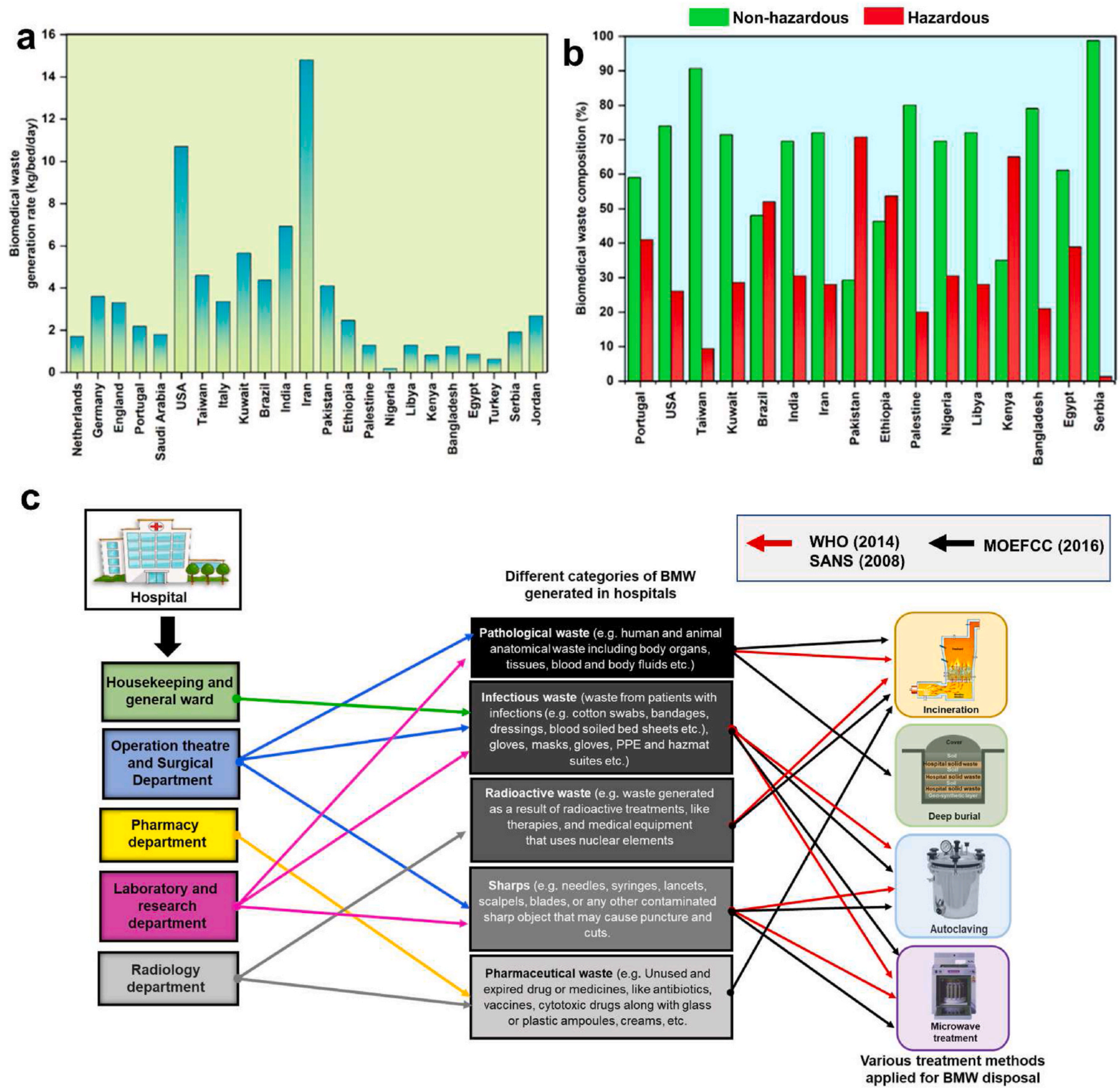

Fig. 6. (a) Worldwide BMW generation rate (kg/bed/day) and (b) hazardous and the non-hazardous component of the BMW generated among the selected countries [Data source: Table S4 in Supplementary Material]. (c) Different categories of BMW generated by hospitals based on different international organizations and regulatory authorities, as well as various disposal strategies proposed by them [Data source (MOEFCC, 2016; SANS, 2008; WHO, 2014):].

material.

5.3. Regulations and conventions for biomedical waste

The government interventions are mandatory to have a larger impact on improvements in waste management in local healthcare facilities across different countries. The WHO and other statutory agencies have established several treaties, international agreements, and conventions to ensure the safe handling and management of wastes from healthcare facilities.

The WHO guidelines recommend a few strategies (i.e., short-term, medium-term, and long-term) that government agencies should implement to safely handle and manage BMW. The strategies primarily emphasize the recycling of materials used in healthcare facilities. The WHO also recommends the core principles for safe and sustainable BMW management. According to these principles, everyone involved in financing and supporting healthcare activities must account for the costs of managing BMW (WHO, 2014).

The Biomedical Waste Management and Handling Rules (2016) (BWMHR) established a variety of roles and responsibilities for common biomedical waste management (CBMW) disposal facilities and authorities. According to the BWMHR, the CBMW should make sure that microbiological waste, laboratory waste, blood samples, and other infectious wastes are pre-treated through disinfection or sterilization on-site in the prescribed manner. The CBMW are also advised to give proper training, immunization, health check-up, and occupational safety to all the workers employed in the management of BMW. The rules also suggest that barcoding and GPS should be implemented for effective BMW traceability. Furthermore, for the final disposal of BMW, sustainable and eco-friendly technologies, such as plasma pyrolysis, may be used to promote waste to energy (MOEFCC, 2016). The following section discusses some significant conventions made by the different regulatory authorities regarding the effective management of BMW.

5.3.1. The International Solid Waste Association

The International Solid Waste Association (ISWA) is a non-profit organization that works in the public interest to promote and develop sustainable waste management. The primary goal of ISWA is to ensure that countries pay adequate attention to the safe and sustainable management of BMW by best available techniques (BAT), which include segregation, storage, transport, treatment, and final disposal. Due to the widespread drug abuse and the increase in the number of healthcare activities, the ISWA ensures that BMW generated by minor sources is captured and treated appropriately (Capoor and Bhowmik, 2017; WHO, 2014).

5.3.2. The Basel Convention

The Basel Convention on the "Control of Transboundary Movements and Disposal of Hazardous Wastes" is one of the most comprehensive global environmental treaties on hazardous and other wastes. The primary goal of the treaty is to protect human health and the environment from the adverse effects of hazardous and other waste generation, management, transboundary movement, and disposal. This convention actively oversees activities involving the management of infectious and anatomical wastes from hospitals, medical centers, clinics and pharmaceuticals, drugs, and medicines waste (UNEP, 1989). Another convention similar to the Basel Convention is the Bamako Convention. The primary goal of this convention is to prohibit the trade of hazardous and toxic waste, including BMW, to African countries (UNEP, 1998).

5.3.3. The Stockholm Convention

The Stockholm Convention on persistent organic pollutants (POPs) is a global treaty that was established to protect human health and the environment from POPs. The primary goal of the treaty is to reduce or eliminate the release of POPs such as polychlorinated dibenzo-p-dioxins and dibenzofurans by BMW incinerators and other combustion processes using BAT guidelines to promote best environmental practices (BEP) for new incinerators within four years of the party signing the convention.

The convention also focuses on the BMW reduction, segregation, resource recovery and recycling, training, and proper handling and transport using BEP. BMW incinerators emit several toxic substances, such as chlorinated dioxins and furans (Allen et al., 2012; Cebe et al., 2013; Gao et al., 2009). The BAT guidelines have mandated that the concentration of polychlorinated dibenzo-p-dioxins and dibenzofurans should be less than 0.1 ng I- Toxicity Equivalency Quantity/Nm^3 (at 11% O_2), and dioxin and furan concentrations should be less than 0.1 ng I-Toxicity Equivalency Quantity/liter in the wastewater generated from the treatment of flue gas coming out from BMW incinerators (UNEP, 2006).

5.4. Health and environmental risks associated with biomedical waste

The BMW contains a wide range of pathogens and toxic chemicals that can affect the people exposed to these wastes, such as patients, medical staff, BMWM workers, and the general public (Saini et al., 2004; Subramanian et al., 2021). In each stage of BMWM, from the collection and segregation to the final disposal of BMW, there is a risk of disease transmission to the people associated with BMWM through contact with hazardous wastes.

The improper disposal of sharp wastes may introduce pathogens through cuts or pricks, causing bacteremia, which quickly spreads through the bloodstream, causes inflammation and infection of organs, and may cause acute and chronic hepatitis, liver cirrhosis, liver cancer, and HIV/AIDS (Chamberlain, 2019). In addition, the improper disposal of solid wastes from laboratories can cause parasitic infections, such as tuberculosis, influenza, and pneumonia, to the BMW workers and general public as these parasites flourish in the waste can be easily transmitted to humans through respiration and skin contact (Chamberlain, 2019). Meningitis is another risk of transmission through bodily fluids, which contains pathogens that cause swelling of the membranes surrounding the brain and spinal cord (Chamberlain, 2019).

Apart from health risks, BMW is also associated with environmental risks. Improper segregation and disposal of BMW may result in significant environmental pollution. Few studies have reported that most of the countries burn BMW in uncontrolled conditions with no flue gas treatment, posing a significant risk of air pollution (Allen et al., 2012; Gao et al., 2009; Yan et al., 2012). For instance, the release of toxic compounds such as polychlorinated dibenzo-p-dioxins and dibenzofurans, hexachlorobenzene, dioxins, etc., as well as airborne bacteria (*Bacillus subtilis*) from the stack gas emitted by BMW incinerators has been reported by few researchers (Allen et al., 2012; Gao et al., 2009; Yan et al., 2012). Apart from incineration, landfills have been another choice for the disposal of BMW. Although landfills are regarded as one of the simplest and most cost-effective methods for the disposal of BMW, it still falls short in some ways (Reinhart and McCreanor, 2000). For instance, the landfills that are not appropriately constructed or the failure of a landfill liner system might leach harmful leachate and can contaminate the groundwater (Padmanabhan and Barik, 2019).

5.5. Biomedical waste management practices in different countries

BMW must be appropriately collected, segregated, handled carefully, and disposed of properly to reduce the health and environmental risks transmission rate associated with it. As a result, the WHO has proposed a color-coded bag and bin system for effective collection and segregation of BMW based on the type of waste generated by hospitals. According to the system, the infectious, pathological, and sharp waste should be collected in a leak and puncture-proof yellow container. In contrast, the chemical and pharmaceutical waste should be collected in brown containers, and the general non-hazardous waste should be collected in black containers (WHO, 2014). However, in India, the BWMHR (2016) has suggested slightly different color coding for the collection and segregation of BMW. According to the rules, the infectious, pathological, chemical, radioactive, and pharmaceutical waste that is to be incinerated should be collected in yellow bins. Whereas all the recyclable contaminated wastes should be collected in red bins, all the sharps waste should be collected in white bins, and all kinds of glassware waste should be collected in blue cardboard boxes (Iyer et al., 2021; MOEFCC, 2016). In contrast, according to the South African National Standards, the infectious human and animal anatomical waste should be collected in red and orange bins, respectively, sharps waste should be collected in yellow bins, and chemical waste, including pharmaceutical waste, should be collected in dark green bins (SANS, 2008).

Apart from the collection and segregation of BMW, a variety of methods for the safe disposal of hospital wastes have been used by most of the countries, including incineration, landfill, autoclaving or steam sterilization, microwave treatment, and chemical disinfection (Fig. 6c) (Ansari et al., 2019; Iyer et al., 2021; Subramanian et al., 2021). The details about these disposal methods, working mechanism, and their advantages have been discussed briefly in section 2.2 of supplementary material.

Despite the advantages, there are some drawbacks to these disposal techniques. HSW incinerators generate a large number of toxic chemicals and fumes into the environment. These gases can stay in the ambient air for a longer period, posing serious health and environmental hazard (Allen et al., 2012; Cebe et al., 2013; Gao et al., 2009). Whereas, for autoclaving lack of electricity is the biggest barrier as, without electric energy, the autoclave machine cannot be operated. Similarly, for microwave treatment, the complex operation procedures and high cost of the instrument have limited its use in upper and lower-middle-income countries (Pasupathi et al., 2011; Tiwari et al., 2013). However, a few studies are also available that have reported various procedures and modifications to overcome the limitations of these disposal methods. For instance, Kaur et al. (2021) conducted an experiment using *Bacillus halodurans* (gram-positive rod-shaped bacteria) to reduce alkalinity, and heavy metal leaching from hospital incinerated biomedical waste ash and found that approximately 95% bioremediation of these toxic metals occurred. These alkaliphile bacteria have enzymes that allow them to survive in an alkaline environment and help them to biodegrade these toxic metals. In an alkaline pH of 10–13, the cell surface of these bacteria can keep intracellular pH values near neutral. As a result of their natural metabolic process, these bacteria can stabilize the toxic metal content (Kaur et al., 2021). Similarly, Qin et al. (2018) used porous alumina bed material to remove monocyclic aromatic hydrocarbons emissions from the medical waste incinerator in a fluidized bed combustor, thereby reporting a removal efficiency of 91.6% (Qin et al., 2018). Many theoretical and experimental investigations on solar autoclaves have been conducted using various types of thermal solar technology. It uses less expensive materials to lower the overall cost of the sterilizing system and make it easier for rural health facilities to obtain them (Ituna-Yudonago et al., 2021; Tesfay et al., 2019).

6. Hospital wastewater and biomedical waste management in the context of COVID-19

During the ongoing global COVID-19 pandemic, countries implementing frequent hand washing and extensive disinfection had seen a 15%–18% increase in wastewater generation (Quintuña and Marcelo, 2020). Due to the pandemic, the water demand in Asian countries, such as India and Iran, increased by 70% and 40%, respectively. In Latin American countries such as Mexico and Colombia, water demand has increased by 50% and 75%, respectively (Quintuña and Marcelo, 2020). As a result, a significant increase in the generation of HWW is inevitable. Recent studies have reported that SARS-CoV-2 RNA is detected in the urine and stool samples of infected patients (Holshue et al., 2020; Ihsanullah et al., 2021; Liu et al., 2020). The urine and stool of patients can be another possible mode of transmission for this virus. The fecal and mucosal transmission of the virus can be facilitated by poor sanitation at public toilets and drinking water outlets due to frequent touching of the mouth, nose, and eyes without washing hands (Tian et al., 2020).

Previous studies have reported that SARS-CoV-2 can mostly survive when the pH of the HWW is between 6 and 8 (Amoah et al., 2022; Varbanov et al., 2021). La Rosa et al. (2020) have reported SARS-CoV-2 is highly sensitive to alkaline water and can be inactivated in chlorinated water (La Rosa et al., 2020). It was reported that SARS-CoV-2 RNA ceased to exist in a septic tank following disinfection with 6700 g/m^3 of sodium hypochlorite (D. Zhang et al., 2020).

With the global spread of COVID-19 in various countries, including China, India, Italy, Japan, the Netherlands, and others, sewage monitoring can allow early detection of the entrance of the virus into the community (Ahmed et al., 2020; Kumar et al., 2022; Medema et al., 2020; D. Zhang et al., 2020). Hence, the wastewater-based epidemiology/sewage epidemiology and wastewater surveillance approach could be used as a quasi-early-warning tool to alert the public about the severity of the COVID-19 outbreak and assist public health officials in implementing appropriate measures and help them to track the actual source of the virus (Mallapaty, 2020; Mandal et al., 2020; Suthar et al., 2021). This may aid in implementing critical risk-prevention strategies to protect public health (Suthar et al., 2021).

Apart from the acute to chronic health consequences of COVID-19, the pandemic has also triggered severe problems, including psychological, economic, and social effects on the population. Due to the pandemic, people were forced to stay at home, which has resulted in increased solid waste generation at the domestic level (Das et al., 2021; Sarkodie and Owusu, 2021). Furthermore, the outbreak has resulted in an unexpected increase in the number of patients admitted to hospitals. As a result, a huge number of medical equipment and single-use items, such as masks, gloves, hazmat, PPE suites, etc., have been produced in bulk, increasing the overall generation of a large quantity of BMW (Islam et al., 2021; Iyer et al., 2021; Patrício Silva et al., 2021; Sarkodie and Owusu, 2021).

Different countries have conducted many studies to determine the increase in the BMW generation due to the pandemic (Ansari et al., 2019; Das et al., 2021; Sarkodie and Owusu, 2021). In India, according to a report by the Centre for Science and Environment, the BMW generation per day increased by 10.7% between 2017 and 2019, and during the second wave of a pandemic the quantity of BMW generated per day was significantly increased by 46% (CSE, 2021). Similarly, Agamuthu and Barasarathi (2021) have reported an increase in BMW generation by 27% (by weight) during the pandemic in Malaysia. In China's Hubei province, the infectious BMW generation increased by 600%, from 40 tons/day to 240 tons/day during the COVID-19 outbreak (ADB, 2020). Furthermore, according to United Nations Environment Programme and International Environmental Technology Centre (2020) report, there was a rapid increase in the healthcare waste generation in some of the upper and lower-middle-income countries like the Philippines, Indonesia, Thailand, and Vietnam due to the COVID-19 outbreak (UNEP and IGES, 2020). Several studies from high-income countries have also reported a high generation of BMW. For instance, Wei and Manyu (2020) have reported that BMW generation in France and the Netherlands has increased from 40% to 50% and 30%–50%, respectively, due to the COVID-19 effect. Furthermore, Liang et al. (2021) have reported the BMW generation had increased by 350% from mid-march to mid-April in Catalonia, Spain (Liang et al., 2021).

Many countries have implemented various methods to effectively handle the large quantity of BMW generated during the pandemic so that no additional risk is generated for BMW workers and the general public (Agamuthu and Barasarathi, 2021; Sarkodie and Owusu, 2021; Windfeld and Brooks, 2015). For instance, in India, the Central Pollution Control Board provided special guidelines which recommend the use of yellow-colored double-layer bags and bins labeled with "COVID-19 waste" for the collection of all kinds of hazardous waste generated from the health care facilities related to COVID-19, with emphasis on being a priority waste. The guidelines also recommend that solid waste collected from hospitals and nearby health care facilities should be disposed of with extreme caution (CPCB, 2020). Similarly, in China, the Ministry of Ecology and Environment of the People's Republic of China published "Pneumonia Medical Waste Emergency Disposal Management and Technical Guide" guidelines which suggest that the COVID-19 hazardous BMW collection and disposal must be given priority by hospital waste disposal units which are generated throughout the pandemic. The guidelines also recommend that the entire medical waste process should assure the security of worker hygiene (Ma et al., 2020).

Several studies have reported that in some of the upper and lower-middle-income countries, such as Indonesia, Bangladesh, Thailand, South Africa, Malaysia, and Mexico, the most common for the disposal of the BMW generated during the pandemic was incineration. Liner landfills were used if incinerators were not available (far away from the city) (Islam et al., 2021; Marome and Shaw, 2021; Singh et al., 2022; UNEP, 2020). Furthermore, in countries like South Africa, Thailand, and Mexico, autoclaving, radio wave, and microwave treatment were also practiced apart from incineration for the BMW treatment (Marome and Shaw, 2021; Singh et al., 2022; UNEP, 2020).

Several studies from high-income countries have also been reported on the effective management of BMW generation during the pandemic (Das et al., 2021; OSHA, 2020). In Japan and Italy, infectious and non-infectious waste separation, storing infectious waste in strong and leak-proof containers, proper labeling of the infectious waste, maintaining a short storage time, and a separate room for storing infectious waste were practiced (Das et al., 2021).

Similarly, the European Union also suggested guidelines for managing household COVID-related waste, suggesting a separate collection of COVID-19 infected patient waste (mask and tissue) which should be placed in separate double-layered leak-proof plastic bags in separate containers (Das et al., 2021). Furthermore, WHO and US EPA also provided guidelines with a major focus on handling BMW during the pandemic using special hazmat suits, including face covering, mask, apron, boots, puncture-resistant gloves, and long-sleeved gowns (OSHA, 2020; WHO, 2020).

7. Computational modeling

7.1. Computational modeling for risk assessment of potentially carcinogenic compounds in hospital waste

Big data and other data-driven statistical modeling methods can be used to analyze extensive biological data from hospitals, healthcare facilities, and pharmaceutical industries by integrating artificial intelligence with computational methods (Chowdhury et al., 2020; Musavi et al., 2019; Romero et al., 2017). Assessment of the risk related to the presence of dangerous chemicals in the environment is both important and difficult. However, accurate assessment of the impact of a chemical is a complex task (Ekins, 2006). Most widely detected ECs, such as antibiotics, analgesics, contrast media, and BMW incinerator-released pollutants like dioxins and furans have not been addressed with specific regulations. Furthermore, the lack of knowledge about the ecotoxic effects of exposure to such contaminants poses a bigger problem (Allen et al., 2012; Carraro et al., 2016; Ekins, 2006; Gao et al., 2009). Due to insufficient data on their transport and pathways in different environmental matrices, the environmental risk assessment depends on many assumptions. Hence, computational models are used to replace the missing experimental data. Mostly these tools are based on a probabilistic approach using AI techniques. These model-based tools can measure the probability of certain mechanisms, pathways, level of concentration increase, or other scenarios (Chowdhury et al., 2020; Ekins, 2006; Winkler, 2016).

Most of these models generally provide estimates for spatial and temporal data. A critical evaluation of input variables must be carried out to achieve a good quality of output results. Many environmental outcome system architecture and models, such as SCADA, HYDRUS-1D, HYDRUS-2D, IMPAQT, MACRO, PEARL, GEOPEARL, VARLEACH, etc., have been employed for real-time data monitoring and assessment of pollutant exposure in the environment (Ekins, 2006). Furthermore, structure-activity relationships and quantitative structure-activity relationships, collectively known as (QSARs) are theoretical models that can be used to predict the physicochemical and biological properties of chemical compounds. However, these models can also be employed in predicting effluent concentration, toxicology evaluation, and setting up discharge regulation (Ekins, 2006; Winkler, 2016).

In order to assess the risks associated with a particular EC, the computational model requires a set of input data or parameters related to the particular EC. A cancer slope factor is generally used which is also referred to as carcinogenic potency factor (CPF) expressed as $(mg/kg/day)^{-1}$ (Farris and Ray, 2014; USEPA, 2005). The CPF can be considered as a parameter for evaluating the incremental lifetime cancer risk due to the long-term intake of such carcinogenic compounds. It is an absolute measure, approximating a 95% confidence limit, on the increased cancer risk from lifetime ingestion or inhalation of a carcinogen. The risk associated with these compounds is the multiplication of CPF and chronic daily intake (mg/kg/day) (Farris and Ray, 2014; USEPA, 2005).

Hazard quotient (HQ) is another very important parameter used in risk assessment. This parameter is often used by regulatory bodies like the US EPA for the identification of the risk category of a chemical compound based on the dose-response relationship (Chemsafety, 2018). The HQ is evaluated based on the total dose of a potential carcinogen and a reference dose at which no adverse effects are likely to occur (Chemsafety, 2018; USEPA, 1993).

7.2. Computational modeling for effective management of hospital wastewater and biomedical waste

In recent times, computational-modeling methods such as blockchain, fuzzy logic, system dynamics, and so on have played a critical role in the effective management of HWW and BMW. Some of these methods are discussed in the following sections. Computational methods have been used for analyzing data sets that are too large or complex for traditional data-processing application software to handle. Researchers have successfully implemented big data tools and computational technologies to address issues in the water and wastewater utility sector (Choudhury et al., 2021; Chowdhury et al., 2010; Musavi et al., 2019; Romero et al., 2017).

7.2.1. Fuzzy logic

Fuzzy logic, another artificial intelligence-based system, has been frequently used for problem-solving when a numerical solver is insufficient to produce accurate results. It makes use of a soft computing system to deal with extreme situations. The system helps to improve the known entities and converts them to numeric and functional parameters in surface graphs (Choudhury et al., 2021; Chowdhury et al., 2020). Various researchers have implemented fuzzy logic as an objective function for optimizing the best design and prediction of water and wastewater quality by plotting the correlation between input and output parameters. Pai et al. (2009) have employed fuzzy logic for the prediction of the removal of suspended solids and COD from HWW in Taiwan. The results indicated that the logic could predict the effluent variation with minimum mean absolute percentage errors of 11.9% and 12.7% for SS and COD, respectively (Pai et al., 2009). Majumder and Gupta (2020) used fuzzy logic to predict the removal efficiency of 17-β estradiol (Majumder and Gupta, 2020). In the context of the HWW, fuzzy logic may be used to optimize the performance of a treatment system and also predict how the system may perform when there is a sudden change in wastewater flow or quality.

7.2.2. System dynamics

This is a modeling approach commonly employed for capturing nonlinearity in complex systems. This approach primarily aims to model relations among various key elements of each system and develop a top-down representation of the whole system (Aggarwal et al., 2021). These systems can be used to optimize plans and policies for decision-making during a pandemic. Systems dynamics modeling, in combination with experimental computer design and statistical analysis, can provide quick and quantitative results for decision-making (Fair et al., 2021; Jia et al., 2021). Recently, Musavi et al. (2019) evaluated the performance of a system dynamics model by using "Vensim" software for the future prediction of different categories of waste produced from different hospitals of Iran. The fundamental modeling part of the software is an appropriate simulation of stock and flow diagrams. The software was used to plot a general and hazardous waste model for the prediction of BMW production of a complex waste management system. The obtained model effectively overcame the prediction problems using dynamic simulation modeling with only partially available information. The model predicts the quantity of each type of waste produced based on the type of hospital, making it easier for stakeholders and government officials to find ways to reduce the negative effects of such wastes on human health and the environment (Musavi et al., 2019).

7.2.3. Neural network

An artificial neural network is also a tool for modeling complex systems. Researchers have previously employed neural networks in conjugation with genetic algorithms to model, predict, and optimize different wastewater treatment processes (Iyer et al., 2021; Tan et al., 2012). Researchers have recently used a neural network to model and optimize the removal of PhACs, such as ciprofloxacin and 17-β estradiol (Majumder and Gupta, 2020). The data from the neural network can also be used to carry out sensitivity analysis of the systems (Gupta et al., 2021; Majumder and Gupta, 2021; Tan et al., 2012). The sensitivity analysis helps identify the parameters, which strongly influence the system's overall performance. Neural networks may be applied to model HWW management systems, and the most sensitive parameters of the system may be identified. Based on the findings, if proper measures are taken, the system will not stop functioning even during extreme anomalies.

8. Summary of findings

Hospitals are major contributors to the generation of large quantities of wastewater and solid waste due to various activities and services provided. Moreover, it was observed that high-income countries produced higher quantities of wastewater than upper and lower-middle-income countries. However, upper and lower-middle-income countries generated more BMW than high-income countries. Hospital effluents are generally characterized by different physicochemical, biological, nutrients, and organic pollutants. It was found that the concentrations of these parameters in HWW are 2–3 times higher than the MWW, thereby making the HWW treatment more challenging. In addition, HWW also contains a wide range of ECs, such as PhACs, contrast media, detergents, and others. The HWW comprising these recalcitrant contaminants are often released into local sewers and are only partially treated in the municipal WWTPs. The continuous discharge of these ECs with high concentrations to various water bodies can pose a serious threat to aquatic species and humans. The available research works on human exposure to ECs released by HWW are limited and mostly restricted to a specific domain, and there are only limited studies available on the health and environmental effects of HWW. As a result, future research should focus on the occurrence of ECs found in HWW from different regions and the pathways by which they enter into different water matrices. It is recommended that monitoring programs be conducted to measure the concentration of these ECs in the drinking water in selected regions of different countries to assess their effects on aquatic species and human health.

Advanced treatment methods such as AOPs, filtration, and adsorption-based processes must be employed to effectively remove these contaminants to secure public health and the environment. Among the treatment units considered in this study, ASP and MBR were found to be the most effective. The performance of these units was enhanced when tertiary treatment methods such as ozonation, UV treatment, CWAO, Fenton and photo-Fenton oxidation, NF/RO, and PAC were integrated with it to form a hybrid system. However, most of these tertiary treatment techniques are generally used as a polishing unit in HWW treatment because they cannot produce satisfactory results unless the wastewater is pre-treated. Furthermore, these treatment methods are costly, and regular monitoring of operation and maintenance is required. Therefore, more research work is needed before they can be implemented on a field scale.

In addition to HWW discharge, hospitals discharge large quantities of hazardous solid waste. This amount of generation of BMW has increased significantly in the last two years due to the COVID-19 pandemic. Mishandling and improper disposal of such highly contagious BMW can result in severe infections and deadly diseases. Therefore, proper handling and appropriate measures must be taken for their safe disposal. In the present study, the authors have attempted to cover various aspects related to BMW generation and BMWM in various countries, including the bibliometric analysis for evaluating published articles related to BMW generation and their management. Most of the lower and upper-middle countries were the main contributors to BMW generation and their management. Furthermore, the current study reviews prior findings related to the harmful effects of BMW on human health and the environment. Furthermore, the present review also emphasizes the BMW environmental concerns posed by various methods employed for their disposal. These methods release a high amount of toxic chemicals and fumes, such as solvents, acids, dioxins, furans, etc., into the environment, resulting in soil and groundwater pollution. As a result, further research is needed to ensure that BMW is properly managed and disposed of, as they are extremely hazardous to the environment and humans. The present review can provide significant insights for the researchers in the field of HWW treatment in developing novel and innovative methods for the effective removal of ECs, pathogens, and other micropollutants from the HWW. In addition, the study can provide valuable lessons for the regulatory authorities and the policymakers in the design and deployment of BMWM in upper and lower-middle-income countries, where advanced disposal techniques to manage toxic chemicals and gases released from these BMWs are lacking. The paper outlines the various aspects of effective hospital waste management and may be useful during the COVID-19 pandemic when waste generation from all hospitals worldwide has increased significantly.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors are thankful to the project PAVITR funded by the Department of Science and Technology, Government of India, for providing support for this work (DST/IMRCD/India-EU/Water Call2/PAVITR/2018).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jenvman.2022.114609.

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