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Effects of aquatic heavy metal intoxication on the level of hematocrit and hemoglobin in fishes: A review

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Environmental pollution caused due to the presence of heavy metals has become a great concern as it has an adverse effect on almost all types of ecosystem. In this sense, these pollutants have a tendency to pollute the aquatic ecosystem, thus badly affecting the health of aquatic organisms. As a result, toxicological studies believe them to be the most harmful pollutants in the aquatic environment. Among all the aquatic organisms, fish—being a chief organism in this system—become the easiest victim of these pollutants. Heavy metals enter fish bodies through the alimentary system by consumption of polluted food, or through the gills, and skin. They are finally delivered by the bloodstream to the organs and tissues where they accumulate after absorption. Ultimately, in this way heavy metals make their way into humans through the food chain. The fluctuations in the hematological values may serve as an initial indicator of the toxicant's impact on fish health. It has been observed that when pollutants impact the quality of the aquatic medium, the first consequence is apparent in the form of physiological changes in fish, which are reflected in one or more hematological parameters, such as hemoglobin, hematocrit, red blood cell count, white blood cell count, etc. As a result of these alterations, fish become weak, anemic, and more susceptible to diseases. Over the past several decades, a vast number of studies have been reported on the qualitative and quantitative variations in hematological parameters due to the presence of heavy metal intoxication. Heavy metal contamination of water resources not only degrades the water quality but also negatively impacts the quality of food in the form of fish proteins. Therefore, this article sheds light on the effects of heavy metals on hemoglobin and hematocrit of fish hematology and calls for more attention to the protection and preservation of aquatic ecosystems, particularly those contaminated with heavy metals.

KEYWORDS
hemoglobin, hematocrit, heavy metal, environmental impacts, fish hematology

1 Introduction

Aquaculture is a growing part of the world's agricultural economy in general, and of India's agricultural economy in particular, where fisheries are now considered a fast-growing sector with significant medicinal, nutritional, economic, aesthetic, industrial, and religious values, as well as offering employment to a large number of people in the country. Fish are among the most significant vertebrate groups, supplying a valuable supplement in the form of diversified, nutritious diets to the populace. The essentiality of fish in the form of a nutritious diet due to the presence of healthy protein, fats, vitamins, and minerals is well understood. It also has a good source of essential fatty acids, including long-chain omega-3, and other micronutrients important to support healthy life (Skonberg and Perkins, 2002; Nurullah et al., 2003; Deckelbaum and Torrejon, 2012; Thilsted et al., 2016; Hicks et al., 2019; Mohanty et al., 2019; Tacon, 2020). About 20 percent of animal proteins are provided to the world's population by fish, and over 3.3 billion people depend on fish as their main source of animal protein (FAO, 2020). Sustainable, productive fisheries and aquaculture enhance revenue and alleviate poverty, boost the economy, and safeguard the environment and natural resources, ensuring food and nutrition security. As a result, productivity improvement of fisheries and aquaculture in developing countries is crucial to reducing food insecurity. However, due to their delicacy, fish are very sensitive to any environmental impacts triggered by various factors such as physical, chemical, and biological that can immediately affect the ecology and survival of species.

Fish live in close proximity to their surroundings and are thus vulnerable to chemical and physical variations, which could be mirrored in their blood and its components (LeaMaster et al., 1990; Luskova, 1997; Singh et al., 2008; Sheikh and Ahmed, 2016; Witeska, 2021). Abiotic and biotic factors such as parasitic invasions, predator pressure, or strong competition, variations in temperature, dissolved oxygen content, pH, aquatic pollutants namely insecticides, pesticides, and heavy metals, as well as human activities related to fish rearing and harvesting, such as manipulation, transport, and crowding, can all cause stress in fish (Meier et al., 1983; Witeska, 2005; Dekar and Magoulick, 2013; Gebrekiros, 2016; Mateo-Sagasta et al., 2017; Teunen et al., 2021; Seibel et al., 2021). The analysis of hematological indices is an important tool that provides reliable information for monitoring and assessing the alterations in fish physiology and pathology under adverse conditions (Svetina et al., 2002; Pavlidis et al., 2007; Prado et al., 2014; Witeska, 2021). In toxicological investigations and environmental monitoring, fish blood is increasingly being used as a potential indicator of physio-pathological changes in fish populations and disease investigations (Sancho et al., 2000; Barcellos et al., 2003; Fazio, 2019; Lawrence et al., 2020; Witeska, 2021). Hematological parameters can give a reliable evaluation in non-lethal ways, which is significant because there are many ethical concerns about using animals in investigations (Satheeshkumar et al., 2012; Lawrence et al., 2020; Witeska, 2021). Therefore, hematological indices have been used as crucial diagnostic tools to assess the health status of fish (Bhaskar and Rao, 1989; Gabriel et al., 2004; Pradhan et al., 2012; Fazio, 2019; Lawrence et al., 2020; Seibel et al., 2021). Alterations in hematological parameters have been viewed as special signs of the health of fish, and are strongly associated with the way fish respond to environmental variations. Thus, they're useful for monitoring the health of fish exposed to different types of toxicity in aquatic habitats (Omoregie and Oyebanji, 2002; Adhikari et al., 2004; Al-Akel and Shamsi, 2000; Cicero et al., 2014; Hamidipoor et al., 2015; Fazio, 2019; Lawrence et al., 2020).

The term hematological analysis refers to the assessment of the cellular components of blood, including the measurement of hemoglobin (Hb), red blood and white blood cell counts, hematocrit (Hct), mean corpuscular volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), and erythrocyte sedimentation rate (ESR), which are considered as primary diagnostic methods for the analysis of fish health (Fazio, 2019). Fish hematological indices have been used to track metal contamination in the aquatic environment for years (Shah and Altindag, 2005; Authman et al., 2015). There is no doubt that some blood parameters serve as reliable indicators of the health of fish. So, in the present review, we focus on the Hct and Hb among the hematological parameters as an indicator for evaluation of the stress. The Hct is the percentage of blood that is made up of red blood cells in terms of volume or the ratio of red blood cell volume to whole blood volume. Gallaugher (1994) defined Hct as a measure of the capacity for blood to carry oxygen. Then theoretically, the higher the Hct, the greater will be the capacity for oxygen transport. The Hct is expressed in percentage. The micro-hematocrit constitutes the parameters frequently studied, probably because it is easily undertaken and interpreted. Since the environmental toxicants mainly targeted the fish among aquatic organisms, due to these pollutants, the health of fish deteriorates with the passage of time, therefore in the present review, an attempt has been made to correlate the impact of these pollutants on the fish's initial health markers i.e., selected hematological parameters.

2 General aspects of heavy metals and fish hematology

Aquatic pollution is considered a major load/burden facing both freshwater and marine environments; the main sources of this great problem include expansion in population density, heavy industrialization, and agricultural activities, as a result, more and more waste finds its way towards the aquatic bodies. These wastewaters contain large quantities of heavy metals which are consequently harmful to the health of aquatic animals

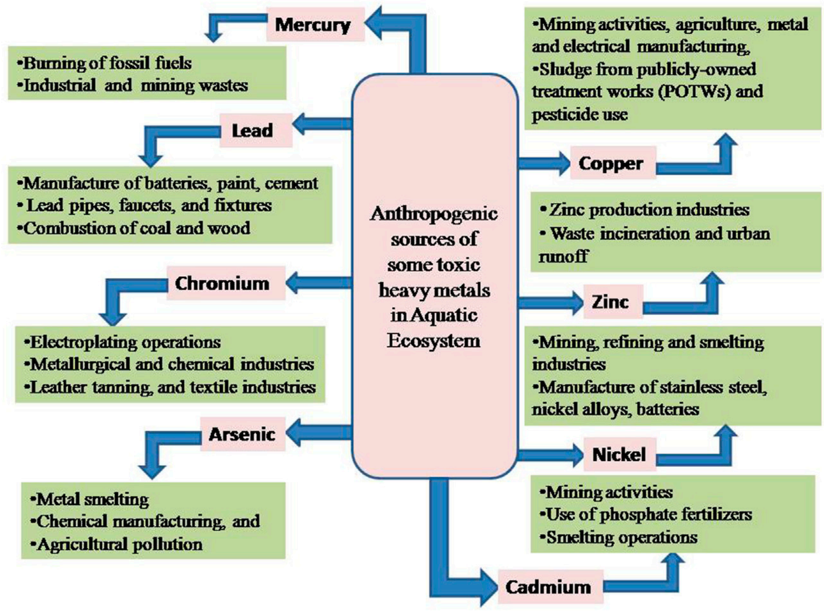

FIGURE 1
Illustrative depiction of anthropogenic sources of some toxic heavy metals in the Aquatic Ecosystem.

(Al–Masri et al., 2002; Karbassi et al., 2006), besides affecting the health of fish (Vutukuru, 2005; Vinodhini and Narayanan, 2008; Authman et al., 2015). Heavy metals are now posing a threat to living beings due to their widespread use in agricultural, chemical, and industrial operations. Heavy metals are defined as metals with a density of at least 5 g/cm^3 and an atomic number of at least 11 that pose a concern to the environment and/or humans (Tchounwou et al., 2012). The major source of heavy metal pollution in the aquatic ecosystem is anthropogenic activity, principally smelting, mining, and foundries, as well as the leaching of metals from different sources, including waste dumps, excrement, runoffs, livestock droppings, and the use of pesticides, insecticides, fertilizers, and other agricultural chemicals (Figure 1). Heavy metal pollution can also be caused by natural causes (Figure 2) such as corrosion of metals, volcanic activity, sediment re-suspension, metal evaporation from soil and water, soil erosion, and geological weathering (Herawati et al., 2000; Tchounwou et al., 2012; Gautam et al., 2016; Masindi and Muedi, 2018). Their presences pose a disastrous effect on both ecological balance and the diversity of aquatic organisms. Many heavy metal ions are toxic or carcinogenic in nature, making them dangerous to human health and the environment (Farombi et al., 2007; Briffa et al., 2020; Balali-Mood et al., 2021). Excessive use of heavy metals in recent decades has probably resulted in increasing metallic component discharge into the aquatic environment (Yang and Rose, 2003; Li et al., 2011). Researchers from all around the world have been drawn to the poisoning of the aquatic environment by heavy metals and pesticides (Dutta and Dalal, 2008).

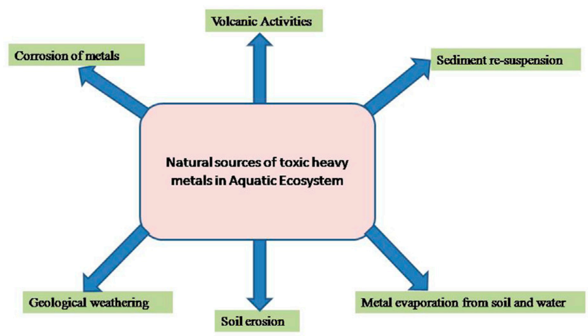

FIGURE 2
Illustrative depictions of natural sources of toxic heavy metals in the Aquatic Ecosystem.

Heavy metals are absorbed by fish either through their gills or their guts, after which they move into the bloodstream and are eventually deposited in various organs (Oliveira Ribeiro et al., 2005; Javed and Usmani, 2012; AL Taee et al., 2020). Consequently, fish accumulate large amounts of metals from the water, and their accumulation rate is influenced by both their absorption and elimination rates (Mansour and Sidky, 2002; Ahmed et al., 2016). Thus, metal accumulation in fish has been studied and monitored in several countries around the globe

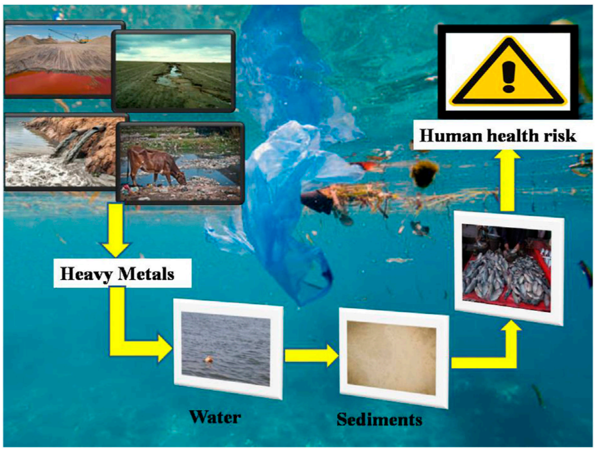

FIGURE 3
Illustrative depictions of bioaccumulation of heavy metals in fish and its transmission through the food chain.

(Ahmed et al., 2016). The intake of aquatic food contaminated with toxic heavy metals has increased the risk of human health problems globally; particularly in underdeveloped countries such as India (Figure 3). As a result, fish are considered one of the most important indicators in aquatic systems for monitoring trace metal pollution and its possible health impacts on humans (Vieira et al., 2011; Pan and Wang, 2012; Ahmed et al., 2016). Since heavy metals first manifested themselves in the bloodstream, it is critical to investigate the hematological parameters that are used to determine the fish's health and the state of the environment (Shah and Altindag, 2005; Javed and Usmani, 2015; Lawrence et al., 2020). The poisonous impact of excessive metals on both metabolic and hemopoietic processes in the animal was demonstrated by the relative up/down in hematological parameters, as previously reported (Hanan et al., 2013). Therefore, blood indices are considered pathophysiological indicators of the whole body, and therefore are helpful in determining whether fish have suffered structural and functional damage as a result of toxic exposure (Adhikari et al., 2004; Fazio, 2019). Hematological parameters can also be a valuable pointer for exposure to chemical contaminants and predict the deadly impacts of toxicants within the aquatic medium. Identically as for non-aquatic life forms, the hematological data of a fish have been used in evaluating the effect of heavy metals. According to studies, when pollutants alter the quality of the aquatic medium, any physiological changes in aquatic animals are reflected in the values of one or more hematological parameters (Gabriel et al., 2004; Akinrotimi et al., 2007; Adewumi et al., 2018). Different workers have done lots of work to designate the consequence of heavy metal intoxication on numerous hematological variables counting Hb, Hct, Rbc's, and Wbc's of particular fish species from various corners of the globe. Consequently, the present review paper has been made to collate all the data about the major impacts of heavy metals on the level of Hb and Hct of a variety of fish species inhabiting different parts of the world. This survey ought to be valuable for a variety of investigators counting fishery researchers and controllers, and may offer assistance to characterize the magnitude of heavy metal-induced hematological modification in exposed piscine populations.

3 Impacts

3.1. Impacts of different heavy metals on the hematocrit(Hct) and hemoglobin (Hb) of fishes

It is evident that each heavy metal has its own properties that set it apart from the others. Because of this, the level of their toxicity to fish also varies. In addition, the toxicity of metals in various water sources also varies significantly. In toxicological research, certain elements like lead (Pb), mercury (Hg), cadmium (Cd), copper (Cu), nickel (Ni), iron (Fe), cobalt (Co), manganese (Mn), chromium (Cr), zinc (Zn), and arsenic (As) are considered as the deadliest at high concentrations for aquatic ecosystems due to their low biodegradability and long-lasting qualities, as well as their toxicity to ichthyofauna and humans (Yousif et al., 2016; Rajeshkumar and Li, 2018; Hong et al., 2020; Balali-Mood et al., 2021). Meanwhile, copper (Cu), nickel (Ni), iron (Fe), cobalt (Co), manganese (Mn), chromium (Cr), and zinc (Zn) are essential micronutrients/metals included in the active centers of enzymes and are essential regulators of a wide range of biological functions, but at high concentrations they become toxic. Therefore, it is also important to monitor the concentrations of these essential metals in aquatic environments. Heavy metals can be absorbed and accumulated by fish either directly by ingestion of polluted water or indirectly via polluted food such as phytoplankton, zooplankton, and crustaceans (Polat et al., 2015). Fish have the ability to tolerate stress before developing a major physiological change. In the case of minor stress, the inner equilibrium is normally restored but in the case of severe or protracted stress, the organism's compensating skills may be overwhelmed, resulting in physiological abnormalities or even mortality. The various impacts of heavy metals on the above-selected blood parameters of fish have been documented by several authors in different countries around the world in the past several decades (Jaishankar et al., 2014; Authman et al., 2015; Rajeshkumar and Li, 2018; Hong et al., 2020; Naz et al., 2021).

Heavy metal exposure can induce an increase or reduction in the levels of blood parameters in a fish. Heavy metals affect the oxygen-carrying capacity of the blood by affecting the Hb and Hct levels in different ways depending on the metal type, the species, and the duration of exposure. In aquatic environments, several hematological indices, including Hb, Hct, RBCs, etc., have been used as indicators of metal pollution and are often used to assess the functional status of the oxygen-carrying capacity of the bloodstream (Fazio, 2019). In the present review, we will summarize the present knowledge on the toxic effects of heavy metals on the hematological parameters of various fish species, which is shown in Tables 1-7.

3.1.1 Effect of lead (Pb) on the level of Hct and Hb in fishes

Lead (Pb) is one of the heavy metals that are non-essential, non-beneficial, and highly toxic to several organisms at relatively low concentrations (Tchounwou et al., 2012; Rajeshkumar and Li, 2018; Balali-Mood et al., 2021). This unfavorable factor has been shown to change the hematologic system of hosts by blocking the activity of several heme production enzymes (Agency for Toxic Substances and disease Registry ATSDR, 2005). Pb is highly persistent in the environment and has been classified as an important hazardous substance (Sfakianakis et al., 2015). Additionally, several authors also agree that contaminants such as Pb accumulate in many fish species and cause harm to their physiology, behavior, and biochemistry, as well as causing damage to their central nervous system (CNS), peripheral nervous system (PNS), hematopoietic system, cardiovascular system, and organs such as the liver and kidney (Guo and Hsu, 2002).

Exposure to Pb can cause many effects depending on its level and duration (Table 1). As recoded in *Oncorhynchus mykiss* (Johansson-Sjobeck and Larsson, 1979) and *Barbus conchonius* (Tewari et al., 1987), chronic Pb exposure causes a reduction in Hb content and Hct values. Ciftci et al. (2008) examined the impact of two different Pb doses of 0.06 mg/L and 0.12 mg/L,

TABLE 1 Influence of lead (Pb) on Hb and Hct in different fish species.

Fish Species	Lead dose	Duration (h)	Alteration in Level of Hb and Hct	References
A. anguilla	0.06 mg/L	360 and 720	Hct↑	Ciftci et al. (2008)
	0.12 mg/L		No alteration	
Arrhina mrigala	-	-	Hct↓ Hb↓	Iqbal et al. (1997)
B. conchonius	0.0474 mg/L	720 and 1440	Hct↓ Hb↓	Tewari et al. (1987)
C. carpio	10 mg/L	3	Hct↑	Witeska (2005)
	10 mg/L	3	Hb↑ (Day 16)	Witeska et al. (2010)
			Hb↓ Hct↓ (Day 4)	
	6.2 mg/L	360	No alteration	Khalesi et al. (2017)
C. gariepinus	0.1 and 0.4 mg/L	672	Hct↑ Hb↓(1st7 days)	Oluah and Omerebele (2010)
			Hct↓(after 7 days)	
Clarias batrachus	3.6 mg/L	384	Hb↓	Muneesh and Mansa. (2016)
O. aureus	10 mg/L	168	Hct↓	Allen (1993)
O. niloticus	1.5 mg/L	336	Hct↑ Hb↑	Zaki et al. (2008)
	0.1 mg/L	240	No alteration	Cogun and Sahin (2013)
		480	Hct↓ Hb↓	
	0.2 mg/L	720	Hct↑	Ciftci et al. (2015)
	1 mg/kg	144	Hct↓ Hb↓	Dos Santos et al. (2016)
	26.4 mg/L	720	Hct↓ Hb↓	Abdel-Warith et al. (2020a)
O.mykiss	0.3 mg/L	720	Hb↓	Sjobeck and Larsson (1979)
P. lineatus	126 and 95 mg/L	96	No alteration	Martinez et al. (2004)
	71 and 24 mg/L	96	No alteration	
Salmo coruhensis	5 mg/Land 10 mg/L	3	Hb↑	Serezeli et al. (2011)
Tinca tinca	300 mg/L	48	Hct↑ Hb↓	Shah (2006)
	30 mg/L	504	Hct↑ Hb↓	
	75 mg/L	504	Hct↓ Hb↓	
	300 mg/L	48	Hct↑	
	30 mg/L	24	Hct↑	
	30 mg/L	96	Hct↑	
	75 mg/L	504	Hct↓ Hb↓	

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

which is 5 and 10% of the 96 h LC50 value (1.17 mg/L), on the Hct level of *Anguilla anguilla* for 360 and 720 h. They reported that a Pb concentration of 0.12 mg/L had no effect on Hct levels, however, 0.06 mg/L of Pb elevates the level of Hct. Cogun and Sahin (2013) conducted a toxicological study in *Oreochromis niloticus* for 240 and 480 h exposure respectively at 0.1 mg/L Pb, however, no significant changes in hematological parameters such as Hct and Hb count were observed after 240 h of exposure. On the other hand, the levels of these hematological indicators exhibited a downward trend at the end of the 480 h exposure period. Allen (1993) also noted a decrease in Hct values in *Oreochromis aureus* administered with 19 mg/L Pb. Martinez et al. (2004) did not observe any hematological changes in *Prochilodus lineatus* after acute Pb exposure to LC50 for 96 h. Khalesi et al. (2017) reported similar findings in carp, *Cyprinus carpio*, when exposed to sub-lethal Pb (6.2 mg/L) over a 360 h period. No significant change in the Hct level of *P. lineatus* and *C. carpio* exposed to Pb concentrations indicated that despite gill lesions, the fish were not exposed to internal hypoxia. Abdel-Warith et al. (2020a) found that the Hct and Hb values of *O. niloticus* exposed to sub-lethal concentrations of Pb during 720 h were higher than in the control group. They finally observed that the values of Hb and Hct showed a decreasing trend with respect to the increase of Pb concentration. The same trend has also been exhibited for *Clarias gariepinus* (Abdel-Warith et al., 2020b). The reason for the decrease in the values of Hb and Hct might be hemodilution, hemorrhagic anemia (blood loss), hemolytic anemia (erythrocyte destruction), and hypoplastic anemia (poor erythropoiesis) which resulted due to the exposure of fish species to heavy metal. Increased hematocrit levels are due to the release of erythrocytes from erythropoietic tissues following Pb stimulation. Zainuddin et al. (2017) investigated the effects of sub-lethal Pb levels on the hematological parameters of Nile tilapia, *Oreochromis niloticus* at different salinity levels and found that fish exposed to Pb had lower levels of Hb than fish raised without Pb. Whereas at salinity levels of 0, 5, and 10 ppt, the level of Hct in the Pb-exposed fish was lower than that in the control fish.

3.1.2 Effect of mercury (Hg) on the level of Hct and Hb in fishes

Mercury (Hg) can be toxic to both humans and animals, depending on its chemical form. It has been shown that organic methylated mercury is more toxic than organic mercury

TABLE 2 Influence of mercury (Hg) on Hb and Hct in different fish species.

Fish Species	Mercury Dose	Duration (h)	Alteration in Level of Hb and Hct	References
Aphanius dispar	1.0 mg/L	96 and 720	Hct↓ Hb↓	Hilmy et al. (1980)
Channa punctatus	0.034–0.136 mg/L	-	Hct↑	Juneja and Mahajan (1983)
C. batrachus	0.02, 0.04, 0.06, 0.08 and 0.10 mg/L	840	Hb↓	Maheswaran et al. (2008)
C. gariepinus	0.1 mg/L	-	Hb↓	Saroch et al. (2012)
C. idella	0.005 mg/L	At 1st 2 Weeks of Exposure	Hct↓ Hb↓	Shakoori et al. (1994)
Cyprinus carpio	0.30 mg/L	90	Hct↓ Hb↓	Beena and Viswaranjan (1987)
	5 mg/L	1	No alteration	Witeska and Jezierska (1994)
	10 mg/L	1–3	Hct↑	
Hypophthalmichthys molitrix	0.09 mg/L and 0.27 mg/L	96	Hct↓ Hb↓	Hedayati and Ghaffari. (2013)
O. niloticus	0.02,0.002 and 0.0002 mg/L	336	No alteration	Ishikawa et al. (2007)
	0.05 mg/L	504	Hct↓ Hb↓	Elseady and Zahran (2013)
O. aureus	0.5 mg/L	24	Hct↑ Hb↑	Allen (1994)
	0.1 mg/L	168	Hct↓ Hb↑	
Oreochromis mossambicus	0.1 and 0.15 mg/L	120 and 168	Hct↑ Hb↑	Cyriac et al. (1989)
P. platessa	0.3 mg/L	168	Hct↓	Fletcher and White (1986)
Scyliorhinus canicula	25 mg/L	24	Hct↓ Hb↑	Tort and Torres (1988)
Salmo trutta caspias	0.0035, 0.0048 and 0.01 mg/L	840	Hct↓ Hb↓	Mousavi and Yousefian, (2012)
T. tinca	1 mg/L	48	Hct↓ Hb↓	Lal Shah (2010)
	0.1 and 0.25 mg/L	504	Hct↓ Hb↓	
	1.0 mg/L	24	Hct↓ Hb↓	Shah and Altindag (2004)
	0.1 mg/L	48	Hct↑	
	0.1 mg/L	504	Hct↓ Hb↓	
	0.25 mg/L	96	Hct↑ Hb↑	

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

(Sorenson, 1991; Hong et al., 2012). In fish, Hg is mainly present as methylmercury (CH_3Hg) (Spry and Wiener, 1991; Li et al., 2010). Fish can get CH_3Hg in two ways: directly from the water (sulfate-reducing bacteria convert first-hand Hg into an organic form) or by eating other creatures (biomagnification of the food chain). The conversion of inorganic mercury by anaerobic bacteria to CH_3Hg occurs most efficiently in aquatic ecosystems (Ullrich et al., 2001; Bravo and Cosio, 2019). Mercury serves no biological purpose in the body and has major metabolic and physiological consequences (Calabrese et al., 1975; Jarup, 2003; Rajeshkumar and Li, 2018). Several hematological parameters of fish have been affected by exposure to different levels of mercury.

Several studies have been conducted to observe the influence of different concentrations of Hg on various hematological indices in different fishes across the world (Table 2). Shah and Altindag (2004) investigated the effect of acute lethal (1.0 mg/L Hg/48 h) and chronic sub-lethal (0.25 mg/L Hg/3 weeks) Hg doses on the hematological parameters of Tench (*Tinca tinca*). These results observed a sharp decline in Hb and Hct levels at both higher acute lethal (1.0 mg/L Hg/48 h) and higher chronic sublethal (0.25 mg/L Hg/3 weeks) treatments, but at lower acute sublethal (0.1 mg/L Hg/24 h) treatment, a significant increase in Hct value was observed. Maheswaran et al. (2008) reported a drop in Hb content of *Clarias batrachus* when administered to various concentrations of mercuric chloride ($HgCl_2$) for 840 h. Hedayati and Ghaffari (2013) observed reductions in Hb content and Hct value of Silver Carp, *Hypophthalmichthys molitrix* treated with low (10% LC50) and high (50% LC50) concentrations of $HgCl_2$ for 96 h. Cyriac et al. (1989) studied the short-term influence of Hg on the Hb and Hct level of the fish *Oreochromis mossambicus* and revealed a considerable increase in the Hb and Hct values in Hg-exposed fish at 120 and 168 h respectively. Following exposure to three mercury treatments (one acute lethal and two chronic sub-lethal), Lal Shah (2010) found a significantly lower Hb and Hct level in fish *Tinca tinca*. Contrary to this, no significant variation in Hb and Hct has been observed at different Hg concentrations (0.02, 0.002, 0.0002 mg/L Hg) in *Oreochromis niloticus* (Ishikawa et al., 2007). Observations by Shakoori et al. (1994) demonstrated that the content of Hb and Hct in grass carp, *Ctenopharyngodon idella*, decreased in the first 2 weeks after exposure to $HgCl_2$. The same results were also reported for carp, *Cyprinus carpio* exposed to $HgCl_2$ (0.30 mg/L) for 90 h (Beena and Viswaranjan, 1987), *Aphanius dispar* exposed to the same product (1.0 mg/L) for 96 and 720 h (Hilmy et al., 1980), *Channa punctatus* (Juneja and Mahajan, 1983) and *O. aureus* (Allen, 1994) exposed to sub-lethal concentrations of $HgCl_2$ (0.034–0.136 and 0.5 mg/L, respectively).

3.1.3 Effect of cadmium (Cd) on the level of Hct and Hb in fishes

Cadmium (Cd) is not a dietary essential element in fish nutrition. It is one of the most toxic heavy metals because of its non-biodegradable nature and non-beneficial effect and causes toxicity in aquatic organisms even at very low levels (Cicik and Engin, 2005). The average natural concentration of Cd in unpolluted natural waters is below 0.001 mg/L (Nordberg et al., 2007). Researchers have studied a variety of fish species from around the world and found that the exposure of a fish to Cd may alter their Hb and Hct values (Table 3). Mekkawy et al. (2011) observed a remarkable decline in the Hb content and Hct value of *Oreochromis niloticus* after exposure to Cd for 360–720 h. However, when Cd-exposed fish were treated with vitamin E or tomato paste, they saw a considerable rise in the falling value of Hb and Hct. Finally, they concluded that supplementing Cd-exposed fish with vitamin E and tomato paste phytonutrients counteracts the negative effects of Cd on the examined features. A decrease in blood Hb and Hct values has also been reported in *Channa punctatus* exposed to Cd (29 mg/L) for 168, 360, and 720 h (Karuppasamy et al., 2005). Drastichova et al. (2004) expose the fish *Cyprinus carpio* to Cd (12.5 mg/L) for 96 h and found higher Hb content and Hct value than the control group and concluded that the rise in Hb and Hct values in Cd-exposed fish might be due to a response to impairment of gas exchange in Cd affected gills. Similarly, Ghazaly (1992) observed a significant rise in Hb content and a sharp decline in Hct value in *Tilapia zillii* after exposure to 17.70 and 24.78 mg/L for 24 h Cd concentrations. Haux and Larsson, (1984) revealed a sharp decline in the value of Hct in *Onchorhynchus mykiss* with the increasing concentrations of Cd (0.01 mg/L). After being exposed to 0.05–0.5 mg/L of Cd, the amount of Hb and Hct in *Pleuronectes flesus* (flounder) fell dramatically (Johansson-Sjobeck and Larsson, 1978). Contrary to these findings, it has been reported that acute Cd exposure of 5 mg/L for 1 h had almost no influence on Hct value in *C. carpio*, but Cd concentration of 10 mg/L for 24h resulted in a reduction in Hct levels of *C. carpio* (Witeska and Jiezierska, 1994). *O. niloticus* was subjected to various doses of cadmium chloride ($CdCl_2$) for a period of 240, 480, and 720 h and found that the Hb and Hct values were decreased in exposed fish to all periods (Al-Asgah et al., 2015). Naz et al., 2021 have reported that the Hb and Hct show a significant decrease upon exposure to Cd.

3.1.4 Effect of chromium (Cr) on the level of Hct and Hb in fishes

In the environment, Chromium (Cr) occurs naturally as trivalent (CrIII) and hexavalent (CrVI). Hexavalent Chromium(CrVI) is considered the most hazardous among them, as it easily penetrates through biological membranes before being reduced to trivalent form, which then combines with several macromolecules, such as genetic material inside the

TABLE 3 Influence of Cadmium (Cd) on Hb and Hct in different fish species.

Fish Species	Cadmium Dose	Duration (h)	Alteration in Level of Hb and Hct	Reference
Anguilla rostrata	0.15 mg/L	1344	Hct↓ Hb↓	Gill and Epple (1993)
Catla catla	0.000669 mg	600	Hb↓	Remyla et al. (2008)
Channa punctatus	29 mg/L	168, 360 and 720	Hct↓ Hb↓	Karuppasamy et al. (2005)
Cyprinus carpio koi	92.5 mg/L	720	Hct↓ Hb↓	Ali et al. (2018)
Cyprinus carpio	0.02 mg/L	96–1608	No alteration	Palaekova et al. (1994)
	12.5 mg/L	96	Hct↑ Hb↑	Drastichova et al. (2004)
	8.4 mg/L	360	No alteration	Khalesi et al. (2017)
	5 mg/L	1	No alteration	Witeska and Jezierska (1994)
	10 mg/L	1–3		
Notemigonus crysoleucas	1.35 and 2.40 mg/L	96	No alteration	Benson et al. (1987)
O. mossambicus	0.1–10.0 μg/L	24–1080	Hb↓	Ruparella et al. (1990)
Oreochromis niloticus	5.5 mg/L	168, 504 and 1080	Hct↓ Hb↓	Al-Attar (2005)
	4.64 mg/L	360 and 720	Hct↓ Hb↓	Mekkawy et al. (2011)
	1–5 mg/L	96	Hct↓ Hb↓	Parekh and Tank (2015)
	1.68, 3.36 and 5.04 mg/L	240, 480 and 720	Hct↓ Hb↓	Al-Asgah et al. (2015)
Parachanna africans	10 mg/L	504	Hct↓ Hb↓	Siakpere and Ikomi. (2011)
Scyliorhinus canicula	0.025 mg/L	24	Hct↓ Hb↑	Tort and Torres (1988)
Tilapia zillii	17.70 and 24.78 mg/L	24	Hct↓ Hb↑	Ghazaly (1992)

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

cytosol, exposing the toxic and mutagenic variations owing to the presence of toxicity (Velma et al., 2009; Ahmed et al., 2013). In an aquatic ecosystem, Cr makes its way through effluents mostly discharged from various sources such as metal finishing, dyeing and printing industries, leather tanneries, mining, photographic, pharmaceutical, electroplating, ceramic, and textile industries, etc. (Arunkumar et al., 2000; Tadesse and Guya, 2017; Grace Pavithra et al., 2019; Ukhurebor et al., 2021). Poor treatment of these effluents, on the other hand, might result in the presence of heavy metals like CrVI in nearby water bodies, where it is regularly detected at levels that are potentially dangerous to fish (Li et al., 2011; Bhatia, 2017; Lellis et al., 2019). The

TABLE 4 Influence of Chromium (Cr) on Hb and Hct in different fish species.

Fish Species	Chromium Dose	Duration (h)	Alteration in Level of Hb and Hct	References
Cirrhinus mrigala	3.4, 5.2 and 10.4 mg/L	1440	Hct↓ Hb↓	Mallesh et al. (2015)
Labeo rohita	39.4 mg/L	24 and 96	Hb↓	Vutukuru (2005)
	6 mg/L	720	Hct↓ Hb↓	Bhatkar (2011)
	10 mg/L	168 and 720	Hct↓ Hb↓	Praveena et al. (2013)
	96 h (LC50)	24, 48 and 96	Hct↑ Hb↑	Venkatachalam and Natarajan (2014)
Onchorhynchus mykiss	2.0 mg/L	504	Hct↑ Hb↑	Van Der Putte et al. (1982)
Platichthys stellatus	400 ppb	336	Hct↓ Hb↓	Ko et al. (2019)
Pangasianodon hypophthalmus	20, 30, and 40 mg/L	96	Hct↓ Hb↓	Majharul Islam et al. (2020)
Salmo gairdneri	20 mg/L	-	Hct↑ Hb↑	Schiffman and Fromm (1959)
	4.2–0.125 mg/L	2160–2400	Hb↑	Svobodova et al. (1994)
Saccobranchus fossilis	0.1, 1.0 and 3.2 mg/L	672	Hct↓ Hb↓	Khangarot et al. (1999)
Tilapia sparrmanii	0.098 mg/L	-	Hb↓	Wepner et al. (1992a)

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

concentration of Cr ranges from 0.005 to 0.8 mg/L in sea water, and from 0.026 to 5.2 mg/L in rivers and lakes (Jacobs and Testa, 2005). According to the EPA, the total Cr including CrVI in drinking water must be less than 0.1 mg/L. In general, both biotic and abiotic variables influence Cr toxicity in aquatic ecosystems. Age, species type, and developmental stage of an individual are all biological factors. Abiotic parameters include pH, temperature, Cr concentration and oxidation state, water hardness, and alkalinity. Hematological abnormalities, morphological and histological changes, formation of reactive oxygen species (ROS), inhibition/reduction of growth, and reduced immunological function are all toxic effects of Cr in fish (Reid, 2011; Vera-Candioti et al., 2011).

Several variations in the hematologic indices of numerous fish species subjected to the presence of Cr are well documented (Table 4). *Labeo rohita* showed a significant decrease in Hb and the total erythrocyte count after 24 and 96 h of exposure to 39.4 mg/L CrVI (Vutukuru, 2005). Wepener et al. (1992a) recorded a marked decline in the blood Hb concentration of *Tilapia sparrmanii* exposed to 0.098 mg/L of CrVI. After rainbow trout were exposed to CrVI of 2.0 mg/L for 504 h, the levels of Hb and Hct in their blood dramatically increased, according to Van Der Putte et al. (1982). Venkatachalam and Natarajan (2014) investigate the hematologic alteration in the blood of a freshwater teleost *L. rohita* after being exposed to both CrIII and CrVI for 96h, and their finding revealed a significant rise in the value of Hb and Hct values. Similarly, Gill and Pant (1987) observed significant polycythemia in the acutely intoxicated fish *Barbus conchonius* with a marked increase in Hb and Hct. Furthermore, chronic exposure led to significant erythropenia with a reduction in Hb and Hct values. A similar trend in the Hb content and Hct value was also found in *Salmo gairdneri* exposed to Cr (20 mg/L) (Schiffman and Fromm, 1959). Various fish species have also been reported to have higher hematological indices after being exposed to 10 mg/L of CrVI for 360 h (Strik et al., 1975). Even after short-term (96 h), as well as long-term (2160–2400 h), treatment with potassium bichromate, the levels of Hb and Hct in the blood of *C. carpio* remain the same, whereas long-term exposure to Cr concentrations of 4.2–0.125 mg/L increased Hb content in *Oncorhynchus mykiss* (Svobodova et al., 1994). Moreover, *Saccobranchus fossilis*, a freshwater fish, was subjected to CrIV concentrations of 0.1, 1.0, and 3.2 mg/L for 672 h and demonstrated a dose-dependent drop in Hb and Hct levels (Khangarot et al., 1999). Majharul Islam et al. (2020) investigated the effects of Cr on the hematological indexes of the striped catfish, *Pangasianodon hypophthalmus*, and discovered that Cr concentrations of 30, 40, and 60 mg/L dramatically reduced Hb and Hct levels after 96 h. Mallesh et al. (2015) exposed the fish *Cirrhinus mrigala* to sub-lethal concentrations of Cr (3.4, 5.2, and 10.4 mg/L) for 1440 h and observed a marked drop in Hb and Hct values, which leads to anemia in fishes. Praveena et al. (2013) studied the impact of sub-lethal Cr concentrations on the hematological indices of *L. rohita*. They found considerably decreased values of Hb and Hct after 168 and 720 h of exposure. Similarly, after Cr exposure, Hb and Hct values in *C. carpio* were also found to be much lower (Shaheen and Akhtar, 2012). It is clear from the decreased hematological parameters that heavy metal exposure leads to anemic fish with erythropenia. The decline in hematological values could also be ascribed to heavy metals (pollutants) damaging the structure of RBCs, causing fewer oxygen molecules to bind to Hb, reducing RBC oxygen carrying capacity, lowering Hb levels, and even resulting in anemia (Javed et al., 2016).

3.1.5 Effect of copper (Cu) and zinc (Zn) on the level of Hct and Hb in fishes

Copper (Cu) and zinc (Zn) are critical trace elements for fish and are necessary in small amounts for the normal development and metabolism of aquatic species, including fish. However, if the concentrations of Cu or Zn exceeds the physiological limits, they become toxicant and can even be lethal for almost all organisms, including fish (Heath, 1995). The US EPA (2009) issued water quality criteria for Zn, which stipulated that the criteria for freshwater aquatic organism protection were 0.12 mg/L (short-term hazardous concentration) and 0.12 mg/L (long-term hazardous concentration), while the criteria for human health were 7.4 mg/L (ingested potable water + edible aquatic organisms grown in the water) and 26 mg/L (only edible aquatic organisms). The toxicity of Zn and Cu to fishes is well documented and investigation has found that elevated doses of Zn and Cu may become acutely or chronically toxic to aquatic life, including fish, affecting growth, survival, and development, accruing structural damage, having an adverse effect on tissue respiration leading to death by oxygen deprivation, changes in heart and ventilator physiology as well as having a negative impact on fish hematological indices. The present intensive industrial developments have increased the concentration of Zn and Cu in aquatic ecosystems and make them one of the most common pollutants in natural waters. In the last few decades, the usage of these metals has increased significantly, by virtue of which the probability of accumulation of these elements increased in various aquatic environments. Because of these concerns, it is crucial to understand the toxicity of these metals on aquatic organisms before they lead to harmful effects on them.

The impact of these essential trace elements on the hematological parameters of fishes has been widely studied and a considerable number of experimental data are available (Table 5). Ciftci et al. (2015) examined the impact of Cu (4.0 mg/L) on the hematological parameters of *O. niloticus* and noticed that the value of Hct had raised significantly during the exposure periods of 168 and 360 h, later they also reported a decline in the value of Hct at 720 h exposure period. They revealed that the increase in Hct levels was reported to be

TABLE 5 Influence of Zinc (Zn) and Copper (Cu) on Hb and Hct in different fish species.

Fish Species	Factor	Metal dose (Cu and Zn)	Duration (h)	Alteration in Level of Hb and Hct	References
Channa punctatus	Zn	Sub-lethal	3240	Hct↓ Hb↓	Tyagi and Srivastava (2005)
	Cu	0.36 mg/L	1080	Hct↓ Hb↓	Singh et al. (2008)
Clarias gariepinus	Cu	_	At 48	Hb↓	Van Vuren et al. (1994)
			After 48 h	Hb↑	
	Zn	30–50 mg/L	96	Hct↓ Hb↓	Ololade and Ogini (2009)
	Zn	0.08 mg/L and 0.15 mg/L	120	Hct↓ Hb↓	Olurin et al. (2012)
Colisa fasciatus	Cu	3 mg/L	90	Hct↑ Hb↑	Mishra and Srivastava (1980)
	Zn	100 mg/L	90	Hct↓	Mishra and Srivastava (1979)
C. carpio and *O. mykiss* yearling	Cu	Close to LC50	_	Hct↑ Hb↑	Svobodova et al. (1994)
Cyprinus carpio	Zn	High Zn Conc	Short period	Hct↓ Hb↓	Svobodova et al. (1994)
		Low Zn Conc	Long period	No alteration	
	Zn	Sub-lethal	Acute exposure	Hb↑	Tishanova and Ilieva (1994)
	Zn and Cu	Sub-lethal Conc	720	Hct↓ Hb↓	Dhanapakiam and Ramasamy (2001)
	Cu	2 mg/L	336	Hct↓ Hb↓	Roja et al. (2013)
	Cu	1000 mg/kg	1008	Hct↑ Hb↑	Ajani and Akpoilih (2010)
		2000 mg/kg	1008	Hct↓ Hb↓	
Heteroclarias sp	Zn	5 and 10 mg/L	360	Hct↓ Hb↓	Kori-Siakpere and Ubogu (2008)
Ictalurus nebulosus	Cu	3.4–104 µg/L	720	Hct↑ Hb↑	Christensen et al. (1972)
Mugil cephalus	Cu	0.79 and 1.57 mg/L	504	Hct↓ Hb↓	Akbary et al. (2018)
Oreochromis mossambicus	Cu	0.1 mg/L and	24	Hb↓	Cyriac et al. (1989)
		0.2 mg/L	72, 120 and 168	Hct↑ Hb↑	
	Zn	1, 2.5 and 5 mg/L	336	Hb↑	Celik et al. (2013)
				Hct↓(5 mg/L)	
				Hct↑(1and2.5)	
O. niloticus	Zn	15, 30 and 45 mg/L	24, 48 and 72	Hct↓ Hb↓	Shokr (2015)
Oncorhynchus mykiss	Cu	0.0269 mg/L 26.9 µg/L	504h	Hct↑ Hb↑ (at day 3)	Dethloff et al. (1999)
				Hct↓ Hb↓ (after day 3)	
		0.125–0.5 mg/L	_	Hct↑	Vosyliene (1996)
		4.9 mmol/L	24	Hct↑ Hb↑	Wilson and Taylor (1993)
Puntius parrah	Cu	0.05 mg/L	672	Hct↓ Hb↓	Ciji and Bijoy Nandan, (2014)
	Zn	0.9 mg/L	672	Hct↓ Hb↓	
Prochilodus scrofa	Cu	0.029 mg/L	96	Hct↑ Hb↑	Mazon et al. (2002)
		0.025 mg/L		Hct↑	
	Cu	0.098 and 0.088 mg/L	-	Hct↑ Hb↑	Carvalho and Fernandes (2006)
		0.016 and 0.014 mg/L			
Salvelinus fontinalis	Cu	24, 39 and 67 mkg/L	During 1st3week	Hct↑ Hb↑	McKim et al. (1970)

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

a result of either hemoconcentration or stimulation of erythropoiesis by feedback mechanisms. A freshwater teleost, *Colisa fasciatus* showed significantly elevated Hb and Hct values after 96 h exposure to 3 mg/L of Cu (Mishra and Srivastava, 1980). Contrary to this, the same fish (*C. fasciatus*) showed a significantly lowered Hct value after 90 h exposure to 100 mg/L of zinc (Mishra and Srivastava, 1979). Hilmy et al. (1987) observed that the Hb and Hct contents of catfish, *Clarias lazera*, and tilapia, *Tilapia zilli* had significantly increased after 96 h exposure to 22 mg/L and 32 mg/L of Zinc. It was demonstrated by Celik et al. (2013) that Zn (1, 2.5, and 5 mg/L) negatively affected the hematology of *Oreochromis mossambicus* and their findings revealed that in all groups of exposure, the Hb content increases with the increase of exposure dose, while the Hct value decreases at high exposure dose but increases at low and medium doses of Zn. Cyriac et al. (1989) noted an increase in Hb and Hct concentrations of *O. mossambicus* after 24 h exposure to substantially lower Cu concentrations (100 and 200 mkg/L). Their findings demonstrated that the rise in Hb and Hct content in the blood of fish acutely exposed to Cu was generally triggered by erythrocyte enlargement or the spleen's release of giant red blood cells. The Hb content of catfish (*Clarias gariepinus*) is significantly reduced at 48 h acute exposure to background copper concentrations, although after 48 h exposure the Hb content slightly increases (Van Vuren et al., 1994). The results of Dharam et al. (2008), who examined the hematological data in *Channa punctatus* following acute sublethal exposure to Cu (0.36 mg/L) revealed a substantial drop in Hb (down from 10.73 to 6.60%) and Hct levels (down from 31.00 to 23.33%), when compared to control, after 1080 h. Their study revealed that the reduction in blood Hb and Hct is primarily the result of increased destruction and decreased synthesis of Hb due to Cu (a heavy metal). The Hb an oxygen-carrying module serves as a marker for anemia in fish (Parekh and Tank, 2015). Therefore, the significant drop in Hb in *C. punctatus* reveals that the fish has anemia due to metal toxicity. Cu and Zn toxicity have shown detrimental effects on almost all physiological systems of fish, yet fish of different species had varying tolerance levels.

3.1.6 Effect of manganese (Mn), nickel (Ni), and cobalt (Co) on the level of Hct and Hb in fishes

Manganese (Mn) exists in the aquatic environment in two main forms: soluble MnII and insoluble MnIV oxidation states, with the latter being less bioavailable and toxic. In small amounts, Mn is essential for organisms, including fish, since it is a constituent of important enzymes and cofactors; however, at concentrations exceeding the threshold level, it is potentially harmful (Vieira et al., 2012). The acute toxicity of these elements has been recorded in fish ranging from 2.4 mg/L for coho salmon (*Oncorhynchus kisutch*) to 3350 mg/L for Indian catfish (*Hippocampus fossilis*) (Howe et al., 2004). The range of Mn concentrations that cause toxicity varies by species of fish, age group, and the composition of the surrounding water (Fish, 2009). Mn is considered to be less of an environmental hazard than other heavy metals, with evidence from the literature indicating that Mn's acute and chronic toxicity to many freshwater biotas is low.

Many researchers have studied the influence of a high concentration of Mn on the hematological parameters of fish and found negative impacts on hematological indices (Table 6). A considerable drop in the Hb and Hct concentration was found in *Tilapia sparmanii* after exposure to Mn at pH5 (Wepener et al., 1992b). At 23°C, the freshwater fish *Oreochromis mossambicus* was exposed to both acute (345 mg/L for 96 h) and chronic (259 mg/L for 624 h) toxicity of Mn (Barnhoon, 1996). Acute Mn exposure increased Hb and Hct levels significantly. Whereas, an oxygen deficiency developed after chronic Mn exposure, resulting in hypoxia and increased hematologic data related to Hb and Hct contents.

In freshwaters, the dominant form of nickel (Ni) is soluble Ni^{2+}, but other forms also exist, predominantly as complex forms with sulfate and chloride. In many aquatic ecosystems, Ni contamination results from various human processes, including extraction, casting, refining, and the production of steel materials and Ni-Cd batteries, etc. In unaffected water, Ni concentrations are normally below 10 g/L, but in heavily contaminated water, they can exceed several hundred g/L up to even 1000 g/L (Eisler, 1998). Despite the fact that Ni is an important trace element for a wide range of living creatures, at elevated concentrations, it can be very harmful to all living organisms. Ni and its compounds have high acute and chronic toxicity to aquatic life including fish.

Several studies reported Ni-related variations in the hematological indices of fishes (Table 6). Ololade and Oginni (2010) reported a significant decrease in the hematological indices such as Hb and Hct contents of *C. gariepinus* after exposure to 8.87 mg/L Ni for 96 h. Similarly, when Musa and Omoregie (1999) subjected *C. gariepinus* to a contaminated environment under laboratory conditions, the fish's hematological profile was likewise reduced. The considerable fall in hematological markers indicates that experimental fish were exposed to Ni in the water, which produced severe anemia. After short-term exposure to high Ni concentrations in *C. carpio*, Al-Ghanim (2011) discovered a considerable drop in Hb and Hct levels.

Cobalt (Co) is a mineral that is necessary for the survival of fish and other species and plays a crucial role in the growth of all living organisms. Co is required by all animals, including fish, in trace amounts. Its high concentration, on the other hand, can be harmful to the health of the fish. As a result of their persistence and propensity to bio-magnify in the aquatic food chain, Co pollution poses a serious threat to aquatic life (Ubaidullah et al., 2004). Co, which is an integral part of vitamin B_{12} or cobalamin, has an important role in fish nutrition and aquaculture. Since fish and all other animals are unable to synthesize this vitamin, therefore, they must rely on bacterial production to meet their nutritional needs. Co compounds that dissolve easily in water are generally more dangerous than those that do not. Co is dispersed throughout the body, but especially in the liver, kidneys, and bones, once it enters the body (ATSDR, 2004). Several investigations have found Co-related variations in fish blood parameters (Table 6). Atamanalp et al. (2011) examined the hematological data in Co exposed fish, *O. mykiss*. Their findings revealed a significant rise in Hb

TABLE 6 Influence of Manganese (Mn), Nickel (Ni), and Cobalt (Co) on Hb and Hct. in different fish species.

Fish Species	Factor	Metal Dose	Duration (h)	Alteration in Level of Hb andHct	References
C. gariepinus	Ni	8.87 mg/L	96	Hct↓ Hb↓	Ololade and Oginni (2010)
Carassius auratus	Ni	80% of LC50	96	Hct↓ Hb↓	Moosavi and Shamushaki (2015)
Cirrhinus mrigala	Ni	Sub-lethal conc	672	Hct↓ Hb↓	Parthipan and Muniyan (2013)
Colisa fasciatus	Ni	45 mg/L	90	Hct↑ Hb↑	Agrawal et al. (1979)
	Co	195 mg/L	90	No alteration	Srivastava and Agrawal (1979)
	Mn	2500 mg/L	90	No alteration	Agrawal and Srivastava (1980)
Cyprinus carpio	Ni	2 and 20 mg/L	168	No alteration	Canli (1995)
		6, 9, 12, 15 and 18 mg/L	96	Hct↓ Hb↓	Al-Ghanim (2011)
Garra gotyla gotyla	Mn	20%, 40 and 60% of LC50	1512	Hct↓ Hb↓	Jyoti and Seema (2014)
H. fossilis	Mn	120 mg/L	720	Hct↓ Hb↓	Garg et al. (1989)
O. mossambicus	Mn	Acute treatment	96	Hct↑ Hb↑	Barnhoon (1996)
		Chronic treatment	624	Hct↑ Hb↑	
O. mykiss	Co	0.18 mg/L	672	Hct ↓ Hb↑	Atamanalp et al. (2011)
O. niloticus	Ni	27.2 mg/L	96	Hct↑ Hb↑	Alkahem (1994)
Salmo trutta fario	Co	0.18 mg/L	672	Hct↑ Hb↓	Atamanalp et al. (2010)
Tilapia nilotica	Ni	19.2, 32 and 51.2 mg/L	96	Hct↑ Hb↑	Ghazaly (1992)
Tilapia sparmanii	Mn	4.43 mg/L	96	Hct↓ Hb↓	Wepener et al. (1992b)

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

concentration and a declining trend in Hct value after exposure to 0.18 mg/L for 672 h.

3.1.7 Effect of arsenic (As) on the level of Hct and Hb in fishes

Arsenic (As) is one of the major global environmental toxicants that is delivered either directly or indirectly into aquatic ecosystems (Agency for Toxic Substances and disease Registry ATSDR, 2002). The poisoning of aquatic ecosystems by this worldwide environmental contaminant, as well as its influence on aquatic creatures, has now become a major environmental issue all over the world (Allen and Rana, 2004). As is found in abundance in our environment and is known to come in different chemical forms. In general, As exists in both organic and inorganic forms; the latter exhibit the highest toxicity level, while the former are usually less toxic (Luh et al., 1973). Arsenate (AsV+), arsenite (AsIII+), arsenic (As0), and arsine (AsIII−) are the most common oxidation states (WHO, 2011). In most As-contaminated locations in India, arsenic trioxide (As_2O_3) was the dominating species, accounting for over half of the total As level (Chatterjee et al., 1993). Arsenical toxicity in animals varies according to inorganic or organic forms, exposure duration, exposure dose, sex, species, age, valence state, and other factors (Allen and Rana, 2004; Amsath et al., 2017). Fish can act as the most effective bioindicator of arsenic toxicity in the aquatic environment because their gills and diet are continuously exposed to As (Ahmed et al., 2008).

In general, As exposure in the aquatic environment induces bioaccumulation in aquatic fauna, which can lead to biochemical and physiological problems such as poisoning, tissue damage, liver lesions, cell death, and reduced fertility (Bears et al., 2006). As influences a number of parameters, including biochemical, hematological, and ionoregulatory, and their changes can be utilized to monitor As pollution in the environment (Lavanya et al., 2011). Fish have been regularly utilized as a model organism to assess the toxic burden of environmental pollutants for several decades. Blood in fish exhibits the early effects of As toxicity because it enters the blood primarily through the vast gill surface area, at which the barrier between the blood and the metal salt is much thinner, and also through the buccal cavity (Romeo et al., 1999; Kumar and Banerjee, 2012). Tripathi et al. (2003) reported a decreased level of Hb and Hct in *C. batrachus* exposed to water-borne arsenic (Table 7). Their findings revealed that a decline in Hb and Hct contents of *C. batrachus* is an indication of an anemic condition due to the poisoning effects of arsenic.

3.1.8 Effect of heavy metal mixture on the level of Hct and Hb in fishes

The effects of single metals on fish have been investigated in the majority of ecotoxicological investigations; however, studies

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TABLE 7 Influence of Arsenic (As) on Hb and Hct in different fish species.

Fish Species	Arsenic dose	Duration (h)	Alteration in Level of Hctand Hb	Reference
Catla catla	43.78 mg/L	96	Hct↓ Hb↓	Kavitha et al. (2010)
	4.378 mg/L	840	Hct↓ Hb↓	
	2.041 mg/L	840	Hct↑ Hb↑	Lavanya et al. (2011)
Channa punctatus	2.42 mg/L	720	Hb↓	Amsath et al. (2017)
Clarias batrachus	5, 10 and 15 mg/L	120	Hct↓ Hb↓	Tripathi et al. (2003)
	1 mg/L	1440	Hct↓ Hb↓	Kumar and Banerjee (2016)
Clarias gariepinus	19.2 and 38.3 mg/L	360	Hct↓ Hb↓	Mekkawy et al. (2020)
Heteropneustes fossilis	1.10 and 0.78 mg/L	1440	Hct↓ Hb↓	Singh and Srivastava (2015)
Mystus vittatus	10 and 30%	720	Hct↓ Hb↓	Verma and Prakash (2019)
Platichthys stellatus	0.6 mg/L	672	Hct↓ Hb↓	Han et al. (2019)

"Upward and Downward Arrows in column "Alteration in level of Hb and Hct" indicate direction of change; Hb, Hemoglobin; Hct, Hematocrit".

evaluating the biological responses of fish to the influence of a blend of heavy metals are rare. Numerous reports have shown that the effects of metal mixtures on living life forms differ from the effects of single components in terms of toxicity. The toxicity of heavy metal complexes is determined by their quantities, composition, and duration of exposure to fish (Vosyliene and Jankaite, 2006). The impact of a model mixture of five heavy metals (copper, zinc, nickel, chromium, and iron) on *Oncorhynchus mykiss* (rainbow trout) during short-term exposure was investigated, and it was discovered that the most sensitive hematological parameters, such as Hb and Hct, changed depending on the concentration of the mixture and the duration of the exposure to it (Vosyliene, 1999). But the fish adapted to low concentrations of the mixture after prolonged exposure (from 10 days to 3 months), and variations in hematological markers could only be seen in blood smears. In perch, *Perca fluviatilis* was exposed for 288 and 648 h to the model heavy metal mixture (zinc, copper, lead, cadmium, and mercury) the Hct and Hb concentrations declined, according to the dosage of the metal mixture (Larsson et al., 1984)

4 Conclusion

In this review, an endeavor is made to understand the disparate evidence on the hazardous consequences of heavy metals to the selective hematological indices of various fish species. From the review of literature available, it is concluded that heavy metals impose a huge alteration in hematological parameters (specifically Hb and Hct) of fishes. Therefore, it is recommended that the assessment of heavy metals using hematological parameters might be helpful in the early analysis of fish health status before it becomes more severe. Thus, the scientific data discussed in this review provide a basis for understanding the potential effect of heavy metals on the hematological index (Hb and Hct) of a fish species and will aid the research community to assemble advanced information on the ecotoxicology and risk assessment of hazardous metal. It has been revealed that heavy metals can induce a variety of unfavorable impacts at histological, physiological, biochemical, enzymatic, hematological, and genetic levels in fish. These heavy metals will ultimately enter the food web via water and food, creating negative health impacts in humans and other animals, just as they do in indicator organisms. Therefore, one of the most important approaches to addressing the issue of heavy metal contamination in aquatic ecosystems is to prevent them from occurring in the future. Uncontrolled release of sewage and industrial wastes has seriously weakened the aquatic ecosystem in general and water quality in particular which ultimately influences the biochemical and physiological status of the aquatic flora and fauna including the fish. For maintaining ecological balance, it is therefore advisable that industrialists do not dispose of their waste unless it has been treated first. Ultimately, if the pollution from these point sources is reduced, the heavy metals in fish will be reduced as the degree of pollution in their habitat decreases. In order to provide a solution to this problem, such strategies or measures must be developed. Therefore, it is crucial to act now in order to ensure that future emissions and releases of heavy metals in aquatic ecosystems are minimized to the maximum extent possible in order to prevent contamination of aquatic ecosystems globally and to prevent hazardous impacts on fish and humans.

Author contributions

IA supervises the study and contributed in conceptualization, reviewing and editing. AZ wrote the original draft. FF contributed in reviewing and editing. All authors helped to revise the manuscript, read it, and approved the final version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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