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A review on enhanced microplastics derived from biomedical waste during the COVID-19 pandemic with its toxicity, health risks, and biomarkers

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ABSTRACT

The COVID-19 pandemic led to the explosion of biomedical waste, a global challenge to public health and the environment. Biomedical waste comprising plastic can convert into microplastics (MPs, < 5 mm) by sunlight, wave, oxidative and thermal processes, and biodegradation. MPs with additives and contaminants such as metals are also hazardous to many aquatic and terrestrial organisms, including humans. Bioaccumulation of MPs in organisms often transfers across the trophic level in the global food web. Thus, this article aims to provide a literature review on the source, quantity, and fate of biomedical waste, along with the recent surge of MPs and their adverse impact on aquatic and terrestrial organisms. MPs intake (ingestion, inhalation, and dermal contact) in humans causing various chronic diseases involving multiple organs in digestive, respiratory, and reproductive systems are surveyed, which have been reviewed barely. There is an urgent need to control and manage biomedical waste to shrink MPs pollution for reducing environmental and human health risks.

1. Introduction

The world is fighting the COVID-19 pandemic caused by a novel coronavirus (SARS-CoV-2), an extreme respiratory syndrome, since December 2019 (Ghebreyesus, 2020). COVID-19 is highly contagious and spread through oral-fecal transmission, airborne respirational droplets, and direct interaction with contaminated surfaces and medical waste, causing a wide range of adverse effects on the human body (Coil and Fretz, 2020; Heller et al., 2020). The increasing mutation capability of SARS-CoV-2 is a serious concern for governments, medical professionals, the scientific community, and the public in terms of control and transmission prevention. Various precautionary measures have been implemented to prevent the spread of the virus including social distancing, lockdown, restrictions on gatherings and travel, and frequent use of hand sanitizers. In addition, the use of plastic-based personal protective equipment (PPEs) such as face shields, face masks, surgical masks, gloves, gowns, and aprons (Islam et al., 2020; Kahlert

and Bening, 2020), increase drastically as a necessity for frontline health workers and the general public (Parashar and Hait, 2021a). WHO predicted a monthly demand of 89 million face masks, 76 million gloves, 30 million gowns, 1.6 million goggles, and 2.9 million hand sanitizers for the frontline health worker to battle the pandemic, while a 40% rise in the supply chain of various medical safety goods worldwide was reported during the pandemic (Duer, 2020; WHO, 2020). As a result, face masks (e.g., N95 or FFP2), boots, water bottles, food containers, plastic bags, and single-use plastic products in the environment have increased significantly (Rajesh et al., 2020; WHO, 2020). For a population of 7.8 billion, monthly usage of face masks and medical gloves is reported to be about 129 and 65 billion, respectively (Kalina and Tilley, 2020). In February 2020, China's facemask production increased to 116 million per day, more than 12 times the usual level (Bermingham and Tan, 2020). In the United Kingdom, 39,500 facial masks, 11,500 medical gloves, 1500 gowns, and 4200 FFP3 masks were used in February 2020 (Duer, 2020). The magnitude of PPEs and other healthcare items during

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the pandemic contributed to the sudden increase in biomedical waste and municipal solid waste globally. A significant rise in biomedical waste was reported in Spain (Catalonia) and China, increasing 350 and 370%, respectively (Klemeš et al., 2020). Another study reported 10-fold increase in biomedical waste in Jordan (Abu-Qdais et al., 2020), while a 600% increase was observed in Hubei province in China, the epicentre of the COVID-19 pandemic (ADB, 2020). In the Philippines and Indonesia, the generation of hazardous medical waste has reached 280 and 212 tons per day in Manila and Jakarta, respectively (Ramteke and Sahu, 2020). Plastic waste production in Thailand increased by 62%, from 2120 tons in 2019 to 3440 tons per day in April 2021 (Godbole, 2021). Before the COVID-19 pandemic, the average rate of plastic waste generation in Southeast Asian countries was about 5500 tons per day, which has now risen to 6300 tons per day, with Thailand, the region's top plastic polluter, expecting a 30% increase in its annual plastic waste level (Promchertchoo, 2020). The whole scenario of biomedical waste production and its increasing use worldwide during and before pandemic is summarized in Table 1.

Intensified usage of PPE and other protective materials were not disposed of following a safe disposal guide. When the disposal strategy for used PPEs is not followed, PPE waste makes its way to the seas and oceans and leads to harmful environmental effects (Sam ball, 2021). Therefore, the production and the use of the enormous amount of biomedical waste lead to a large amount of plastics in the terrestrial and aquatic environment owing to the mismanagement of biomedical waste worldwide. Even though plastic pollution existed in the terrestrial and atmospheric ecosystems before the COVID-19 pandemic (Xanthos and Walker, 2017), with about 5 trillion pieces of plastic waste floating around in the world's oceans (Eriksen et al., 2013), the large number of PPE items (i.e., including masks, gloves, and splash-proof garments) were abandoned on the beaches, coastal regions, rivers, and cities since the beginning of the pandemic (Canning-Clode et al., 2020). For example, used face masks have been discovered along a 100-m stretch of beach on Hong Kong's Soko Island (Saadat et al., 2020).

Among many other adversities, the COVID-19 pandemic has deteriorated the environmental problem related to plastic pollution. Over time, environmental factors such as waves, rain, turbulence, wind, and sun cause plastics to break into smaller fragments, called microplastics (<5 mm; MPs). Biomedical waste and other plastic wastes degraded by mechanical and photodegradation processes can be a source of MPs in the environment (Aragaw, 2020). MPs have been observed in lakes (Vaughan et al., 2017; Xiong et al., 2018), estuaries (Gray et al., 2018), oceans (Tuncer et al., 2018; Zhou et al., 2018), and even polar regions (Kanhai et al., 2018). Despite the recent increase in number of studies on harmful effects of MPs in aquatic and terrestrial ecosystems, no review on biomedical waste and MPs derived from biomedical waste during COVID-19 are available to date. Therefore, this review aims to focus on the recent increase in plastic made biomedical waste, the transformation of biomedical waste to MPs, the detrimental impacts of MPs on human health and other environmental organisms, and biomarkers for the health hazards of MPs.

2. Source, elements, and transformation of biomedical waste

2.1. Sources

Hospitals, medical schools, and labs are the primary sources of biomedical waste (Pasupathi et al., 2015). However, biomedical waste can also be produced domestically as part of home health care such as home dialysis, self-administration of insulin, and recuperative care (Emmanuel et al., 2001). Due to the prolonged pandemic, biomedical waste from the local pharmacy (e.g., packages of various medicine) also increased significantly (Cordova et al., 2021). Typical biomedical waste including testing kits, surgical facemasks, diagnostic kits, hand gloves, disposable wipes, cleaning agents, hand sanitizer, trays, plastic medical bottles, plastic cups, syringes and accessories, sterile liquid containers,

Table 1Worldwide production and increased demand for biomedical waste during the COVID-19 pandemic.

Continent	Country	Production and increased demand	Time	Reference
Asia	Bangladesh	Produced 1.63–1.99 kg per day per bed in the hospital in Dhaka city.	Peak pandemic	Rahman et al. (2020)
	China	Produced 116 million facemasks per day	February 2020	Yudell et al. (2020)
	China	12.5% demand for medical gloves is increased	During pandemic	Nazario (2020)
	China	200 tons of medical	February	Saadat et al.
	(Wuhan)	waste produced per day	2020	(2020)
	Indonesia	30% demand for medical waste is increased	During pandemic	Nurhati et al. (2020)
	India	600 metric ton per day	May 2020	Ramteke and Sahu (2020)
	Malaysia	Increase of 27%	During	Muhamad
	751 111 1	medical waste	pandemic	(2020)
	Philippine	280 tons per day produced in Manila	Peak pandemic	Ramteke and Sahu (2020)
	Thailand	Demand for	January to	(DW 2020)
		medical waste is 62% increased	April 2020	(511 2020)
	Jakarta	Produce 212 tons of medical waste per day	Peak pandemic	Ramteke and Sahu (2020)
	Japan	600 million face masks a day	April 2020	METI (2021)
	China	600% increase in	During	ADB (2020)
	(Hubei) Southeast	hazardous waste 1000 tons of	pandemic During	Bridges
	Asia	medical waste	pandemic	(2020)
		produced per day		
	Jordan	650 kg medical	During	Abu-Qdais
Europo	Mostom	waste, which is tenfold higher.	pandemic	et al. (2020)
Europe	Western Europe	Increase of 27% medical waste	During pandemic	Parashar and Hait (2021b)
	UK	Plastic medical kit needs 7.5–12 million daily, 39,500 face masks, 1500 surgical	February 2020	Duer (2020)
	France	gloves and gowns 40 million surgical masks per week	During pandemic	BoF (2020)
	Catalonia &	350% medical	During	Klemeš et al.
	Spain	waste increased	pandemic	(2020)
North America	USA	Increase 312% growth rate of face shields	During pandemic	(Richard Gray, 2020)
Africa	-	Produced 700 million facemasks	January 2020	Nzediegwu and Chang (2020)
Worldwide	-	40% increase of medical masks per month	Peak pandemic	WHO (2020)

tubing, medical bags, eye shields, face shields, gown, and vinyl gloves are being used every day during the pandemic (Ilyas et al., 2020; Sharma et al., 2020; Geyer et al., 2017) (Fig. 1). Since the beginning of pandemic, some additional forms of medical waste such as raincoat, medical masks (surgical, N95), and used-cotton sponge masks became more common as a replacement for hazard suit (Cordova et al., 2021). Biomedical waste can be categorized into various groups, based on source, physical, chemical, and biological characteristics, i.e., (1) general waste: domestic waste, kitchen waste, packaging material, and

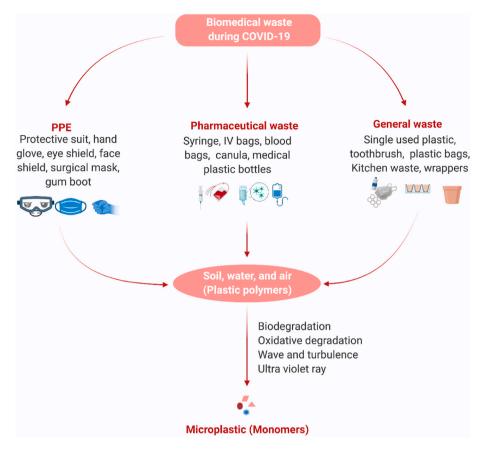


Fig. 1. Illustration of plastic-made biomedical waste during COVID-19 and how the biomedical waste transforms into MPs through the biological (biodegradation) and non-biological (oxidative degradation, wave and turbulence, and ultraviolet ray) processes before reaching the environment.

wrappers; (2) pharmaceutical waste: drugs and pharmaceutical goods (syringe, plastic medicine bottle, IV bag, sachet and so on); and (3) infectious waste: surgical waste culture, stocks from labs, and waste from contagious patients (Hirani et al., 2014). Biomedical waste can also be classified into three categories based on its nature, i.e., (1) absorbent cotton: cotton sheets, bandages, plastic diapers, and bedding soaked in human and animal fluid; (2) discarded medical plastics: plastic syringe, blood bag, and dialysis waste; and (3) infectious waste combined with other waste: wastes that are not included in the above categories but are mixed with absorbent cotton (Parashar and Hait, 2021b). The existing studies identifying the sources of biomedical waste are inadequate which requires systematic documentation worldwide.

2.2. Elements

Most medical instruments, equipment, and other services are plasticbased, making plastic as the predominant element of biomedical waste (Parashar and Hait, 2021a). While plastics are popular and widely used in the healthcare industry because of their excellent strength to weight ratio, toughness, and versatility, plastics in biomedical waste causes a significant rise in plastic pollution in the environment (Chen et al., 2020). Polyvinyl chloride (PVC) is the most commonly used plastic in biomedical waste, but polypropylene (PP), polyacrylonitrile, polystyrene (PS), polycarbonate (PC), polyester, polyurethane (PU), and low-density polyethylene (LDPE) can also be found in the chemical composition of plastic-made PPEs (Parashar and Hait, 2021b). In contrast, packing materials comprise of high-density polyethylene (HDPE), low-density polyethylene (LDPE), PS, and polyethylene terephthalate (PET), and so on (Chua et al., 2020; Klemeš et al., 2020). While N95 masks are made of PP and PET, surgical gloves and masks are made of nonwoven products (e.g., KN95 melt-blown fabrics) containing polymers like PE, PP, and PET (Silva and Nanny, 2020). Helmets and face shields are also made of various plastic polymers including polyethylene terephthalate glycol (PETG), acetate, and PVC (Roberge, 2016). The major plastic elements and components in biomedical waste are shown in Table 2. Since most plastics are resistant to biodegradation/decomposition, they degrade upon landfill disposal or release into the atmosphere (Geyer et al., 2017). Therefore, composition/elements of biomedical waste made from plastic should be specified for the regulatory agencies to employ proper responses both in terms of waste management as well as human health risk assessment, particularly based on their degradability.

2.3. Transformation of biomedical waste into MPs

Biomedical waste is one of the predominant sources of plastic pollution, especially in the COVID-19 pandemic, posing a great risk of MPs pollution in the environment (Peng et al., 2021). The overwhelming increase in biomedical waste generation makes the waste management difficult and inadequate, and thus the unmanaged plastic-made

Table 2Biomedical waste and corresponding generation of plastic components (Geyer et al., 2017; Parashar and Hait, 2021a).

Biomedical waste	Plastic component
Masks, Face shield, Eye shield	Polypropylene (PP), Polycarbonate (PC), Polystyrene (PS)
Gowns	Low-density polyethylene (LDPE)
Hand sanitizer bottles, Aprons, Gloves, Goggles	Polyvinyl chloride (PVC)
Packaging materials	PP, PS, LDPE, High-density polyethylene (HDPE), polyethylene terephthalate (PET)
Plastic bottles	PET, PP

biomedical waste is dispersing in the environment (Eriksen et al., 2013; Xanthos and Walker, 2017; Krystosik et al., 2020; Mol and Caldas, 2020; Oceans Asia, 2020; Prata et al., 2020b) and produces a large amount of MPs thorough breakdown (Fadare and Okoffo, 2020; Prata et al., 2020b). There are two types of MPs in the environment, i.e., (1) primary MPs with a size of <5 mm diameter and (2) secondary MPs resulting from the weathering and ageing of larger plastic (Guo and Wang, 2019). Biodegradation is caused by biological agents (virus, bacteria, fungus, and algae), while non-biodegradation process is caused by environmental factors such as sunlight, moisture, heat, wind, thermal degradation, physical degradation, photodegradation, thermo-oxidative, and hydrolysis, changing the chemical and physical structures of the larger plastic (Veerappapillai and Muthukumar 2015). Biodegradation is predominant in transforming the plastic particle to MPs in nature (Guo and Wang, 2019). For example, polyester polymers can be transformed into their monomer fragments, bonded via ester linkages. Major biomedical waste including masks, face shields, and eye shields, is made of various plastic polymers like PP, PS, and PC (Geyer et al., 2017), which are potential sources of MPs in the aquatic and terrestrial environment. Previous studies reported degradation of polyethylene by Brevibacillus borstelensis borstelensism (degraded up to 11%; 30 days) (Hadad et al., 2005), Rhodococcus rubber (8%; 30 days) (Gilan et al., 2004), Penicillium simplicissimum YK (functional groups facilitated biogreadation, 3 months) (Yamada-Onodera et al., 2001), Comamonas acidovorans TB-35 (produce esterases and catalyzes the polyester degradation; 8-days) (Nakajima-Kambe et al., 1997); and degradation of PS by Phanerochaete chrysosporium, Streptomyces, Phanerochaete chyrsosporium (20% elongation, 20 days heat (70 $^{\circ}$ C) treated) (Lee et al., 1991). Several fungi including Phanerochaete chrysosporium, Lentinus tigrinus, Aspergillus niger, and Aspergillus sydowii were also reported to grow on PVC with possible biodegradation (Roberts and Davidson, 1986; Sabev et al., 2006). Bacteria and fungus utilize plastic elements as the sole carbon and energy source during biodegradation. Environmental degradation can be initiated by abiotic hydrolysis in synthetic polymers like carboxylates, polyethylene, terephthalate, and polylactic acids as well as their copolymers (e.g., polydimethylsiloxanes) (Shah et al., 2008). The photodegradation process (e.g., sunlight, especially to ultraviolet light) transforms plastics by changing the color, physical properties, and surface characteristics; by forming visible defects such as cracks; and breaking the plastic material into smaller particles that eventually form MPs (Zhu et al., 2020; Dissanayake et al., 2022). Previous studies reported that HDPE, PS, PP, PE, and nylon 6 exposed to UV light in air and ultrapure simulated seawater contained increased numbers of oxidized functional groups and broke down into microfibers (Naveed et al., 2019; Naik et al., 2020). The reaction medium exhibited rates of photochemical weathering through crack and flake formation, which are standard features of weathering (Zhu et al., 2020; Eom et al., 2021). Due to the active transformation of plastics in the environment by biotic and abiotic factors, the growth of biomedical waste during the COVID-19 pandemic is projected to surge MPs pollution globally. The changing climate can worsen the situation by expediting the biomedical waste transformation into MPs by increasing UV radiation and changing biodiversity. Therefore, threat of MPs is intensifying, which requires rigorous investigation in terms of its toxicity to terrestrial and aquatic organisms.

3. Health risk of biomedical waste and microplastics during COVID-19

Because of abundance in the environment and food chain, animal exposure to MP through ingestion, inhalation, and dermal contact is a concern. Although MPs' effects on marine animals (i.e. zooplankton, mussels, and copepods) have been widely studied, toxicity in mammals including human is limited (Deng et al., 2017; Suman et al., 2021; Kim et al., 2022). Various organs and systems in human body can be affected by MPs through oxidative stress, inflammation, and/or translocation to

chronic inflammation and neoplasia. An illustration of how MPs affect different organs of the human body is shown in Fig. 2.

3.1. Effect on the digestive system

Human exposure to MPs is thought to be mainly through ingestion (Dris et al., 2017; Joana C. Prata et al., 2020a, 2020b; Joana Correia Prata et al., 2020a, 2020b; Waring et al., 2018; Wright and Kelly, 2017). Ingestion of MPs affects digestive activity by reducing food intake and modulating metabolism (Prata et al., 2020b). After absorption in the intestine, particles may be absorbed by specialized M-cells (specialized epithelial cells of the mucosa-associated lymphoid tissues) surrounding the intestinal lymphoid tissue - Peyer's patches (Wright and Kelly, 2017). High adherence improves particle clearance rate based on adherence to the gastrointestinal mucus (Schwabl et al., 2019). Adsorption allows insoluble MPs particles to pass into the intestinal mucus (Powell et al., 2007), that may change the gastrointestinal microbiota, which adversely affects the growth of unhealthy microbial organisms with enhanced intestinal permeability and endotoxemia (West-Eberhard, 2019). The paracellular passage of particles via the single layer of the intestinal epithelium is another potential cause for particle internalization (Volkheimer, 1977). MPs can infiltrate human gastric adenocarcinoma cells and may influence gene expression after internalization, inhibit cell viability and cause pro-inflammatory responses and morphological changes (Forte et al., 2016). Larger polyethylene particles with MPs (0.3 mm) were shown to induce cytokine activity like interleukin 6 (IL-6), interleukin 1 Beta (IL-1b), and tumour necrosis factor α (TNF-α) (Green et al., 1998). In chronic cases, MPs can cause colorectal cancer (Green et al., 1998; Wright and Kelly, 2017; Waring et al., 2018) (Table 3).

3.2. Effect on the respiratory system

Several studies focused on the effects of MPs on the respiratory system. Inhalation is considered one of the major routes by which MP particles enter the human body (Dris et al., 2017; Kosuth et al., 2018; Joana C. Prata et al., 2020a, 2020b; Joana Correia Prata, 2018; Vianello et al., 2019). According to air sampling using a mannequin, a male individual with light exercise could inhale 272 particles of MPs per day (Vianello et al., 2019). Human lung biopsies, including cancer biopsies, have also been revealed with 250 μ m fibers (Pauly et al., 1998). Several studies found MPs cause variable lung diseases.

Dust overload is caused by the high surface area of MPs in the respiratory system, characterized by persistent inflammation due to the rapid surge of chemotactic factors that inhibit macrophage migration and improve permeability (Donaldson et al., 2000). Airway and interstitial lung disease, with lesions, have been documented in staff in the synthetic garment, flock, and vinyl chloride or PVC industries due to the occupational hazards caused by airborne MPs (Agarwal et al., 1978; Porter et al., 1999; Xu et al., 2004; Atis et al., 2005). This inhaling particulate matter causes autoimmune disorders by causing particle translocation, oxidative stress, immune modulator release, and immune cell activation, which leads to sensitivity to self-antigens and the formation of autoantibodies (Farhat et al., 2011). MPs have cytotoxic and inflammatory impacts and cause respiratory discomfort (Liepins and Pearce, 1976; Steukers et al., 2004; R. Liepins and E. M. Pearce 2015; Dehghani et al., 2017; Prata, 2018; Dong et al., 2020). On pulmonary epithelial cells and macrophages, PS particles in 50 nm cause genotoxic and cytotoxic impact (Calu-3 and THP1) (Paget et al., 2015). Furthermore, MPs can trigger a wide range of diseases: from immediate (asthma-like) bronchial reactions to diffuse interstitial fibrosis and fibre-inclusive granulomas (extrinsic allergic alveolitis, chronic pneumonia), inflammatory and fibrotic changes in bronchial and peribranchial tissue (chronic bronchitis), and interaxial tissue (pneumothorax) (Prata, 2018) (Table 3).

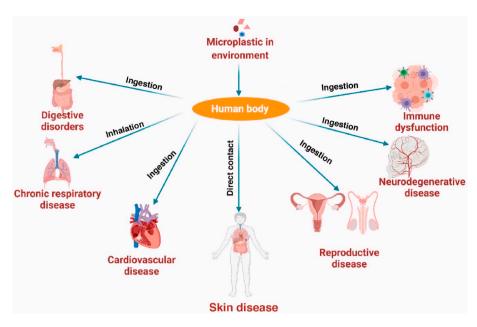


Fig. 2. A schematic diagram of how microplastics enter into the human body and the potential impact on the various organs and systems (digestive, respiratory, cardiovascular, skin, reproductive, nervous, and immune).

3.3. Effects on other systems

MPs can be absorbed through the skin by crossing the dermal barrier (Dris et al., 2017; Kosuth et al., 2018; Revel et al., 2018). Since the human skin prevents MPs and other chemicals from passing directly in sweat glands, exposed skin burns and hair follicles are still potential entrance points (Schneider et al., 2009). Persorption is the mechanical kneading of rigid objects through the circulatory system across openings in the single-layer epithelium at the villus tips of the gastrointestinal tract (desquamation zones). It triggers cytotoxicity, hypersensitivity, unfavorable immune responses, and severe reactions such as hemolysis (Hwang et al., 2019). MPs in the bloodstream have also been linked to inflammation, pulmonary hypertension, artery occlusions (Prata, 2018), raised coagulability (Churg and Brauer, 2000), cytotoxicity of blood cells (Canesi et al., 2015), systemic lupus erythematosus systemic (Fernandes et al., 2015), and autoimmune rheumatic disease (Bernatsky et al., 2016). MPs are also associated with an increased chance of developing Alzheimer's disease (Ranft et al., 2009), with a greater risk of dementia (Chen et al., 2017). MPs have also been associated with breast and prostate cancer in animals, suggesting promoting the same cancers in humans (Michałowicz, 2014). Many plastics used in the mask, PPE, and other medical waste, such as PC, PS, and PVC, have been shown to release toxic monomers linked to reproductive toxicity, mutagenicity, and cancer (Peng et al., 2017). Hazardous elements present in biomedical waste are shown in Table 4. MPs can also interfere with the function of lipoprotein lipase, aromatase, and lipogenesis regulators, causing changes in fat tissue hormone levels (vom Saal et al., 2012). In addition, MPs can affect human health through indirect mechanisms: materials such as metals on MPs' surface or chemicals (e.g. phthalate esters and polycyclic aromatic hydrocarbons (PAHs)) from their surroundings could be adsorbed and ultimately create toxicity to humans and other organisms (Eom et al., 2021; Sun et al., 2021).

Plastic fragments, by their very nature, have more durable surfaces than wood or any other natural particles (Oberbeckmann et al., 2018) that are quickly colonized by microorganisms, forming biofilms and collecting a large number of pathogens (Feng et al., 2020), including Vibrio sp. (Zettler et al., 2013). The film provides an ideal habitat for microbe colonization on the surface of MPs (Rummel et al., 2017). Proteobacteria sp., Bacteroides sp., Actinobacteria sp., Firmicutes sp., Cyanobacteria sp., and Diatom sp. are examples of certain bacteria

(Oberbeckmann et al., 2014). Vibrio and Pseudomonas, all belonging to the Proteobacteria sp. family, were the most prevalent bacteria on the soil (Oberbeckmann et al., 2014; Kirstein et al., 2016; Li et al., 2019). Chemical toxins, microbes, fungi, and algae, such as Rhodobacteraceae, are often found on the surface of MP (Dang et al., 2008; Zettler et al., 2013; Rodríguez-Seijo et al., 2018). Bacillariophyta (Carson et al., 2013; Oberbeckmann et al., 2014; Reisser et al., 2014), Campylobacteraceae (McCormick et al., 2014) and Sphingopyxis (Sphingomonadaceae) are also present on MP's surface and is thought to be a reservoir for antibiotic resistance (Vaz-Moreira et al., 2011; Iredell et al., 2016). However, the contribution of MPs towards antibiotic resistance is believed to be another alarming issue related to MPs pollution that required more investigation but is out of the scope of this review.

4. Bioaccumulation, toxicity, and biomarkers for risk assessment of MPs

4.1. Bioaccumulation and toxicity of MPs to various organisms

Bioaccumulation is the net uptake of a pollutant such as MPs from the environment through viable routes (e.g., respiration, touch, and ingestion) from water, air, and soil (Maher et al., 2016). It happens when the uptake becomes higher than the egestion of an organism. Bioaccumulation of MPs can occur within each trophic level (Miller et al., 2020). It suggests that accumulation in upper trophic levels is the output of consumption of prey in lower trophic levels (Kelly et al., 2007; Miller et al., 2020). Deep oceans, coastal waters, pelagic zones, coastal sediments, beaches, lakes, rivers, and terrestrial environments are the potential sites for MPs buildup (Prata et al., 2018; Jiang et al., 2019; De Silva et al., 2021). The increased contamination and following accumulation of MPs resulted in a detrimental impact on aquatic and terrestrial biota, becoming a severe threat to public health globally through the food chain (Fig. 3; Table 5) (Jiang et al., 2019; De Silva et al., 2021; Rahman et al., 2022).

The abundance of MPs affecting the growth of plants is widespread. Accumulation of MPs surrounding the seed coat or root hair causes blockage of imbibition with subsequent reduction of the seed germination rate and growth (Jiang et al., 2019; De Silva et al., 2021). MPs were found responsible for reducing the root and shoot growth by obstructing water uptake of pores in the seed capsule with a

Table 3Health consequences of biomedical waste and/or microplastics in human.

System	Effect	References
Digestive system	Reducing nutrient	Prata et al. (2020a)
,	consumption and metabolism	
	Inhibits cell viability, pro-	Forte et al. (2016)
	inflammatory responses, and	
	morphological changes	
	Altered gut microbiota and	West-Eberhard (2019)
	unhealthy species	
	proliferation, and increased	
	bowel permeability Gastrointestinal mucus	Ensign et al. (2012)
	adherence and increased	Elisigii et al. (2012)
	particle clearance	
	Colorectal cancer	(Wright and Kelly, 2017;
		Waring et al., 2018)
Respiratory	Inflammatory response,	(Smith et al., 2018; Cox et al.,
system	oxidative stress, cell damage,	2019)
	and size-related toxicity	
	Particle translocation,	(Farhat et al., 2011; Dris et al.,
	oxidative stress, immune	2017; Wright and Kelly, 2017)
	modulator release and	
	immune cell activation	
	resulting in self-antigenation	
	and autoantibodies formation Respiratory distress,	(Staukers et al. 2004: P
	cytotoxic, inflammatory, and	(Steukers et al., 2004; R. Liepins and E. M. Pearce 2015;
	men's autoimmune disorders	Dehghani et al., 2017; Prata,
	men s autommune alsoraers	2018; Dong et al., 2020)
	Genotoxic and cytotoxic	Paget et al. (2015)
	impact on pulmonary	
	epithelial cells and	
	macrophages	
	Asthma, extrinsic allergic	Prata (2018)
	alveolitis, chronic pneumonia	
	Chronic bronchitis,	
	pneumothorax, pulmonary cancer	
	Induce intense chemical	Donaldson et al. (2000)
	release, chronic inflammation	Donaidson et al. (2000)
	Chronic inflammation and an	Prata et al. (2020a)
	increase in the risk of	
	neoplasia	
Cardiovascular	Cytotoxicity, autoimmune	(Brown et al., 2001; Canesi
system	reactions, and rapid	et al., 2015; Bouwmeester
	hemolysis responses	et al., 2015; Forte et al., 2016;
		Hwang et al., 2019; Jung
	To Classical and and an array	et al., 2020)
	Inflammation and pulmonary	Zagorski et al. (2003)
	hypertension Vascular occlusions	Prata (2018)
	Increased coagulability	Churg and Brauer (2000)
Reproductive	Toxicity, mutagenicity, and	Peng et al. (2017)
system	cancer	
Endocrine	Alter testosterone ratio,	Michałowicz (2014)
system	adverse effect on hormones	
	level.	
	It affects fatty tissue receptors	(vom Saal et al., 2012)
	Mammalian breast and	Michałowicz (2014)
Immuno acatam	prostate cancer	Powerteless et al. (2016)
Immune system	Systemic autoimmune rheumatism	Bernatsky et al. (2016)
	Systemic lupus erythematosus	Fernandes et al. (2015)
	Decrease in immune response	Wright and Kelly (2017)
Nervous system	Rising likelihood of	Ranft et al. (2009)
oud by been	Alzheimer's disease	
	Dementia	Chen et al. (2017)
		•

concentration-dependent manner: the reduced seed germination was 67%–38% for 50 nm, 50%–30% for 500 nm and 55%–17% for 4800 nm MP in *Lepidium sativum* (Bosker et al., 2019). Accumulation of MPs (concentration of 50 and 100 mg/L) was found in the root tips of terrestrial plants, Bean (*Vicia faba*) (Jiang et al., 2019). The harmful effect of MPs on aquatic plants is comparatively higher. Algae species (i. e., *Chlorella* and *Scenedesmus*) are prone to adsorb MPs resulting in

Table 4Hazardous elements in biomedical waste in different environmental matrices (Water, Soil, and Air).

Environmental matrices	Hazardous Elements	Country reported	References
Water Soil	Cd, Zn, Pb, and Cu Hg, Pb, Cd, Cr, Ag	China Ghana	Shang (2002) (Ali et al., 2014; Adama et al., 2016)
	Salt like Al, Ca, Fe, K, Mg, and Na.; Heavy metals (As, Cd, Cr, Cu, Ni, and Pb)	China	Zhao et al. (2009)
	Fe, Cu, Zn, Cr, Pb, Ni	Nigeria	Auta and Morenikeji (2013)
Air	Pathogenic bacteria	Nigeria	Ogbonna (2011)
	Dioxin and furan (Incineration)	Portugal	Coutinho et al. (2006)
	Particulate matter, Metals, Acid gases, Oxides of nitrogen, and sulfur	India	Sharma et al. (2013)

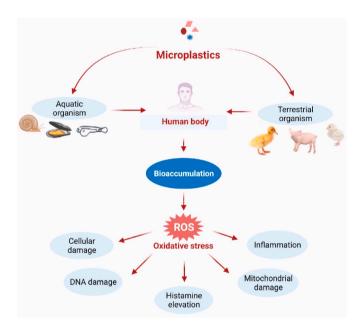


Fig. 3. A plausible mechanism of translocation and accumulation of MPs in various organisms (i.e., producer to consumer, prey to predator) in a food chain with their subsequent bioaccumulation in the human body. MPs can induce cellular dysfunction by inducing oxidative stress and ROS production and lead to cell membrane damage, DNA disruption, elevated histamine, mitochondrial damage, and induction of pro-inflammatory cytokines IL-6 and TNF-α (Modified and adapted from (Lu et al., 2019; Yong et al., 2020; Suman et al., 2021).

decreased photosynthesis activity and growth rate due to the generation of reactive oxygen species (ROS) (Bhattacharya et al., 2010). Mao et al. reported reduced growth rate and photosynthetic activity of algae (Chlorella pyrenoidosa) under three different concentrations (10, 50, 100 mg/L) of PS-MPs (0.1 and 1 µm) (Mao et al., 2018). There are great risks of MPs accumulation in plants to terrestrial organisms through trophic transfer (Dissanayake et al., 2022; Sarkar et al., 2022) which demands further research on how MPs pollution affects local food webs. MPs can pose serious risk to soil organisms (i.e. earthworms, mites, and collembola) which play key role for maintaining soil health and ecological balance (Qi et al., 2020). MPs ingestion by invertebrates can invoke oxidative stress and spark antioxidant upregulation leading to disrupted redox homeostasis (Trestrail et al., 2020). In earthworms, histopathological impairment was detected even at a low concentration of MPs (62.5 mg/kg), while severe gut damage was observed at 125 mg/kg

Table 5Bioaccumulation of microplastics (MPs) in various organisms and their correspondence responses.

Organism	Features of MPs	Tissue accumulation or cellular uptake	Observation	References
Daphnia (<i>Daphnia</i> magna)	1 μm MP (12.5–400 mg/L)	Uptake and immobilization	- MPs ingested and caused immobilization.	Rehse et al. (2016)
Microalgae (Tetraselmis chuii)	$15~\mu m$ MP (0.75, 1.5, 3, 6, 12, 24 and 48 mg/L) with Procainamide (104 and 143 mg/L) and Doxycycline (22 and 14 mg/L)	Uptake and localization	Integrated solutions had higher toxicity than individual solutions. Combined solutions significantly diminished growth rate and chlorophyll content.	Prata et al. (2018)
Algae (Chlorella pyrenoidosa)	0.1, 1 μm MP	Uptake	- Photosynthetic activity and growth rate reduced.	Chua et al. (2020)
Diatom (Skeletonema costatum)	MPs of 1 μm and 1 mm	Adsorption and aggregation	-Retardation of growth up to 39.7% in 1 μ m MP; however, no effects on algal growth in 1 mm MP.	Zhang et al. (2017)
Bean (Vicia faba)	100 nm, 5 μm MP	Uptake	- Increased genotoxic and oxidative damage with subsequent reduced growth.	Jiang et al. (2019)
Wheat (Triticum aestivum)	50, 250, 500, 1000 μm MP	Uptake, translocation	 Both upper-ground and below-ground organs of the wheat plant were affected during vegetative and reproductive growth. 	Qi et al. (2018)
	PS microbeads of 0.2, 2, 7 μm MP	Transportation of 0.2 µm MP to stem and leaves via the vascular system	- Imbibition affected.	Li et al. (2020)
Blue mussel (Mytilus edulis)	4–10 μm MP	Uptake and persistence	-Existed in different organs.	Rist et al. (2019)
	2 μm MP		-Deformity and abnormal development were observed, although the growth of mussel larvae was not affected.	Rist et al. (2019)
Oyster (Crassostrea gigas)	2 and 6 μm MP	Transcriptomic and proteomic responses	 -38% decreased in oocyte number and 23% reduction in sperm velocity. -Development of offspring larvae is hampered. 	Sussarellu et al. (2016)
Medaka (Oryzias melastigma)	10–11 μm PS MPs	MPs assemblage in digestive tracts of larvae and intestines of adults.	-Fecundity declined significantly Enhanced mortality and reduced lengths and weights of larvae and adult fish.	Cong et al. (2019)
Zebrafish (<i>Danio rerio</i>)	PS MPs of 70 nm, 5 $\mu m,$ and 20 μm (20 mg/L)	Only 5 μm MP accumulated in gills, gut, and liver.	Inflammation and lipid accumulation. Increased anti-oxidative stress enzymes. Altered liver metabolomics profile.	Lu et al. (2016)
	PS MPs of 10–45 μm (20 mg/L)	Ingestion of MPs in larvae gut.	-Significant altercation in the transcriptome of zebrafish larvae -Derangement of genes linked with metabolism.	LeMoine et a (2018)
Red tilapia (Oreochromis niloticus)	PS MPs of 0.1 $\mu m,$ at 1, 10, and 100 $\mu g/L$	MPs gathered significantly in gut and gills compare to liver and brain.	- Acetylcholinesterase activity inhibition of the brainAltercation of liver enzyme profile.	Ding et al. (2018)
Crucian Carp (Carassius carassius)	24 and 27 nm MP	Trophic transfer to fish in the aquatic food chain, from algae through <i>Daphnia</i>	-Deformity in feeding and shoaling behavior -Disrupted metabolism and brain morphology.	Ding et al. (2018)
Other wild fishes (Dicentrachus labrax, Trachurus trachurus, Scomber colias)	MPs observed in 49% of fishes	Assemblage of MPs in gills, gastro-intestine and dorsal muscle.	-Enhanced lipid. peroxidation found in the brain, gills, and dorsal muscleStimulated acetylcholinesterase activity of the brain.	Barboza et a (2020)
Human (Faeces)	50–500 μm MP	Retained in faeces.	-Various types of MPs are excreted in faeces suggesting their potent entrance into the body through the digestive system.	Schwabl et a (2019)
Mice	PS MPs of 5 μm and 20 μm (0.01–0.5 mg/day)	Accumulation of MPs recorded in the gut, liver, and kidney.	Lipid profile changed, and ATP levels declined. Liver oxidative stress elevated, decreased acetylcholinesterase.	Deng et al. (2017)
	PS MPs of 5 μm	Gathered in gut and liver.	acetylchomesteraseSignificant alterations in both the richness and diversity of the intestine microbiome Induced bile acids metabolism dysfunction, declined gut mucus secretion.	Jin et al. (2019)

(Rodriguez-Seijo et al., 2017). Size-dependent neurotoxic effect in cholinergic and GABAergic neurons was reported in nematodes (*Caenorhabditis elegans*) when they were exposed to nano- and micro-PS (Lei et al., 2018).

Ingestion and toxicity mechanisms of MPs have been widely studied in aquatic organisms at different trophic levels (Rehse et al., 2016; Jiang et al., 2019). Coexistence of metals and MPs can adversely affect physiological activities of organisms from the molecular to the cell, organ, even at population level since MPs can act as vectors for metals (Rochman et al., 2013; Galloway et al., 2017; Eom et al., 2021). Being filter feeders, most of the bivalves (e.g., oysters, clams, and mussels) are easily exposed to plastic and, thus, generally ingests MPs (Bouwmeester et al., 2015; Sussarellu et al., 2016). Blue mussel (*Mytilus edulis*) consumed MPs smaller than 10 μ m, which accumulated in the gut and were

absorbed into their circulatory system (Bouwmeester et al., 2015). Tissue accumulation of MPs can cause multiple deleterious impacts: physical damage (De Stephanis et al., 2013), retardation of growth and development in children (Snoj Tratnik et al., 2019), immune deficiency (Avio et al., 2015), oxidative stress (Browne et al., 2013), genetical, neurotoxic and metabolic malfunction (Deng et al., 2017). Daphnia (Daphnia magna), a small crustacean, has been used in biological research to assess toxicity in aquatic environments. Among four types of MPs exposures (1 μ m, 63–75 μ m, 100 μ m, 20–250 mm), only 1 μ m MP induced alteration of immobilization in a short-term (96 h) exposure of 12.5–400 mg/L PE MPs (Rehse et al., 2016). MPs have adverse impacts on reproduction at the higher trophic level of food chain hierarchy. For example, reduced oocyte number (38%) and sperm velocity (23%) of oysters were reported when exposed to PS MPs (2 and 6 μ m) (Sussarellu

et al., 2016). PVC MPs of 1 μ m retarded 40% growth after 96-h exposure while 1 mm particle size of PVC had no significant impacts on growth of marine microalgae, *Skeletonema costatum* (Zhang et al., 2017).

Among the few study on freshwater organisms, Rochman et al. (2013) observed hepatic stress as well as glycogen shortage, fatty vacuolization, and cell necrosis in Japanese medaka (Oryzias latipes), exposed to PE MPs. Zebrafish (Danio rerio) exposure to the MPs (PA, PE, PP, PVC, and PS) induced little mortality with villi deformation during 10-day-exposure (Lei et al., 2018). Likewise, evidence showed that bioaccumulation of MPs (PS) alters fatty acid and energy function of D. rerio (Lu et al., 2016). Such studies clarify the MPs bioaccumulation triggering toxicity in freshwater ecosystems, thereby demanding future research. There is limited research on the combined impact of MPs and metals on the aquatic invertebrates. Nevertheless, elevated malondialdehyde with concurrent induction of oxidative stress was observed in zebrafish (D. rerio) with co-exposure to Cu and PS MPs (0.1 μm) (Qiao et al., 2019). Exposure to metals (As, Cd, Cu, Pb, and Zn) premixed with PS MPs (10 µm) increased toxicity through bioconcentration and impaired cholinergic response and antioxidant defense in a marine mysid (Eom et al., 2021). In common goby (Pomatoschistus microps), chromium toxicity was increased in the presence of PE MPs, leading to inhibition of AChE activity (Luís et al., 2015). Co-exposure of European sea bass (Dicentrarchus labrax) to 1-5 µm MP and mercury resulted in increased lipid peroxide levels (3-fold) in brain which disturbed the function of energy-related enzyme and triggered neurotoxicity (Barboza et al., 2018).

MPs can transmit from prey to predators (lower to higher trophic levels) in food webs (Eom et al., 2022). Artemia sp. nauplii were exposed to different sizes of MPs (1-20 µm) and benzo [a] pyrene additives which were then used in zebrafish diets. Eventually, these MPs and benzo [a] pyrene were detected in zebrafish fed with these nauplii indicating the transfer of MPs and additives at various trophic stages (Batel et al., 2016). Small particles of MPs can easily transfer to the tissues of fish and other marine organisms during digestion of MPs associated with surrounding chemicals (Hirai et al., 2011). For instance, uptake and accumulation of hazardous substances adsorbed on MPs by the marine fish O. latipes, subsequently induced oxidation, pathological toxicity, and liver inflammation (Rochman et al., 2013). Upon ingestion of biosolids or polyurethane foam by earthworms resulted in the aggregation of polybrominated diphenyl ether (PBDE) in their organs. This PBDE is applied as a source of flame retardant which is hazardous to humans as well. This finding infer that MPs additives could be released in the surrounding environment and affect terrestrial organisms including humans (Gaylor et al., 2013). MPs accumulation and concurrent depletion of intestinal mucus secretion causing impairment of gut barrier function were found in 6-week exposure of male mice to 5 μm PS MPs. Furthermore, modification of intestinal microbiota led to metabolic dysfunction of mice (Jin et al., 2019). Moreover, detection of MPs in human placental portions (maternal, fetal, and amniochorial membranes) raised great concern about exposure in uterus (Ragusa et al., 2021). Thus, relevant information on the tissue accumulation of MPs in mammalian models is required to determine and assess the potent threat of MPs in human health.

4.2. Biomarkers for risk assessment

Biomarkers are biological criteria (i.e., ROS and cellular response) that are easy to diagnose and categorized as indicators of negative impacts in biological systems (Hamza-Chaffai, 2014). Biomarkers are practical tools for assessing MPs accumulation and bioavailability risks at the cellular and molecular levels (Jiang et al., 2019; Chang et al., 2020; Suman et al., 2021). Currently, evidence on the toxic effects of MPs on human cells and tissues is limited. Despite toxicity data scarcity for humans *in vivo*, few studies have evaluated the impacts of MPs on human cells in culture. The experiments with pristine MPs have found low to medium-level adverse effects on human cells based on the cell

type, cellular uptake, and size of MPs (Yong et al., 2020). Schirinzi et al., (2017) reported that MPs generated low but measurable levels of ROS, including cytotoxicity in T98G and HeLa cells. In Caco-2 cells, PS (0.1 and 5 μ m) were found to stimulate mitochondrial depolarisation and inhibition of ATP-binding cassette (ABC) transporter, while PS (5 μm) enhanced arsenic toxicity (Wu et al., 2019). Cytotoxicity in association with ROS production, induction of pro-inflammatory cytokines IL-6 and TNF-α from PBMCs (peripheral blood mononuclear cells) were reported in several types of human cells and mice at a concentration of 20 μm PP MPs (Hwang et al., 2019). Another in vitro study revealed cytotoxicity, oxidative stress, and inflammatory responses in human lung epithelial cells with disruption of the epithelial cell layer (Dong et al., 2020). Generally, the detrimental effects of MPs on metabolic, histochemical, and physiological functions are evaluated by monitoring the variation and changes in biochemical, histopathological, and molecular biomarkers. Table 6 demonstrates significant and most used biomarkers for the assessment of MPs toxicity in humans. Consequently, it is important to do further research focusing on biomarkers associated with MPs

Table 6Potential biomarkers and toxicity associated with microplastics (MPs) in human cells.

Cell models of Human	Biomarkers	Toxicity	References
Human lung epithelial cells (BEAS-2B)	ROS	-Epithelial cell disruption, inflammation, oxidative pressure at PS MPs (4.06 μm).	Dong et al. (2020)
Human mast cell line 1 (HMC-1); human basophilic leukemia cell line (RBL-2H3); Peripheral blood mononuclear cells (PBMCs)	ROS, IL-6, TNF- α	- High levels of smaller size (20 μm) particles induced ROS HMC-1 and RBL-2H3 cells promulgated enhanced histamine Low level of stimulated cytokines IL-6 and TNF-α from PBMCs.	Hwang et al. (2019)
Human epithelial colorectal adenocarcinoma cell line (Caco-2)	ABC, oxidation, DNA strand breaks	- Plasma membrane ATP-binding cassette (ABC) transportation restrainedIncreased derangement of mitochondrial DNAReduced toxicity on cell permeability, oxidative stress, and fluidity.	Wu et al. (2019)
Human cervical adenocarcinoma cell line (HeLa); human glioblastoma cell line (T98G)	ROS, Cytotoxicity	- Provoked cytotoxic responses, with PS showing a higher EC50 value than PE in T98G and HeLa cellsIncreased ROS with PE of 3–16 μm and PS; particles of 10 μm MP exposure.	Schirinzi et al. (2017)
Human fibroblasts (Hs27)	ROS, DNA strand breaks	Elevated ROS.DNA disfiguration with genotoxic stress.	Poma et al. (2019)
Caco-2	Macrophagic, cellular response	- MPs of 1, 4, and 10 μm do not affect either macrophage separation or polarization No impact on cell viability except the exposure to a high concentration of MP (1 μm).	Stock et al. (2019)

toxicity to human.

5. Conclusion and future direction

Due to the prolonged prevalence of COVID-19, significant quantities of biomedical waste are generated and added to the environment. Biomedical waste made of various plastic polymers can transform into MPs through different biological and non-biological processes in the environment. With the surge in biomedical waste and MPs during the pandemic, bioaccumulation of MPs can also amplify in aquatic and terrestrial organisms across the trophic levels. Biomedical wastetriggered MPs pollution may largely influence food safety and security and eventually cause various chronic diseases in multiple human organs. Considering the limited data available and discussed in this review, further research is needed to precisely evaluate how MP exposure creates a threat for public health and find effective biomarkers of MPs. The current understandings are inadequate regarding the bioavailability and toxicity of MPs in human health; however, interest in exploring MPs is increasing. Future work should directly monitor biomedical waste, which increases the plastic in the environment during and after the pandemic. The following are essential research needs for monitoring the biomedical waste and MPs impacts on human health:

- Close monitoring of the production and proper disposal of biomedical waste during and after the pandemic
- Strong policies, sustainable pathways, and efficient initiatives should be dispensed
- Development of long-term biomedical waste management policy and best biomedical waste management practice for a safe and better future
- Various treatment techniques (e.g., incineration, pyrolysis, gasification, and thermal conversion) should be encouraged to reduce the biomedical waste in the environment
- Education, information, and communication campaigns among citizens are essential for creating awareness of biomedical waste disposal
- The interaction of MPs with other contaminants such as metals and their combined effects on the organisms and human health
- Data on the translocations of MPs through the food web is necessary
- Developing biomarkers and specific biomonitoring processes for easier detection and remediation of MPs effect on human and ecosystem

Author's contribution

Md Rony Ibne Masud, Kamrul Hassan Suman, Shadia Tasnim, and Md. Niamul Haque: Conceptualization and original draft writing; Mahmudul Hasan Sikder, Most Shirina Begum, and Md Jamal Uddin: review and editing; Md Jamal Uddin: Visualization, and Md. Niamul Haque: Supervision. All authors read and approved the final version of the manuscript.

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.

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