Hematological and Biochemical Alterations Incorporated in Freshwater Fishes due to Several Industrial Effluents in River Water: A Review

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Abstract- Rapid growth of industries and mills have caused overall increase in economy and contributed to the development of world. But this fact can never be ignored that after industrial revolution has not only cut the workload on humans, also, they have caused great menace to life and health of people as well as organisms from single celled to multicellular. Harmful substances such as pesticides, heavy metals, paper mill waste, polychlorinated biphenyl and crude oil and heavy metal contaminants are often released into the aquatic environment. When large quantities of these pollutants are released, there are visible amount of changes seen in large amount of sudden mortalities of aquatic organisms especially fishes. Also, several species of aquatic organisms are extinct leading to loss of great biodiversity. Lower levels of discharge result in an accumulation of the pollutants in body composition of fish. The polluted water have undesirable colour, odour, taste, turbidity, harmful chemical contents, toxic and heavy metals, pesticides, industrial waste products, domestic sewage, and other physico chemical properties not in the reference range assigned by WHO (World Health Organisation) and CPCB (Central Pollution Control Board). Fish species show a number of morphological, biochemical and hematological changes in their body which can be made clear from the several research papers. the aquatic pollution now-a days have become hot topic for the discussion and debates in various institutions, research papers, books and several manuscripts.

Indexed Terms- Industrial Effluents, Beheavioral Alterations, Acetylcholinesterases, Transaminases, Hematology

I. INTRODUCTION

Water is a most vital requirement and natural resource that exists on our planet and is essential for survival and the development of modern technology [1]. The problems related to sanitation, hygiene and drinking water differ fundamentally. Biochemical reactions and hormonal signaling which occurs in our body and also in other living systems require water for the reaction processes. All water pollution affects organisms that live in the water bodies and in almost all cases the effect is damaging not only to the individual species and populations but also to our rich aquatic biodiverse communities [2]. Water is absolutely necessary for all forms of life. The pollution of water bodies poses a potential threat to public health and aquatic ecosystems. It has become a valuable concern to realize the importance of water qualitatively and quantitatively [3]. Additional natural micropollutants are biologically produced taste and odor compounds [2], which are not primarily a toxicological problem but are of great aesthetic concern. There are also the millions of municipal and, particularly, hazardous waste sites, including abandoned industrial and former military sites, from which toxic chemicals may find their way into natural water, especially into groundwater.

Finally, when considering that more than 100,000 chemicals are registered and most are in daily use [4], one can easily imagine numerous additional routes by which such chemicals may enter the aquatic environment.

Fish play a indistinguishable role in our economy, trophic food chain and serve as an excellent ecological indicator. During the passage of time, increase in incidence of mass mortality caused by aquatic pollution has increased as these fish play important role for the carrier of toxicant and pathogen leading to gradually a significant decline in their population. The effect industrial pollution on our rich diversity of fish is still increasing day by day. Thus, aquatic pollution has turned to be highest cause of concern in developing countries [4,5].

For natural growth, survival and reproduction of fishes and other organisms a correct balance of physical and chemical properties should be maintained in the water system. these chemical parameters include TS (Total Solids), TSS (Total Suspended Solids), DO (Dissolved Oxygen), BOD (Biochemical Oxygen Demand), COD (Chemical Oxygen Demand), along with the physical properties such as colour, odour, temperature and pH of the inhabited water body. Fish are undoubtedly, act as a very important ecological tool to act as useful experimental models for assessing aquatic ecosystems that are expose to environmental pollution and associated beheavioral, morphological, biochemical as well as hematological changes so and so forth. The discharge of industrial effluents into receiving water bodies invariably results in the presence of high concentrations of pollutant in the water and sediment. Solid waste management policies and enforcement of sanitation laws in various should be practiced. Effluents have considerable negative effects on the water quality of the receiving water bodies and as such, they are rendered not desirable for fish health and survival, as it has been made clear by the studies done above. So, it has become our prior duty to save our natural resources which are on the verge of getting destroyed.

Physico-chemical properties due to toxicants in aquatic media exerts its adverse effect on fish physiology and directly or indirectly affecting human health via food. Release of heavy metals pesticides, fertilizers, radioactive and industrial waste into atmosphere has resulted in gradual contamination of aquatic habitat. Heavy metal pollution has been reported to affect the fish ovary and an increase incidence of follicular atresia [6].

Fish act as a very important tools for studying water pollution because any change in their surrounding directly or indirectly affects their overall change in behavior, morphology, biochemistry and hematological properties in their internal mileau. The fishes are one of the organisms that can be used to measure environmental degradation for some reason. First, fishes are sensitive to the wide array of direct stresses and second, they integrate the adverse effect of complex and varied stresses on other components of the aquatic ecosystem [7].

The heavy metal concentration in fish tissues reflects past exposure via water and/or food and it can demonstrate thecurrent situation of the animals before toxicity affects the ecologicalbalance of populations in the aquatic environment [8]. The obvioussign of highly polluted water, dead fish, is readily apparent, but the sublethal pollution might result only in unhealthy fish. Dupuy in 1998 reported that the fish health status in some polluted systems (estimated by the condition factor) indicated that the fish have a lower condition. Very low-levels of pollution may have no apparent impact on the fish itself, which would show no obvious signs of illness, butit may decrease the fecundity of fish populations, leading to a longterm decline and eventual extinction of this important natural resource [9]. Also, heavy metals are known to induce oxidative stress and/or carcinogenesis by mediating free radicals/reactive oxygen species [8,9]. In general, metals can be categorized as biologically essential and non-essential. The nonessential metals (e.g., aluminum (Al), cadmium (Cd), mercury (Hg), tin (Sn) and lead (Pb)) have no proven biological function (also called xenobiotics or foreign elements), and their toxicity rises with increasing concentrations [9]. Essential metals (e.g., copper (Cu), zinc (Zn), chromium (Cr), nickel (Ni), cobalt (Co), molybdenum (Mo) and iron (Fe)) on the other hand, have a known important.

- Morphological and beheavioral alterations

Mill effluents discharged in water bodies cause alterations and visible changes in their beheavioral patterns as compared to normal. Studies done on cyprinus carpio and mystus vittatus showed that sub-lethal concentrations of effluents showed that they were in stress conditions and they tried to resist in changing water environment ad reducing the harmful effects of effluents.exposure to effluents in fishes included initial hyper activity ,rapid opercular movements, frequent surfacing . other noticeable characters which implied a true picture of stress on the affected fishes were muscular spasm, more saliva secretion, labored breathing, loss of balancing and lethargy [8]. The initial increase in opercula movement can be taken as index of the stress felt by the fish exposed to pulp and paper mill effluent. the decrese in the opercular movement and the rate of oxygen consumption in fish suggestthe respiratory distress [8,9,10]. Since, the respiratory potentiality of the respiratory tissues are significantly altered, it can be expected that various industrial and textile mill discharges should have caused these types of anomalies. The rise in mucous secretion in the fish act as defence mechanism by which the fishes try to escape from the toxic compounds from entering inside their body [9].

Similar results were obtained in the studies done the fishes, some of the well noticeable morphological changes were red tints appeared around the jaws, due to hemorrhage.in later stages, opercular movements of fishes were slowed down although they try to stay at upper water surface. This was due to the hypoxic conditions because sufficient oxygen supply is not available for cellular respiration, as the copious amount of mucous secretion by fishes formed a thin film on delicate and sensitive tissue, thus, minimizing exchange of gases. Due to inability to respire, fishes are not able to maintain their balance and finally sink at the bottom which cause mortality in fish population [10,11,12].

The nature and rapidity of the beheavioral response towards any threshold stimulus indicates that varied types of industrial and mill effluents contains some amount of neurotoxin which, amomngst other things, might be active at the neuromuscular junction of the exposed animals [13]. It is abundantly clear that metals induce an early response in the fish as evidenced by alterations both at structural and functional levels of different organs include enzymatic and genetic effects, thereby affecting the innate immune system of exposed fish and/or increasing susceptibility to multiple types of disease.

Biomarkers can offer additional biologically and ecologically relevant information, a valuable tool for the establishment of guidelines for effective environmental management. So, it can be stated that fish biomarkers are necessary for monitoring environmentally induced alterations to assess the impact of xenobiotic compounds (i.e., heavy metals) on fish. Also, it is recommended that treatment of all kinds of Waste waters, sewage and agricultural wastes must be conducted before discharge into the aquatic systems. Also, enforcement of all articles of laws and legislations regarding the protection of aquatic environments must be taken into considerations.

- Hormonal alterations

The endocrine system regulates hormone-dependent physiologic functions necessary for survival of the organism and the species. Industrial and mill effluents can have either direct adverse effects on the endocrine glands and tissues, or their effects can be indirect through alterations of homeostasis and activities of non-endocrine organs [14]. Their effects are predominantly found on corticosteroid hormones, which together with the catecholamines epinephrine and norepinephrine, are the endocrine effectors of the physiologic response to stressors [15,16]. Cortisol, the major corticosteroid of teleost fish, is synthesized and secreted by the interrenal tissue situated in the head kidney or pronephros. The principal stimulant of cortisol secretion by the steroidogenic inter renal cells is adrenocorticotropic hormone (ACTH) released from the pituitary gland. Polishing treatment of wastewater effluent has the advantage that the aquatic environment, including the water resources, is protected from human pharmaceuticals and endocrine-disrupting compounds. Alternatively, if the presence of these compounds in drinking water is the major concern, various drinking water treatment processes, such as granular or powdered activated carbon, oxidation, and nanofiltration/ reverse osmosis, can be used for the removal of these compounds [15].

The activity of pituitary corticotropes, cells that synthesize ACTH, is regulated by corticotropin-releasing hormone (CRH) and other hypophyseal peptides [15]. Photoperiod and temperature are some of the environmental cues that modulate the activity of the HPI axis in fish [16]. A negative feedback effect exerted by cortisol at the level of the hypothalamus and the pituitary also regulates the production of ACTH. A similar organization of the HPI axis is evident in amphibians, although the major corticosteroid secreted is corticosterone and the interrenal tissue, organized in islets, lies on the ventral surface of the kidney [17]. Cortisol and corticosterone are synthesized from cholesterol, the precursor of all steroid hormones. Synthesis of corticosteroids involves first a cleavage of the cholesterol side chain, then hydroxylations mediated by several enzymes, including cytochrome P-450 [14].

- Physiological and biochemical changes

The gill epithelium is the very important site of gas exchange, ionic-regulation, acid-base balance, and nitrogenous waste excretion for fishes [11,12]. It serve a vivid multitude of vital functions for these aquatic animals. Gill anomalies are common symptoms of toxic effects on fishes of a wide variety of aquatic pollutants, including organochlorines, petroleum compounds, organophosphates, carbamates, miscellaneous herbicides, acidification, nitrogenous compounds, heavy metal salts, and chemotherapeutic agents [13]. According to various studies performed on gill histology and physiology from the fishes obtained from polluted water bodies all over the world showed the common morphological anomalies includeing hyperplasia with lamellar fusion, epithelial hypertrophy, telangiectasia which is marked dilation of terminal blood vessels, edema with epithelial separation from basement membranes, general necrosis, and epithelial desquamation [13].

Environmental stressors such as contaminants can cause a variety of biological responses in fish ranging from the biomolecular and biochemical to population and community-level effects. The growth in fish as influenced by principal ecological factors in the environment, such as seawater environment they inhabit, competition and food availability [18]. The physical size of the fish determines blood glucose levels, the larger of fish body size requires more energy to support their life and as a result, equally higher secretion of glucose. Hyperglycemia condition is not only influenced by the total length or weight but also depends on the environmental conditions and habitat quality.

Low dissolved oxygen can cause any toxic gases such as ammonia gas. High levels of ammonia can cause damage to gill tissue, where gill plates swell so that the respiratory system will be disrupted [19]. The effect of suspended solids on fish is directly on the gills of the fish [19] and therefore oxygen which enters the body is reduced due to gills that are covered in solids. This can interfere the process of respiration so that fish need more high energy to survive.

Based on the quality standard according to the Regulation No. 82/2001 on the Management of Water Quality and Water Pollution Control, the pH value in the research area, belongs to the category good enough for fish life ranging from 6-9 [16]. However, the high BOD indicates that the amount of oxygen needed by microorganisms to oxidize organic matter in the water is high; it means that the water is already in a deficit of oxygen. Meanwhile, the high number of microorganisms multiplies in the water due to the abundance of food available (organic matter). Therefore, BOD always indirectly associated with levels of organic matter in the water. This is supported by the discovery of a lot of rubbish in the surrounding area. The garbage is heavily stagnant on the beach and some are drowned in the bottom such as baby's diapers. This can affect the physical condition of the seawater such as decreasing the value of DO and increasing the need for O_2. Domestic waste usually contains high organic matter, which will cause the decrease of dissolved oxygen so that it can cause respiration of disturbed fishes [18]. If dissolved oxygen is unbalanced, then the fish will experience stress and may cause death. This is because the body's tissue cannot bind the dissolved oxygen in the blood and the brain does not get enough oxygen supply, a common condition called anoxia. Low dissolved oxygen can lead to the presence of toxic gases such as ammonia. High levels of ammonia can cause tissue damage to the gills, where the gill plates to swell so that the respiratory system will be disrupted [15].

Suspended Solid is one of stress factor in fish on the east coast of Pangandaran beside ammonia; organic chemicals (demand oxygen) and low dissolved oxygen. Many physiological changes that occur in response to environmental disturbances are now used routinely for assessing stressed states in fish. Stress responses are mediated through neuronal and endocrine pathways, known as the primary response, following initial perception of the stressor. The response to stress in fish is characterized by the stimulation of the hypothalamus, which results in the activation of the neuroendocrine system and a subsequent cascade of metabolic and physiological changes [20]. These changes enhance the tolerance of an organism to face an environmental variation or an adverse situation while maintaining a homeostasis status [24].

In hyperglycaemic conditions insulin inactivation occurs so that the process of glycogen formation is inhibited, glucose cannot enter the cells and cause high blood glucose levels. The rise in blood glucose is primarily generated by cortisol- mediated gluconeogenesis that also inhibits cellular uptake of circulating glucose thus increasing the levels in blood circulation.

Blood glucose levels can be used as an indicator of environmental stresses [19]. Under conditions of stress, the body of the fish emits immediate responses recognized as primary and secondary responses. The primary responsibility is the perception of an altered state by the central nervous system (CNS) and the release of the stress hormones, cortisol and catecholamines (adrenaline and epinephrine) into the bloodstream by the endocrine system. Secondary responses occur as a consequence of the released stress hormones [4], causing changes in the blood and tissue chemistry, e.g., an increase of plasma glucose [7]. This entire metabolic pathway produces a burst of energy to prepare the fish for an emergency [8]. Normally, the formed glucose will enter the cell will stimulate glycogenesis and lipogenesis. In the stress condition occurs response of receptors that have received stimulation, then the response will be forwarded to the hypothalamus and secrete catecholamine hormone that allows glucose into the cell. In hyperglycaemic conditions insulin inactivation occurs so that the process of glycogen formation is inhibited, glucose cannot enter the cells and cause high blood glucose levels. The rise in blood glucose is primarily generated by cortisol- mediated gluconeogenesis that also inhibits cellular uptake of circulating glucose thus increasing the levels in blood circulation. The increased level of glucose is a manifestation for the higher needs of tissues to fuel the metabolic needs of osmoregulation and an important source of energy for maintaining homeostasis in fish during chronic stress [18]. Thereby, blood glucose levels can be used as an indicator of environmental stresses [19]. In conclusion, the increase in level blood glucose in fish indicates that seawater, where were fish inhabit, were contaminated by pollutants.

The activity of transaminase enzymes sGOT/AST (serum glutamate oxaloacetate transaminase / aspartate aminotransferase) and sGPT /ALT (serum glutamate pyruvate transaminase/ alanine aminotransferase) indicate the impact of pollutants on fish health.generally ,these enzymes are distributed in the cells of vital organs such as liver,kidney, heart and gills.but an increase in their level in blood serum is an indication of tissue injury. Hence, it act as bio-marker to test the tissue injury and liver dysfunction [23].

Previous studies done on T. zilli and M. capito in Qaran lake in year 2019 suggest that under influence of different heavy metals and pollutants causing physiological and endocrinological stress, ultimately, leading to damage of tissue with concomitant liberation of transaminase enzymes into circulation [20].

Acetylcholinesterase enzyme serve as very important biomarker to assess the pollution status. acetylcholine esterase enzyme is vital for regulation of neurotransmitter acetylcholine in sensory and neuromuscular system of fish and other organisms [19]. Its main function is to break AchE into choline and acetic acid and then, to facilitate nerve impulse transmission from one cholinergic neuron to next one [22]. due to its inhibition, there is an spurt in the level of acetylcholine in circulation causing prolonged neural stimulation finally leading to tetany and death of organism.

Proteins play an important role in physiologically and biochemically. Enzymes which are engaged in metabolic pathways are in the form of protein and these proteins are made up of several blocks carbon compounds called amino acids which has amino group and carboxylic group. pollution causes declinement in proteins due to catabolism of protein into aminoacids to cope up with the hostile environment due to effluent stress. the reduction in protein content indicates that tissue protein undergoes proteolysis which results in production of amino acids and are used in TCA cycle for energy production during stress condition [22].

- Hematology alterations

Hematological techniques have been utilized to determine sublethal impacts of pollutants during the clinic diagnosis of fish physiology [19]. Blood

parameters are considered good physiological indicators of the whole-body conditions and therefore can be used in diagnosing the structural and functional status of fish exposed to toxicants [20]. Fish blood is very much susceptible both to internal and external environment fluctuations because pollutants majorly make their entrance inside body via these pathways.
Hematocrit values, hemoglobin content, number of red blood cells, white blood cells and other hematological parameters such as MCH (Mean Corpuscular Hemoglobin) and MCHC (Mean Corpuscular Hemoglobin Concentration) are the indicators of toxicity with wide potential for use in environment monitoring and toxicity studies [24]. Hematology may be a helpful tool in monitoring stress levels of aquatic pollution on fish. Hematological parameters are increasingly used as indicators of the physiological stress response to endogenous and exogenous changes in fish exposed to a complex mixture of available pesticides/pollutants in water bodies.

According to Pamila et al. [24] the reduction in hemoglobin content in a fish exposed to toxicant could be due to the inhibitory effect of those substances on the enzyme system responsible for synthesis of hemoglobin. The decline in Hb content of Cyprinus carpio L. was also observed by Chauhan et al. [25] and Ramesh and Saravanan [26] after exposure to dimethoate and chlorpyrifos respectively. The high hemoglobin content and Packed cell volume or Haematocrit values is related to the large anaerobic metabolic capacity of the species and its preferred environmental conditions and contamination caused by pesticide pollution because of the intensive agriculture dominant in the catchment and by possibly a complex mixture of contaminants could be occurring because of a confluence of both urban and agricultural pollution. This may also be due to impaired oxygen supply to various tissues, resulting in a slow metabolic rate and low energy production. Recently, Ramesh and Saravanan [22] also opined that the decrease in the PCV of C. carpio treated with sublethal concentration of chlorpyrifos was the result of either rapid oxidation of haemoglobin to methaemoglobin or release of oxygen radical brought about by toxic stress of the insecticide. The lowered RBC values would be attributable to the destructive action of pollutants released into the lake, because decreased RBC values are reported to be indicative of accelerated destruction of the cells and hemolysis which occur in response to toxicity [27]. Such destructions results in alteration of the selective permeability of the cell membrane. the discharge of waste may cause serious problems as they impart odour and can be toxic to aquatic animals. Declined RBC count was also reported by Svobodova et al. [28]. After exposure of Cyprinus carpio to chloropyrifos. It was seen that significant increase in the number of leucocytes (leukocytosis) in fish which was directly relative to the severity of stress condition and resulted from the direct stimulation of immunological defense due to the presence of pesticides/pollutants present in their aquatic environment [27].

- Genotoxic and Molecular Anomelies

Increasing loads of industrial, agricultural and commercial chemicals discharged into aquatic habitats could pose a serious public health problem and a threat to the aquatic ecosystem [28]. This increases the interest in studies for the evaluation of the genotoxicity of polluted waters [29]. The exposure of aquatic organisms to a variety of genotoxic chemicals raises the question about the potential effects of exposure on the health status of both current and future aquatic populations [30,32].

The micronucleus (MN) test is a useful method to assess genotoxicity in aquatic environments [33]. Micronuclei arise from chromosomal fragments or whole chromosomes that are not incorporated into daughter nuclei at mitosis [34] and could be easily visualised in peripheral erythrocytes. In addition, there are some nuclear and cellular abnormalities that may be considered as genotoxicanalogues of micronuclei, and may also be due to genotoxic agents [36]. Furthermore, toxic heavy metals could result in injury to cells, which may die from necrosis and/or apoptosis [37].

Cells normally undergo apoptosis in response to mildly adverse conditions, whilst exposure to severe conditions will result in necrosis. Both processes are truly distinct and have important implications. A molecular hallmark of apoptosis is degradation of nuclear DNA into fragments with the size of an oligonucleosome, as a result of activation of endogenous endonucleases, recognised as a ‘DNA ladder' on conventional agarose-gel electrophoresis [38].

Comet assay or alkaline single-cell gel electrophoresis (SCGE) is a very simple, fast, and sensitive technique for assessing genotoxicity by quantifying the amount of DNA damage caused in individual cells. It is used as an important tool for environmental monitoring and assessing health of aquatic animals by detecting DNA damage in fish, clams, shellfish, and mussels. Comet assay is used to detect genetic damage in the form of DNA strand break, which is an additional sensitive indicator. This assay has been applied in aquatic environments to assess and monitor the health and genetic condition of both vertebrate and invertebrate organisms.

Most of the toxic substances which are abundant in various classes of industrial effluents that produce genotoxicity have been found to produce reactive oxygen species as well as electrophilic free-radical metabolites that interact with the DNA and lead to its disruption. Studies conducted by Chandra and Khuda-Bukhsh in 2004 and Klopman, Conttreras, Reosenkranz, and Waters, in 1985 showed that during the metabolism of Azadirachtin, electrophilic ions and free radicals are produced, which interact with the nucleophilic sites in DNA and lead to breaks and other related DNA damage.

It is also reported that the oxidative stress in an organism plays an important role to inducing cytotoxicity and genotoxicity in different vital tissues such as liver, lungs, kidney and brain according to Moore, Yedjou and Tchounwou in 2010.

- Aquatic pollution and human health

A group of chemicals that have been and continue to be of greatest environmental concern are denoted as POPs. They include a diverse set of high-volume production compounds that are intentionally produced as well as compounds that form as accidental by-products of a variety of combustion processes. A compound is commonly classified as a POP if it exhibits the following four characteristics:

1. Persistent in the environment, which means that chemical, photochemical, and biological transformation processes do not lead to a significant removal of the compound in any environmental compartment;
2. Prone to long-range transport, thus to global distribution, even in remote regions where the compound has not been used or disposed, owing to the compound's physical-chemical properties;
3. Bioaccumulation through the food web and
4. Toxic to living organisms, including humans and wildlife.

Some prominent classical POPs (also called "legacy POPs" or "the dirty dozen") have been listed and dealt with in two international conventions (the Aarhus Protocol and the Stockholm Convention) with the goal to assess the POPs' global presence and to reduce their emissions to the environment (29). They primarily encompass highly chlorinated compounds [e.g., dichlorodiphenyltrichloroethane (DDT), PCBs, polychlorinated dioxins and dibenzofuranes] and polycyclic aromatic hydrocarbons (PAHs).

- Diffuse sources:

Widespread activities, with no discrete source, that cause pollution these conventions allow addition of new compounds to the list. Recent examples of such "emerging pollutors" that are under consideration to be added are the polybrominated diphenyl ethers (PBDEs) widely used as flame retardants (31, 32), and a variety of perfluoroalkyl chemicals (PFCs) that, because of their very special properties (33), are used in numerous industrial applications (34).

Regular monitoring, public awareness and strict law enforcement are needed to design an approach to deal with the such a big problem due to these industries and improve environmental protection of the precious ecosystem and our valuable flora and fauna.

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