ISEIS

Journal of Environmental Informatics Letters 13(1) 25-37 (2025)

Journal of Environmental Informatics Letters

www.iseis.org/jeil

Histopathological Changes in Teleost Kidney as Indicators of Aetiopathogenic Involvement

T. Bhattacharyya[1 *], and A. Bardhan[2]

[1] *College of Fisheries, Assam Agricultural University, Raha, Assam 782103, India*
[2] *Department of Aquatic Animal Health Management, The Neotia University, Pargana, West Bengal 743368, India*

Received 11 March 2024; revised 25 June 2024; accepted 19 October 2024; published online 29 January 2025

ABSTRACT. Pathogenic invasion acts as one of the most important aspects of loss of livestock in aquacultural practice across the globe. Different aetiological agents show peculiar differential effects on the vital organs of the fishes and thus are easily detectible through the histological studies of those affected organs. Studies have shown progressive histological changes in fish kidney including changes in the glomerulus as well as the nephric tubules due to pathogenic effect. This review tries to highlight the importance of histological methodologies as the modern instrument of disease diagnosis as well as gives off non-biased information by different authors, that act as both synergistic and antagonistic to each other varying with species and environmental changes. Moreover, comparative gradual changes and the alteration of the function of kidney via pathogenic infestation have also been discussed in detail with relevant case history.

Keywords: nephric tissues, aquaculture, diseases, aetiology, histopathology

1. Introduction

In fish health research, the utilization of histopathological indicators is a common practice, offering valuable insights into both chronic and acute infections caused by pathogens in various organs, as well as aiding in the assessment of fish stress levels. At the cellular level, changes induced by pathogenic invasions provide clear and accessible information of the harmful effects caused by specific pathogens, making them pivotal in pathology studies. Modern technology heavily relies on histology due to its specificity and rapid insights into various disease conditions. Histological studies employ different stains to highlight specific cellular components and stands as the gold standard diagnostic method, offering unparalleled reliability in diagnosing neoplasia and providing essential evidence for reaching conclusive diagnoses (Rastogi et al., 2013). However, it is important to note that even with high-quality slide preparation, mishandling and improper fixation can occur, resulting in tissue alterations termed as "Artifacts". These artifacts pose significant diagnostic challenges but can be minimized or prevented through diligent precautions (Taqi et al., 2018).

For a long time, different studies have been conducted on the different adverse pathogenic effects on fishes and histopathological changes played a major role as the differentiating tool in this aspect. Although the studies are present on limited strains, different species of teleosts tend to show diversified symptoms for a common pathogen. *Aeromonas* infection being common in natural and farmed water bodies, plenty of studies can be found showing diverse effects in case of carps, tilapia and channel catfishes. *Streptococcus* and *salmonella* are found to be fatal whereas the other pathogens like fungal, protozoal and viral case studies are also associated with secondary bacterial infection leading to heavy mortality. Iridovirus is being found to be the most influencing in different trouts and causing heavy hemorrhagic and necrotic changes in cellular level studies. Ornamental fish are found to be heavily infested by viruses and bacterial pathogens both in wild and farmed conditions. Epizootic symptoms due to *Aphanomyces* infestation and protozoal infections impose noticeable changes in studies on tilapia, carp and farmed salmons. However, as the causative pathogenic agent changes, the pathological symptoms of these infectious diseases get changed too. But in all cases, the haemorrhagic conditions remain the same. Fungal diseases are characterized by open necrotic lesions and protozoal diseases can be diagnosed by the sporogenic effects in the tubules and cellular infiltration along with the macrophagic aggregates due to the proliferative disease characteristics. Bacterial infections as mentioned before can be primary and secondary both depending on the causative agents and thus show diverse changes in context to cellular changes on the other hand in different cases of viral infections, directly virion strains are being noticed in the kidney cells and most important and common diagnostic symptoms can be infiltration of lymphocytes and proliferation in in the melano macrophagic centre (MMC). We can find several literatures on the previous studies done on the histopathological studies of fish liver and gills, but such cumulative data are scarce in case of kidney pathology. Moreover, the kidney is the primary

* Corresponding author. Tel.: +91-85839-45217.
E-mail address: avishek.bardhan@tnu.in (T. Bhattacharyya).

ISSN: 1726-2135 print/1684-8799 online
 doi:10.3808/jeil.202400145

haematopoietic organ in fishes and slight histological changes can invariably affect the overall health of the fish as considered to help in generating immunological response. Underlying hypothesis explored in this study posited that teleost's respond to an etiological agent, with the kidney exhibiting the initial and most intense histological alterations when compared to control specimens. This comprehensive review was meticulously crafted to evaluate and document such changes observed in teleost kidneys. Special attention was given to potential artifacts that could potentially impede accurate observations, ensuring a reliable analysis for future research endeavors. The main objective of this review lies in the assembly of all the histopathological studies on fish kidney via an efficient summarization and thus helping the readers to effectively differentiate between different infectious pathogenic effects. This study also aims to elevate the similarities in different case studies in a cumulative manner so that it is helpful for the readers to avoid any further confusion regarding their future research aspects.

2. Teleost Kidney Structure and Function

The kidneys located above the alimentary canal and below the vertebral column, are vital for excretion and osmoregulation in teleost. Despite variations in adult structure among species, they develop embryonically as paired organs. Unlike humans, in teleost, there are three types of kidneys: pronephric, mesonephric, and metanephric. The head kidney is pronephric, functioning as a hematopoietic organ, while the trunk or tail kidney is mesonephric which is also called the ophisthonephros (back kidney) is responsible for excretion and osmoregulation (Khanna and Singh, 2015). Pronephric kidneys are observed in fish embryos and some adult lampreys and hagfish which are believed to be the most anterior part of the archespores or first kidney found in a few larval hagfishes (McMillan, 2011). The kidney consists of haemopoietic, reticuloendothelial, and excretory cellular components, with nephrons comprising Malpighian corpuscles and renal tubules. In fish, the glomerular portion is concentrated posteriorly, whereas the excretory tubules are anteriorly positioned. The glomerulus facilitates the ultrafiltration of blood, removing proteins and sugars. The filtered blood component without proteins and macromolecules is termed the primary filtrate. The kidney's structure and function vary among fish species, adapting to their environments (Khanna and Singh, 2015).

In mature species, the head kidney can transform into a mesonephric structure, demonstrating the adaptability of renal function. The renal tubule is intricately organized into four segments: the ciliated, brush-bordered proximal tubule, further divided into the first and second proximal tubules; an intermediate part (which may be absent in certain species); and the distal ciliated segment, leading to the collecting tubule (Khanna and Singh, 2015). Marine teleost might lack the distal tubule (Khanna and Singh, 2015). The primary role of kidney tubules is to eliminate excess water, electrolytes, waste, and foreign substances from the primary filtrate. Selective reabsorption primarily occurs in the proximal tubule, where active and passive transport mechanisms facilitate the reabsorption of water, glucose, Na^+ ions, and Cl^- ions, returning these vital components to the body through peritubular capillaries. Remarkably, up to 99% of the filtrate materials are reabsorbed here. Conversely, the distal and collecting segments serve as key sites for tubular secretion, involving substances like H^+ ions, ammonia, drugs, and K^+ ions transferred from plasma to the renal tubules, contributing to the formation of urine (Khanna and Singh, 2015). This intricate process ensures the precise regulation of the body's internal environment.

In addition to its excretory function, the kidney serves as a crucial osmoregulatory organ, ensuring the maintenance of ionic balance and water equilibrium in both the intrinsic and extrinsic body environments. Through urine, the kidney excretions and other waste substances, regulating their concentration to create either hypertonic or hypotonic conditions. The renal tubules play a pivotal role in actively absorbing and secreting desired and undesired materials, respectively. Given its dual role in hematopoiesis, nutrient secretion, and absorption, the kidney is highly susceptible to pathogenic invasions (Khanna and Singh, 2015). Consequently, it becomes a prime site for pathogen growth, leading to various histopathological symptoms specific to the infecting pathogen and the diseases it causes. This sensitivity highlights the importance of the kidney in understanding the body's overall health and immune responses (Khanna and Singh, 2015).

3. Histological Differentiation in Different Parts of A Healthy Fish Kidney

In comparative analysis during different case studies, generally the histological structures of the organs of a healthy fish act as the standard specimens to understand the levels of damage due to pathogenic involvement. But according to a few authors, even the fresh fishes might also display some histopathological disorders in addition with a few inflammatory reactions (Bernet et al., 2004). Saraiva et al. (2015) mentioned in their histology-based health assessment study on farmed Sea bass that 27.6% of the specimens showed hyperemia, vacuolar degeneration of tubular epithelium, accompanied with few cases involving necrosis of hematopoietic interstitial tissues. These findings have been corroborated by several authors in both farmed and wild Sea basses (Roberts, 2012).

3.1. Malpighian Corpuscle

Malpighian tubules consist of a glomerulus enclosed by a bowman's capsule. The inner wall of the capsule is in vicinity with the capillaries of glomerulus (Figure 1 and Figure 2). The filter consists of the endothelium of the glomerular capillaries, visceral layer of Bowman's capsule and their combined basal lamina (Figure 3). The afferent tubule, involved in the entry of blood into the glomerulus, has granules in the epithelioid cells which help in regulating the glomerular filtration rate (GFR). The efferent arteriole leaves the glomerulus (Figure 1) making a network all around the tubular part of the nephron. The visceral layer of the Bowman's capsule is composed of podocytes, which form fenestrations acting as filtration slits during the

ultrafiltration process. These podocytes surround the glomerular capillaries (Figure 4) by piercing through the thin endothelium with the help of extended branching arms fringed with foot like processes called the pedicels (Figure 4) The basal lamina sheaths over the endothelial layer on which the pedicels get attached (Figure 5). The fenestrations open into the glomerular space. Mesangial cells are occasionally seen as a part of the endothelium helping in the elimination of the fragments of degenerating material (Figure 3) (McMillan, 2011).

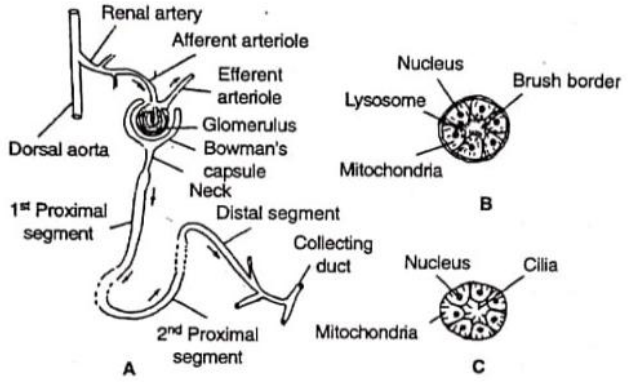


Figure 1. (a) Teleost kidney and its parts, (b) Transverse section (T.S) of proximal segment, and (c) T.S of distal segment. (Source: Khanna and Singh, 2015).

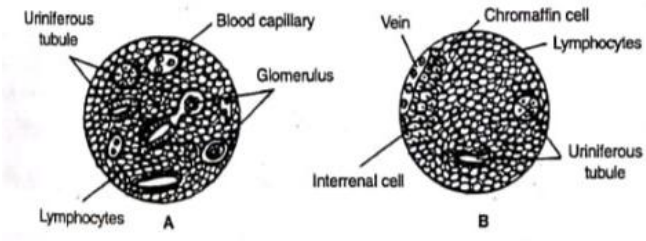


Figure 2. (a) T.S Trunk kidney, (b) T.S Head kidney (Source: Khanna and Singh, 2015).

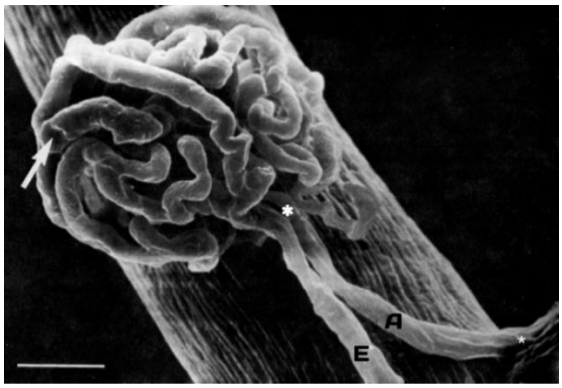


Figure 3. Scanning electron micrograph of a corrosion cast of the glomerulus of a rainbow trout; an arteriole lies behind. A, afferent arteriole; E, efferent arteriole; arrow, indentation from an endothelial cell. Scale = 20 mm. (Source: McMillan, 2011).

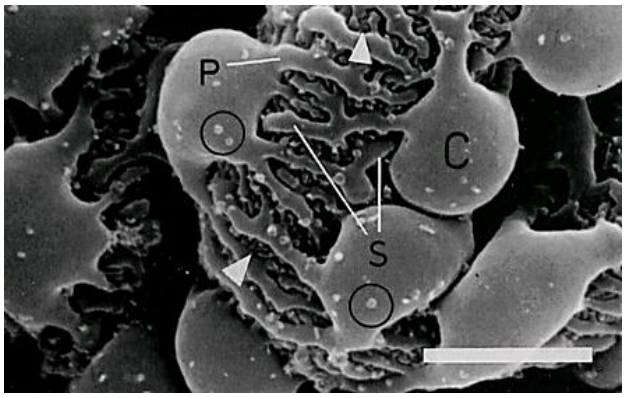


Figure 4. Scanning electron micrograph of podocytes from the glomeruli of rainbow trout (*Salmo gairdneri*). Podocytes embracing the capillaries have rounded cell bodies (C), primary processes (P) branching to secondary processes (S) and tertiary or foot processes (arrowhead). Scale = 2.5 mm. (Source: McMillan, 2011).

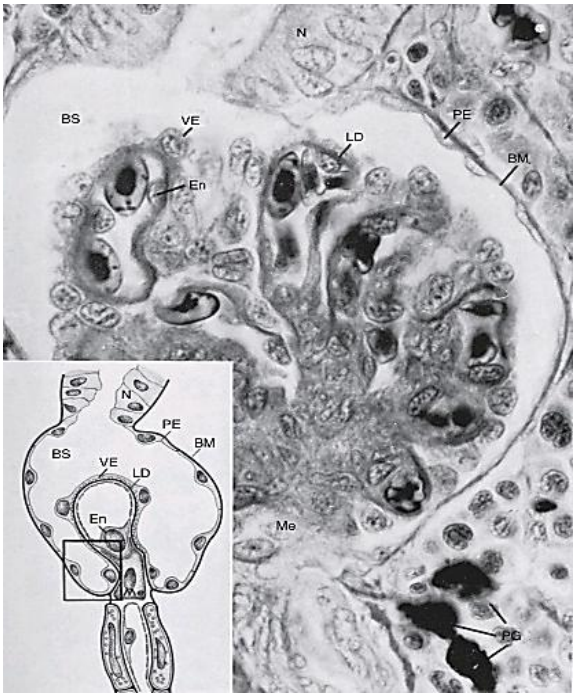


Figure 5. Photomicrograph of a section of the renal corpuscle of a trout. Inset: Schematic drawing of the glomerulus of a freshwater trout. Abbreviations: BM, basal lamina of the parietal epithelium; BS, nephric space; En, endothelial cell of a glomerular capillary; Me, mesangial cell; N, neck segment; PE and VE, parietal and visceral epithelium of the nephric capsule; LD, basal lamina between the endothelium of the capillary and the visceral epithelium; PG, pigment granules. (Source: McMillan, 2011).

The adverse effects on glomerular corpuscles due to pathogenic invasion can include glomerulitis or glomerular necrosis leading to hyperplasia, cellular proliferation, reduction of Bowmen's space, neoplasia etc. These cellular abnormalities

can lead to affect the GFR, can cause interruption in the ultrafiltration of the kidney because of the glomerular necrosis and Bowmen's space reduction. Moreover, neoplasia and cellular proliferation can lead to hemorrhages to the hematopoietic tissue which leads to anaemia, asphyxia etc blood cell related issues. Besides this, the thickening of the basement membrane is another kind of response to the pathogenic infection to prevent the pathogen to invade inside. This kind of response can again lead to decreased passage of primary filtrate into the Bowmen's space. Bowmen's capsules being affected can lead to the entry of blood proteins like Albumin and Globulin inside the filtrate and thus get excreted out of the body. This might affect the osmoregulation as well as the oxygen carrying capacity of the RBCs.

3.2. Proximal Tubule I

PTIs are identified by the presence of columnar epithelium with basal or sub central nuclei, prominent brush border and a well-developed apical endocytic system of vesicles, vacuoles, and lysosomes. Moreover, characteristically present large but scarce mitochondria and multiple peroxisomes can also be seen in Figures 6(b) and 7(c) (Resende et al., 2010).

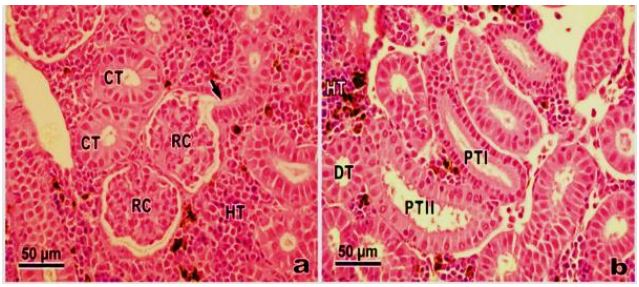


Figure 6. Light micrographs of paraffin sections from brown trout trunk kidney, showing the different stereologically analyzed components. In (a): Among the several structures present in this figure, two renal corpuscle (RC) and two collecting tubules (CT) stand out. Note the connection between one of the renal corpuscles and the initial portion of a proximal tubule, the neck segment (arrow). In (b): Image showing several segments of renal tubules, first (PTI) and second (PTII) segments of the proximal tubule and distal tubule (DT), HT, haematopoietic tissue (Source: Resende et al, 2010).

3.3. Proximal Tubule II

PTIIs are distinct from the other renal tubule segments by having a high columnar epithelium with central nuclei, a brush border and unlike PTI, showing the absence of the apical endocytic system with small cisternae of rough and smooth endoplasmic reticulum and lysosomes in Figures 6(b) and 7(d) (Resende et al., 2010).

The columnar epithelium with its brush border helps in increasing the surface area for the selective absorption of small peptides and simple sugars and the mitochondria helps in generating energy during active absorption and sometimes helping in the secretion of the bivalent ions like Mg^{2+} into the filtrate. Flerova et al. (2023) assume in their studies that the endoplasmmic system acts as the ion pump for the secretion of bivalent ions in the proximate tubules. Studies have shown that thus, proximate tubules act as both absorbing and secretion sites for ions depending on the osmolarity condition.

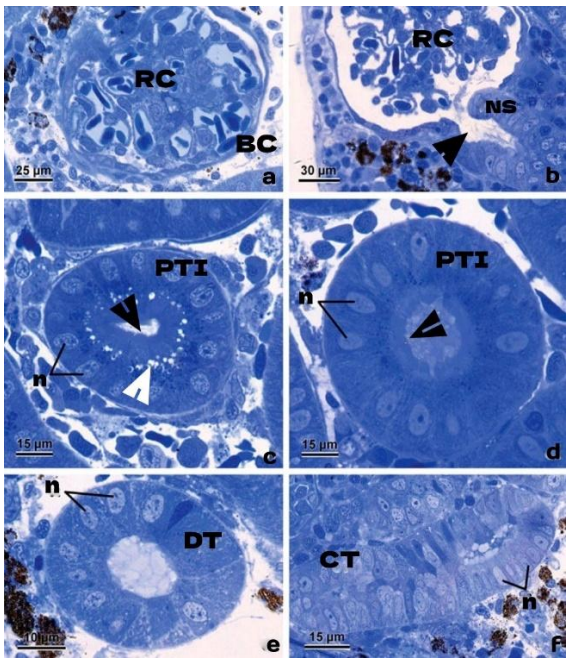


Figure 7. Light micrographs of semithin sections from brown trout trunk kidney showing different nephron portions surrounded with haematopoietic tissue. Note the dark melanin pigment. In (a): Renal corpuscle (RC), with the Bowman's capsule (BC) surrounded capillaries wherein erythrocytes can be depicted. In (b): A renal corpuscle and the initial portion of renal tubule, the neck segment (NS). Verify the presence of cilia (arrowhead) from epithelial cells in the lumen. In (c): PTI. Observe the basally located nuclei (n) and the characteristic apical cell portion, plenty of endocytic vesicles (arrow heads), and an evident brush border (arrow). In (d): PTII showing the epithelial cells with central nuclei (n) and apical brush border (arrow). In (e): Distal tubule (DT), with the characteristic epithelium possessing basal nuclei (n) and devoid of brush border. In (f): Collecting tubule (CT) longitudinal section, showing the columnar epithelium with basal nuclei (n) (Sources: Resende et al, 2010).

Histological changes in the proximal tubules directly affect the osmoregulatory function of fish kidneys. Proximal tubules help in the active and passive absorption of the selective materials inside the blood and thus help in the maintenance of the osmotic pressure in the blood and prevent nutrient loss. Pathogenic infection can lead to hypertrophy, vacuolization and tubular necrosis. The damage to the columnar epithelium and sloughing off the epithelial layer will cause enormous and direct influence on the reabsorption capacity and thus the urine will be hypertrophic and osmoregulatory imbalance will harm

the organism homeostasis. Hypertrophy can lead to degeneration of cellular components, such as mitochondria like cell organelles which will lead to loss of ability to cause active absorption and secretion of ions from and into the filtrate respecttively. The recirculation of the ions will be hampered with the connection blockage with the peritubular capillaries and capillary damage.

3.4. Distal Segment

Distal tubules are devoid of brush border and display a low cuboidal epithelium with basal nuclei, great density of mitochondria arranged perpendicular to the basal lamina and parallel to the cell membrane infoldings and sometimes a few apical micro villi in Figures 6(b) and 7(e) (Resende et al, 2010).

The cuboidal epithelia helps in secretion of ions along with the mitochondrias growing in number with more sectretory in nature. The cuboidal cells are generally taller than usual for the sake of their work function.

The distal segment along with the collecting tubule works for the tubular secretion of ions like K^+ and H^+ ions, ammonia etc. This part mostly secretes the ions in an active manner. So, because of the pathogenic infection, the secretory nature gets hampered. Moreover, multiple necrotic lesions can lead to heavy hemorrhages that have an adverse effect on the organism, leading to fatal condition.

3.5. Collecting Tubule

Collecting tubules typically are characterized by the columnar epithelia with basal nuclei and the presence of some smooth muscle cells additionally with connective tissues around the basement membrane forming an irregular lumen in Figures 6(a) and 7(f) (Resende et al., 2010).

Columnar epithelium again helps in the secretion of other components of the urine into the filtrate. The change of secretory compounds and quantity might be the reason for the cellular change in between distal tubule and collecting duct.

Infection in collecting duct intervenes with the excretion of drugs, ammonia, secretion of ions and water excretion which in turn hampers the osmoregulatory balance and imposes severe fatality inside the organism. The tubules, being one of the most important nutrient rich structures of the kidney, are highly prone to pathogenic infection. These infections can run deep inside the cell and cause abnormality in the cellular organelles which in turn happen to change the major cellular activities of the organism.

4. Cellular Level Changes Seen in Different Parts of Fish Kidney Because of Pathogenic Invasion

Histological changes are observed in the haemopoietic tissues and the kidney's excretory system, specifically in the nephrons, while the tubular systems exhibit minimal histopathological alterations. The haemopoietic tissues, inherently active and sensitive, are profoundly influenced even by toxins originating from other tissue systems (Khanna and Singh, 2015). Viral invasions often lead to cytolytic hematopoietic necrosis and hemolytic anemia. Hyperplasia and hypertrophic changes result in tissue deformation and are indicative of an inflammatory response. Bacterial infections can induce granulomatous lesions and fibrosis in the haemopoietic tissue (Khanna and Singh, 2015). The excretory system primarily involves changes in the glomerulus of the nephron. Proliferative changes encompass hyperplasia and membranous alterations, leading to glomerulonephritis in older fishes. Histological changes include thickening of Bowman's capsule and diffuse thickening of the glomerular basement membrane. Chronic bacterial diseases may result in the formation of fibrinous glomerulus, often accompanied by swelling and sloughing of epithelial cells in Bowman's capsule (Khanna and Singh, 2015). Fungal infections induce osmoregulatory failure due to chronic glomerulonephritis, leading to hyperplasia of glomerular cells and destruction of capillary lumina. In cases of degenerative processes in haemopoietic tissues, the excretory ducts experience tubular necrosis or fibrosis (Khanna and Singh, 2015). Certain protozoans can damage tubular epithelium cells. Table 1 comprehensively briefs about all the cellular changes observed in the nephric tissue. Nevertheless, histopathological identification is solely based on personal interpretations, the table lists possible cellular anomalies during aetiopathogenic infections. Different case studies with respect to the different pathological infections and influence on fish kidney have been discussed below.

4.1. Bacterial Diseases

Bacterial diseases in teleosts are most common and diverse in nature with multiple pathogenic variabilities. *Aeromonas, Vibrio, Salmonella, Staphylococcus, Flavobacterium* and *Streptococcus* infections are generally frequent in case of the freshwater species. In addition to this, *Ranibacterium salmoninarum* causing bacterial kidney disease is another matter of concern for the farmed fish these days. Different species of *Aeromonas* like *A. Hydrophila*, *A. Caviae*, *A. Ddhakensis*, *A. Salmonicida* etc are generally found in different previous studies in a prevalent manner in comparison to the other bacterial genus. *Vibrio* is one of the most threatening pathogens in fresh water as well as marine fishes. Salmonella causes high mortality in farmed fishes with respect to the existing studies. In a few cases, multiple bacterial infections are seen behind a certain disease case like Black Body Syndrome (BBS). Although ample in number, only a few bacterial pathogens are being seen to work repeatedly with different histological studies in fishes most probably due to their extensive case availability. However, most of the bacterial pathogenic infections tend to show a few general histopathologic symptoms associated with the fish kidney, like extensive haematopoietic necrosis, macrophagic aggregations and infiltrations of cells, tubulonephritis, vacuolization sometimes in addition to glomerulopathy and congested tubules.

Bacterial Kidney Disease (BKD), caused by *R. Salmoninarum*, manifests as a chronic bacterial ailment in trouts, characterized by coagulative necrosis, typical granulomas, and open lesions in head kidney and other renal tissues. Necrotic centers

Table 1. Different Histopathological Changes in Parts of Kidney as A Biomarker of Aetiopathogenic Invasion.

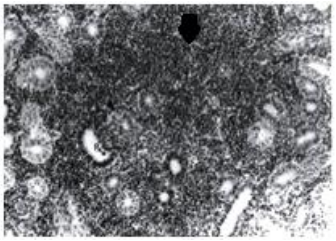
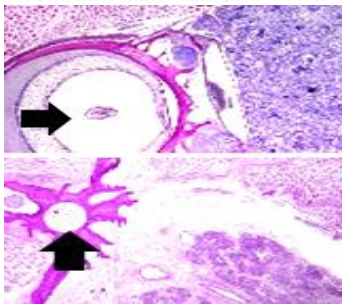
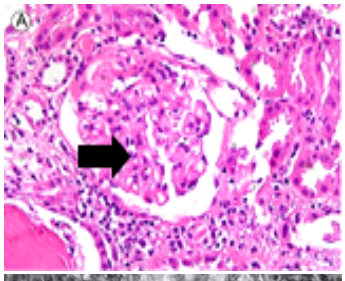
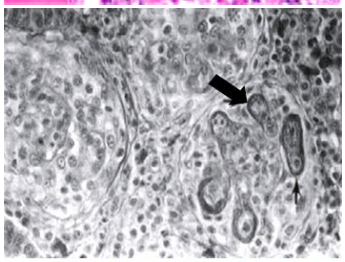
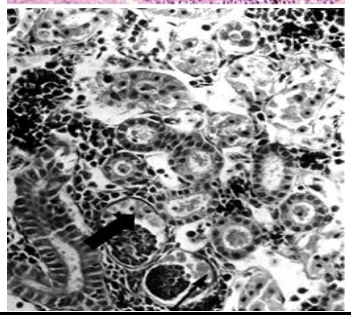
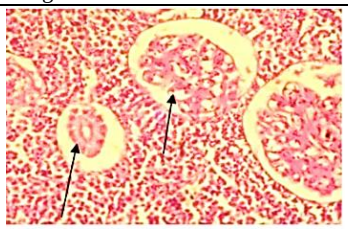
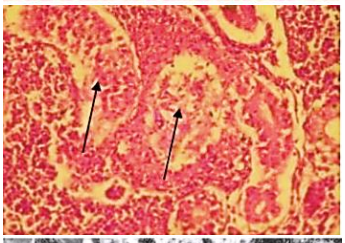
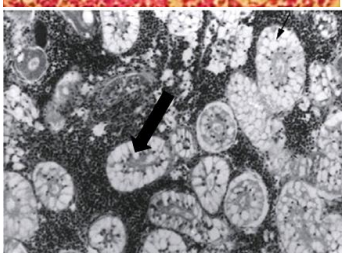
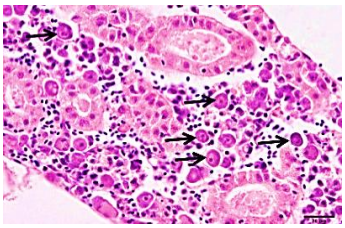
Location	Cellular changes	Images	Reference
Glomerulus	Hematopoietic hyperplasia (Indicative of excessive production of erythrocytes and other associated cells)		Roberts, 2012
	Neoplasia		Lombardini et al., 2014
	Cellular proliferation (Indicative of lymphocyte proliferation or glomerulopathy)		Roberts, 2012
	Thickening of epithelial cells in basement membrane (Preventive measure to limit the entry of pathogens)		Roberts, 2012
Renal tubules	Sloughing off epithelial cells (necrosis of cells leading to their death)		Roberts, 2012

Table 1. Continue

Location	Cellular changes	Images	Reference
Renal tubules	Atrophy and necrosis		Saharia et al., 2018
	Necrosis of tubular cells		Saharia et al., 2018
	Intracellular vacuolation		Roberts, 2012
	Hypertrophy		Jung-Schroers et al., 2016

in renal parenchymal tissues surrounded by a fibrous capsule, with a mixture of epithelioid macrophages, lymphocytes, and frequent giant cells were being observed in Brook trouts by Eissa and Faisal (2014) associated with the multiple scattered creamy nodules throughout the kidney tissues. Gram-positive coccobacilli were observed within the necrotic tissue as well as other layers of the granulomatous tissues. Caseous masses are generally surrounded by a fibroblast layer, often accompanied by fibrosis of the haemopoietic tissue with addition of epithelioid macrophages and lymphocytes in the hematopoietic tissues.

Aeromonas hydrophila, a common freshwater, facultative anaerobic bacterium, causes health issues in farmed freshwater fish species. Studies on *Heteropneustes fossilis* infected with *A. hydrophila* revealed notable histopathological changes in the kidney. Infected fish displayed uniform distribution of bacterial cells throughout the head kidney, haemopoietic tissue system and renal tubules. Atrophy of haemopoietic sinusoids, surrounded by fibrinoid depositions, along with diffused tissue necrosis, was evident (Islam et al., 2008). Additionally, non-infected striped catfish, *Pangasianodon hypophthalmus*, administered oral vaccines of *A. hydrophila* free cells exhibited adverse kidney histological changes, including destruction of Bowman's capsule, glomerular necrosis, tubular necrosis, leukocyte infiltration, and corpuscle tubular degeneration (Mamun et al., 2020). Similar results were observed in Nile tilapia and goldfish studies infected with *A. hydrophila*, including tubular degeneration, mononuclear cell infiltration, necrosis between renal tubules, occlusion of tubular lumens due to hemosiderin deposition, and degradation of Bowman's space (Ibrahim, 2017; Moneim et al., 2019; Rosidah et al., 2020). Studies on channel catfish infected with the same pathogen demonstrated the lysis of cytoplasmic organelles and nuclear structures in the anterior kidney, with degenerated bacterial cells engulfed by phagosomes of phagocytic cells (Abdelhamed et al., 2017). Outer membrane protein antigen vaccination of the same pathogen showed degenerative changes like vacuole formation in the head kidney, melanomacrophagic centre formation, hemocytic infiltration, necrosis constricted lumen of nephric tubules, glomerulopathy with diluted Bowmans's space and inflamed nephric tubules in Labio rohita (Biswas et al., 2021). In Osphronemus gouramy this bacterium shows piknosis and inflamatory necrotic conditions in the kidney (Rozi et al., 2018).

Hemorrhagic septicemia is a disease that can be caused by both bacterial and viral infections. In cases of bacterial infec-

tion, *Aeromonas* spp. is a notable concern (Austin and Austin, 2012). In bacterial septicemia, localized colonies of organisms can be observed in the haemopoietic tissue. These colonies are likely embolic in origin and form within a fibrinous, necrotic glomerulus in chronic stages. Chronic conditions are also marked by the frequent swelling and sloughing of cells in Bowman's capsule. A case study on bacterial septicemia in Rainbow trout caused by *Vibrio anguillarum*, conducted by Ceylan et al. in 2019, revealed various effects on the fish kidney, including siderosis, necrosis, hyperemia, hemorrhage, infiltration of mononuclear cells, and vacuolar degeneration. Siderosis was observed to increase from day 1 of infection until the 15th day post-infection. Roy et al. (2018) working with *Aeromonas* caviae on Nile Tilapia, *Oreochromis niloticus* had shown acute septicemia where the kidney tissues had glomerulopathy with dilated Bowman's space, nephropathy with the loss of tubular epithelial cells, obliterate as well as inflamed nephritic tubules, melanomacrphagic aggregate, necrosis, wide lumen and thickening of lumen lining.

Various species within genera such as *Pseudomonas*, *Vibrio*, and *Bacillus* is responsible for inducing BBS in fishes. It is acknowledged that BBS is linked to five types of pathogenic bacteria (Izwar et al., 2020) causing significant mortality in both farmed and wild species. Bacteria utilize kidneys as a site to obtain nutrients for their metabolic needs, thereby facilitating natural reproduction. Nuryati et al. (2023) conducted a study on *Lates calcarifer* infected by bacteria associated with black body syndrome. They observed that kidney tissues exhibited more pronounced deterioration compared to the liver, characterized by varying levels of necrosis due to different bacterial infections. Among these infections, *Vibrio harveyi* inflicted the most severe damage. Histological analysis revealed extensive immune-related cell infiltration, severe hemorrhagic conditions, swollen renal tubules, and sloughing of epithelial cells into the lumen (Dong et al., 2017).

In a study by Magi et al. (2009), adverse effects of *Pseudomonas anguilliseptica* infection in Turbot, *Psetta maxima* were described with the histological changes in kidney which include dialation of sinusoids, slight inflammatory response underlying the kidney capsule tissue (initial stages of infection); oedema, focal necrosis in interstitial kidney tissue (during progressive period of infection) and lastly leading to extensive necrosis of hematopoietic cells as well as dialation of peritubular capillaries and necrosis of tubular epithelium and glomeruli.

Aeromonas salmonicida is the bacterium responsible for Furunculosis in both freshwater and marine species. This infection predominantly manifests in internal muscle tissues and kidney tissues. Ling et al. (2019) conducted experimental work on crucian carp and observed significant hemorrhagic inflammations in both the haemopoietic and renal tissues.

Aeromonas dhakensis were found to induce inflammation of kidney in hybrid tilapia via extra cellular proteins characterised by infiltration of focal and multifocal lymphocytes and erythrocytes while the bacterial cells caused inflammation by necrosis of erythrocytes in kidney tubules (Soto-Rodriguez et al., 2018).

He et al. (2017) investigated the pathogenic effects of *Streptococcus agalactiae*, a Group *B Streptococcus* (GBS), on Oreochromis niloticus. Infected individuals exhibited histological changes in the kidney, such as tubulonephrosis and a sharp decrease in haemopoietic tissue. The glomerulus became congested, Bowman's capsule accumulated necrotic debris, and the renal tubule epithelial cells exhibited necrosis characterized by decreased nuclear chromatin, as well as swelling and vacuolation of mitochondria. Similar results were observed in the case of Schizothorax prenanti by Geng et al. (2012). Su et al. (2017) demonstrated results due to infection of the same pathogen in different doses in tilapia which included severe hemorrhages in renal interstitia in association with dissolution of tubules, fibrin precipitation and leucocyte infiltration in necrotic foci, low grade interstitial nephritis and granulomas containing necrotic centers surrounded by variable numbers of macrophages and fibroblasts.

Channel catfish virus disease, characterized by secondary bacterial infections such as *Aeromonas* spp. and *Flavobacterium* spp., leads to focal necrosis starting from the posterior kidney. This necrosis rapidly progresses into diffuse necrosis of both haemopoietic and excretory tissues, accompanied by hemorrhage and edema (Noga, 2010).

Velappan and Munusamy (2018) studied the infection from *Streptococcus iniae* on Tiger Oscar and Astronotus ocellatus. Results have shown histopathological changes of kidney which included congested blood vessels in the renal interstitium with numerous inflammatory cells indicating septicemia. Necrosis, oedema in renal interstitial tissue, destruction of tubular epithelium accompanied with cloudy swelling, vacuolization and hyaline droplet degeneration were also seen in the infected fishes.

Bacterial diseases are enormously diverse and mostly treated with antibiotics at times without even knowing the significant causative agent which can lead to antimicrobial resistance. These scenarios are common and lead to mass mortality later adding up with the pathogenicity of the causative bacteria. The histological diagnosis and the present data help in the proper differentiation of the kind of infection and thus lead to specific pathogen resistant measures. Moreover, cumulative and clear datas help in the further research experiments for easy diagnosis of the etiological agent. Table 2 gives a comprehensive brief about all the mentioned bacteral diseases, their causative agents and important alterations in the histology of the fish kidney by these aetilogical agents.

4.2. Fungal Diseases

Fungal diseases are rare and less in number in comparison to the other pathogenic diseases. Still, Epizootic Ulcerative Syndrome has a progressive effect in case of infection in different farmed as well as wild species of teleosts. This is basically a fungal disease with multiple causative agents and thus got the name "epizootic". Vertical transmissions are common in winter seasons in different farmed ponds and thus have an extensive

Table 2 A Comprehensive List of All Reported Bacterial Pathogens in Teleost Affecting Nephric Tissues

Fish species and weight	Bacteria	Histopathological alterations in host kidney	References
Brook trout (varying size)	*Ranibacterium salmoninarum*	Coagulative necrosis, granuloma, caseation, fibrinous exudate	Eissa and Faisal, 2014
Rainbow trout (avg 208.7 +/– 8.11 gm)	*Vibrio anguillarum*	Siderosis, necrosis, hyperemia, haemorrhage, infiltration of mononuclear cells, vacuolar degeneration	Ceylan et al., 2019
Lates calcarifer (sea bass) (avg 5.64+/–0.16 gm)	*Vibrio harveyi*	Massive immune related cell infiltration, severe haemorrhagic condition, swelling of renal tubules, sloughing of epithelial cells into the lumen	Dong et al., 2017; Nuryati et al., 2023
Crucian carp (220 gm)	*Aeromonas salmonicida*	Hemorrhagic inflammations in both the haemopoietic and renal tissues	Ling et al, 2019
Oreochromis niloticus (mean100+/– 5 gm)	*Streptococcus agalactiae*	Tubulonephrosis, sharp decrease in haemopoietic tissue, deposition of necrotic debris in bowman's space, necrotis of epithelial cells of renal tubules (decrease of nuclear chromatin, swelling and vacuolization)	
Oreochromis niloticus (weight 50+/– 2 gm)		Severe hemorrhages in renal interstitia, dissolution of tubules, fibrin precipitation and leucocyte infiltration in necrotic foci, low grade interstitial nephritis, granulomas containing necrotic centers surrounded by variable numbers of macrophages and fibroblasts.	Su et al., 2017
Oreochromis niloticus (weight 14.50 +/– 0.50 & length 11.20 +/– 0.57 cm)	*Aeromonas caviae*	Acute septicemia where the kidney tissues had glomerulopathy with dilated Bowman's space, nephropathy with the loss of tubular epithelial cells, obliterate as well as inflamed nephritic tubules, melanomacrphagic aggregate, necrosis, wide lumen and thickening of lumen lining.	Roy et al., 2018
Oreochromis niloticus (weight 3.3 gm)	*Aeromonas dhakensis*	Infiltration of focal and multifocal lymphocytes and erythrocytes while the bacterial cells caused inflammation by necrosis of erythrocytes in kidney tubules.	Soto-Rodriguez et al., 2018
Heteropneustes fossilis (35 gm)	*Aeromonas hydrophila*	Massive atrophy of haemopoietic sinusoids surrounded by fibrinoid diposits, diffused necrosis,	Islam et al., 2008
Pangasianodon hypophthalmus (0.524 +/– 1.21 to 1.2 +/– 1.13 gm)		Destruction of bowman's capsule, inflamatory exudate, glomerular necrosis, tubular necrosis, infiltration of leukocytes; capillary dialationin glomerulus, reduction of bowman's space.	Mamun et al., 2020
Oreochromis niloticus (80 +/– 2gm) *Carassius auratus* (3 ~ 6 gm)		Tubular degeneration, mononuclear cell infiltration, inter-renal tubular necrosis, occlusion of lumen because of hemosiderin diposition, degeneration of bowman's space.	Ibrahim El-Barbary, 2017; Rosidah et al., 2020
Channel catfish (64.4 +/– 5.8gm)		Lysis of cytoplasmic organelles and nuclear structures in the anterior kidney, with degenerated bacterial cells engulfed by phagosomes of phagocytic cells.	Abdelhamed et al., 2017
Labeo rohita (size 18 ~ 26 cm and weight 80 ~ 100 gm)		Vacuole formation in the head kidney, melanomacrophagic centre formation, hemocytic infiltration, necrosis constricted lumen of nephric tubules, glomerulopathy with diluted Bowmans's space and inflamed nephric tubules	Biswas et al., 2021
Osphronemous gouramy (weight 50 ~ 135 gm and length 13 ~ 20 cm)		Piknosis and inflamatory necrotic conditions	Rozi et al.,2018
Tiger oscar *(Astronotus ocellatus)* (weight 275 gm, length 25 cm)	*Streptococcus iniae*	Congested blood vessels in the renal interstitium with numerous inflammatory cells indicating septicemia. Necrosis, oedema in renal interstitial tissue, destruction of tubular epithelium accompanied with cloudy swelling, vacuolization and hyaline droplet degeneration were also seen in the infected fishes.	Velappan and Munusamy, 2018
Turbot *(Psetta maxima)* (weight 15 ~ 20gm)	*Pseudomonas anguilliseptica*	Dialation of sinusoids, slight inflammatory response underlying the kidney capsule tissue (initial stages of infection); oedema, focal necrosis in interstitial kidney tissue (during progressive period of infection) and lastly leading to extensive necrosis of hematopoietic cells as well as dialation of peritubular capillaries and necrosis of tubular epithelium and glomeruli.	Magi et al., 2009

spread in multiple fish species and has an ability to lead to secondary bacterial infections. Thus, it is highly fatal and raises serious concerns among the fish farmers. The histopathogenic effects include glomerulonephritis, luminal destruction, haemorrhages, and sometimes vacuolization.

Aphanomyces invadans, a fungus, stands as a primary culprit behind Epizootic Ulcerative Disease, often impacting freshwater cultured species severely, especially in the months of De-

cember and January. During infection, fungal spores adhere to the retroperitoneal surface of the kidney, affecting the muscle layer above the haemopoietic tissue, kidney tubules, and glomerulus. As the condition progresses, chronic glomerulonephritis ensues, leading to osmoregulatory dysfunction, glomerular hyperplasia resulting in capillary lumina destruction, and Bowman's space contraction, as described by Meyers and McPhersons (1985). Chronic stages of Epizootic Ulcerative Disease may exhibit tubular necrosis and periglomerular fibrosis. Notably, certain species such as common carp (Cyprinus carpio), Nile tilapia (Oreochromis niloticus), milkfish (Chanos chanos) (Lilly et al., 2008), and European eel (Anguilla anguilla) (Oidtmann et al., 2008) demonstrate resistance to A. invadans. However, Thapa and Pal (2022) documented common histological changes in the kidneys of various freshwater species infected by A. invadans, including tubular breakage and necrosis, tubular cell vacuolation and hemorrhagic conditions.

Fungal diseases can be very confusing to be diagnosed properly as most of them have similar primary etiology. Rather, the severity is being understood on the spreading of the infection at a deeper level when the diagnosis does not seem to help that much. The histological studies in that case are highly efficient for the diagnostic factors. Different fungal diseases like Aspergillosis, Blastomycosis, candidiasis etc each one has its different histological evidence which can help them to get diagnosed separately. Kidney is one of the major sites of infection of fish. So, understanding the different changes of histology will be beneficial for the researchers to discriminate different infections and their causative agents and take the preventive measures accordingly.

4.3. Parasitic Diseases

Parasite infestation is very common in the case of farmed teleosts but most of the ciliates and flagellates have their major adversities associated with skin and gills like *Ichthyophtheria*s spp, *Ichthyobodo* spp., *Chilodonella* spp., *Trichodina* spp etc. Crustacean parasites like *Argulus* spp, *Lernaea* spp etc are associated with gills and skin. Only the metazoans like *Tetracapsuloides* spp. and Myxobolus spp. are the ones which tend to show deformations in kidney and their histological changes include sporogenic proliferation and other characteristic changes.

Proliferative kidney disease (PKD), caused by the myxozoan *Tetracapsuloides bryosalmonae*, manifests extensively in the kidneys of infected trouts in freshwater systems, resulting in significant histological alterations (Roberts, 2012). These changes manifest in three primary ways: haemopoietic hyperplasia, pathological alterations in the vascular system, and diffuse inflammatory changes, collectively affecting tubular and glomerular functions. The aetiological agent behind hyperplasic effects is believed to be the accumulation of myxosporean cells. This accumulation triggers the formation of a whirling effect by epithelioid-like cells around the myxosporeans (Roberts, 2012). Gorgoglione et al. (2016) demonstrated extensive extra sporogenic proliferative changes and alterations in the luminal tissue in the collecting ducts, ureter, and renal tubules of brown trout kidneys. Protozoan infection, such as Myxobolus bramae, studied in Carasobarbus luteus (Mansoor et al., 2020) with a prevalence rate of 5.00%, resulted in various histopathological changes in the kidney.

Parasite infestation, although a very common problem in farmed fishhes, can be of great concern as it gets spread easily. A few cases are the reason for heavy economic loss. So, the diagnosis nees to be quick and precised. Moreover, the molecular level diagnosis takes time and high expenses which cannot be borne by everyone at one go. In that case, these histological diagnosis studies help with efficient work function. The differentiation in spore proliferation and other closely related histological changes bring huge difference in research and diagnosis.

4.4. Viral Diseases

Viral diseases are generally fatal and scarce in daily life as they are highly complicated to be detected. Viruses like Koi carp herpes virus (*Alloherpesviridae*), Infectious haematopioietic necrosis virus (*Rhabdoviridae*), Infectious spleen and kidney necrosis virus (*Iridoviridae*) and Viral haemorrhagic septicemia virus (*Novirhabrovirus*) etc show coagulative necrotic effect along with characteristic lymphocytic infiltration and focal necrotic effects in fish kidney. Generally, the viral infections later lead to secondary bacterial or any other pathogenic infestations which makes the survival of the organism more complicated.

Viral Hemorrhagic Septicemia (VHS), caused by the viral hemorrhagic septicemia virus, poses a significant threat to various trout species, including Rainbow trout, Brown trout, Brook trout, and Golden trout. The kidneys, in particular, are the primary targets during VHS, resulting in damage to haemopoietic tissues. In the acute phase, kidney tissues exhibit focal hemorrhage, necrosis, and lymphocytic inflammation. During the chronic phase, heavy hemosiderin deposition in melanomacrophagic centers is observed, indicating anemia caused by focal hyperplasia and degeneration of haemopoietic tissues, resembling glomerulonephritis.

Iridoviruses, belonging to the family *Iridoviridae* and specifically the genus *Megalocytivirus*, are responsible for severe diseases in ornamental, farmed, and wild fish species. Within this genus, various infectious spleen and kidney necrosis viruses (ISKNV) have been identified, categorized into three genotypes. Studies by Gibson-Kueh et al. (2003) have revealed that ISKNV predominantly infects interstitial organ cells, including hepatic fibroblasts, hepatic perisinoidal cells, and renal interstitial cells. Jung-Schroers et al. (2016) investigated an ISKNV outbreak among ornamental fishes in Germany, specifically angelfish and platys. Zhu et al. (2021) in their study with the ISSKNV genotype II on Lates calcarifer had discovered hispathological changes like enlargement of cells and significant lymphocytic infiltration in the kidney of the infected fishes leading to mass mortality.

Although viral infections are fatal and histology is a major advantage to diagnose it on preliminary level without the use of molecular level diagnosis which is time consuming, very few viruses in fishes show direct effect only on kidney. Still, all the viruses which tend to affect internal organs can be some-

how diagnosed by kidney histopathology. These data are highly specific for viruses are this can be used successfully in diagnosis and cure or prevention. Specific treatment can only be given when proper diagnosis done and its highly important for viral infection as viruses are highly replicative and change their genomic form according to the changing environmental conditions which leads to diverse confusing morphological symptoms in a single organism. Viral infestation can lead to huge immune deficiency which further leads to bacterial infections. Early detection can help preventing such adverse conditions.

5. Conclusion

Histopathological studies are used as the primary and most reliable source for disease detection because of their accuracy and easily detectable results nowadays and thus have been proved highly effective for both clinical and research-oriented studies. Freshwater teleost being exposed to fluctuating physicochemical parameters like temperature, salinity, PH, hardness and presence of other chemical compounds like nitrite, nitrate, ammonia and trace metals, when detected by abnormal behaveioral symptoms are considered as infected by either toxicological effect or pathological infection. There have been several conducted studies on the adverse toxicological effects of heavy metals, pesticides and effluents on the fish biodiversity and ecosystem of freshwater resources in nature. Despite that, the pathogenic studies with specified species with distinguishable characteristics are still limited in number because of diversified effect of one pathogen, its species variation in a single genus and their effects on different fish species. Moreover, pathogenic invasion and adverse effects are accompanied by physical stressors. So, most of the cases remain unsuspected. On the other hand, most of the pathogens cause nearly identical physiological as well as histological changes, so the proper identification needs additional biochemical tests of the cultured pathogen which can be time consuming.

In our review, we have undergone several cases of such pathogenic effects on fish kidneys and have come out to some characterized specific changes in the histology due to specific pathogens. The kidney shows sporogenic proliferation in parasitic disease along with haemorrhagic conditions which appear secondarily due to the increased pathogenic spore formation. Viral diseases are characterized by lymphocyte infiltration and focal coagulative necrotic effects. The melanomacrophagic centres are highly dense and indicative to high order immune response to the viral genome. Fungal diseases are basically epizootic due to further secondary parasitic, bacterial infections and show multiple open lesions indicating decreased strength of the physical barriers and easy infestation of pathogens due to early fugal distribution all through the epithelial system. Bacterial pathogens are highly diverse in effect generation and fall under secondary pathogens in a less effort. Easy breakthroughs inside the body due to other primary infections and showing multiple haemorrhages, necrotic lesions and cellular proliferative effects are common indication of bacterial infestation. In all cases moderate to heavy necrotic lesions, haemorrhagic effect and cellular infiltrations are common symptoms present as inflammatory response. This review gives a brief idea about these changes and their cause to the readers keeping in mind that further research scopes are ample in number as the conducted studies are basically narrow spectrum and repeated on the same pathogens. Future endeavors can easily detect these few species with the cumulative data presented in this review and can go for further acknowledgeable depth of studies as well as can easily differentiate a few common pathogenic species without confusion during practical works. The arguments clear out the contradictions among different studies and seek a clear conclusion which is useful for the readers.

References

Austin, B. and Austin, D.A. (2012). Vibrionaceae Representatives. *Bacterial Fish Pathogens*. Springer International Publishing, pp 357-411. https://doi.org/10.1007/978-94-007-4884-2_11

Abdelhamed, H., Ibrahim, I., Baumgartner, W., Lawrence, M.L. and Karsi, A. (2017). Characterization of histopathological and ultrastructural changes in channel catfish experimentally infected with virulent Aeromonas hydrophila. *Frontiers in microbiology*. 8, 1519. http://dx.doi.org/10.3389/fmicb.2017.01519

Bernet, D., Schmidt-Posthaus, H., Wahli, T. and Burkhardt-Holm, P. (2004). Evaluation of two monitoring approaches to assess effects of wastewater disposal on histological alterations in fish. *Hydrobiologia*. 524, 53-66. https://doi.org/10.1023/B:HYDR.0000036196.84682.27

Biswas, A., Dash, G., Mali, P., Joardar, S.N., Dey, B., Roy, A. and Karmakar, S. (2021). Histopathology of head kidney tissues in challenged rohu, Labeo rohita Hamilton after vaccinating with Aeromonas hydrophila antigens. *Fish and Shellfish Immunology Reports*. 2, 100025. https://doi.org/10.1016/j.fsirep.2021.100025

Ceylan, M., Duman, M., Inan, S., Ozyigit, O., Saticioglu, I.B. and Altun, S. (2019). The study of histopathologic changes of experimental infection with Listonella (Vibrio) anguillarum in rainbow trout. *Journal of Research in Veterinary Medicine*. 38(1), 59-66. https://doi.org/10.30782/uluvfd.423345

Dong, H.T., Taengphu, S., Sangsuriya, P., Charoensapsri, W., Phiwsaiya, K., Sornwatana, T., Khunrae, P., Rattanarojpong, T. and Senapin, S. (2017). Recovery of Vibrio harveyi from scale drop and muscle necrosis disease in farmed barramundi, *Lates calcarifer* in Vietnam. *Aquaculture*. 473, 89-96. https://doi.org/10.1016/j.aquaculture.2017.02.005

Eissa, A.E. and Faisal, M. (2014). Clinical outbreaks of bacterial kidney disease (BKD) in hatchery-raised brook trout (Salvelinus fontinalis) (Mitchill, 1814): Lessons learned. *Journal of Aquaculture: Research and Development*. 5(242), 2-3. http://dx.doi.org/10.4172/2155-9546.1000242

Flerova, E.A., Yurchenko, V.V., Morozov, A.A., Evdokimov, E.G., Bogdanova, A.A., Alekseev, M.Y., Sendek, D.S. and Titov, S.F. (2023). Histology and ultrastructure of the nephron and kidney interstitial cells in the atlantic salmon (*Salmo salar* Linnaeus 1758) at different stages of life cycle. *Biology*. 12(5), 750. https://doi.org/10.3390/biology12050750

Gibson-Kueh, S., Netto, P., Ngoh-Lim, G.H., Chang, S.F., Ho, L.L., Qin, Q.W., Chua, F.H.C., Ng, M.L. and Ferguson, H.W. (2003). The pathology of systemic iridoviral disease in fish. *Journal of Comparative Pathology*. 129(2-3), 111-119. https://doi.org/10.1016/S0021-9975(03)00010-0

Gorgoglione, B., Kotob, M.H., Unfer, G. and El-Matbouli, M. (2016). First proliferative kidney disease outbreak in Austria, linking to the aetiology of Black Trout Syndrome threatening autochthonous trout populations. *Diseases of Aquatic Organisms*. 119(2), 117-128. https://

doi.org/10.3354/dao02993

Geng, Y., Wang, K.Y., Huang, X.L., Chen, D.F., Li, C.W., Ren, S.Y., Liao, Y.T., Zhou, Z.Y., Liu, Q.F. and Du, Z.J. (2012). Streptococcus agalactiae, an emerging pathogen for cultured ya-fish, Schizothorax prenanti, in China. *Transboundary and Emerging Diseases*. 59, 369-375. https://doi.org/10.1111/j.1865-1682.2011.01280.x

He, Y., Huang, J.L., Wang, K.Y., Chen, D.F., Geng, Y., Huang, X.L., Ou-Yang, P., Zhou, Y., Wang, J., Min, J. and Lai, W.M. (2017). Pathogenicity of streptococcus agalactiae in oreochromis niloticus. *Oncotarget*. 5, 401-413. https://doi.org/10.18632/oncotarget.23551

Islam, M.T., Mostafa, K. and Rashid, M. (2008). Histopathological Studies of experimentally infected shing, heteropneustes fossilis with aeromonas hydrophila bacteria. *Progressive Agriculture*. 19(1), 89-96. https://doi.org/10.3329/PA.V19I1.17359

Ibrahim El-Barbary, M. (2017). Serum biochemical and histopathological changes associated with Aeromonas hydrophila isolated from Oreochromis niloticus and Sparus aurata with multiple antibiotic resistance index. *Journal of Biological Sciences*. 17, 222-234. http://dx.doi.org/10.3923/jbs.2017.222.234

Izwar, A., Nuryati, S., Rahman and Purnomowati, R. (2020). Isolation, identification, and pathogenicity tests of pathogenic bacterial associated with black body syndrome in white barramundi Lates calcarifer B. *Jurnal Akuakultur Indonesia*. 19, 39-49. https://doi.org/10.19027/jai.19.1.39-49

Jung-Schroers, V., Adamek, M., Wohlsein, P., Wolter, J., Wedekind, H. and Steinhagen, D. (2016). First outbreak of an infection with infectious spleen and kidney necrosis virus (ISKNV) in ornamental fish in Germany. *Diseases of Aquatic Organisms*. 119(3), 239-244. https://doi.org/10.3354/dao02995

Khanna, S.S. and Singh, H.R. (2015). *A Textbook of Fish Biology and Fisheries*. Narendra Publishing House. pp 171-175.

Lombardini, E.D., Hard, G.C. and Harshbarger, J.C. (2014). Neoplasms of the Urinary Tract in Fish. *Sage Journals, Veterinary Pathology*. 51(5),1 00-1012. https://doi.org/10.1177/030098581351 1122

Lilley, J.H., Callinan, R.B. and Khan, M.H. (2002). Social, economic and biodiversity impacts of epizootic ulcerative syndrome (EUS). *FAO Fisheries Technical Paper*. 127-139.

Ling, X.D., Dong, W.T., Zhang, Y., Qian, X., Zhang, W.D., He, W.H., Zhao, X. and Liu, J.X. (2019). Comparative transcriptomics and histopathological analysis of crucian carp infection by atypical Aeromonas salmonicida. *Fish and Shellfish Immunology*. 94, 294-307. https://doi.org/10.1016/j.fsi.2019.09.006

Mamun, M.A.A., Nasren, S., Abhiman, P.B., Rathore, S.S., Sowndarya, N.S., Ramesh, K.S. and Shankar, K.M. (2020). Effect of Biofilm of Aeromonas Hydrophila Oral Vaccine on Growth Performance and Histopathological Changes in Various Tissues of Striped Catfish, *Pangasianodon Hypophthalmus* (Sauvage 1878). *Indian Journal of Animal Research*. 54(5), 563-569. http://dx.doi.org/10.18805/ijar.B-3814

Moneim, A.A., Elmenshawy, O., Al-Kahtani, M., Sayed, A. and Alfwuaires, M. (2019). Pattern of renal pathology in fish from Al-Hassa waterways, Saudi Arabia. *Indian Journal of Animal Research*. 536, 751-755. http://dx.doi.org/10.18805/ijar.B-910

Mansoor, N.T., Falih, I.B. and Al-Nasiri, F.S. (2020). Diagnosis of *Myxobolus bramae* (Myxosporea: Myxobolidae) in the kidney tissue of Carasobarbus luteus and histopathological changes associated with infection. *Iraqi Journal of Agricultural Sciences*. 51(3), 874-884.

McMillan, D.B. (2011). *Role of the kidneys—Histology of the Kidney. Encyclopedia of Fish Physiology*. Academic Press. pp 1395-1410. https://doi.org/10.1016/B978-0-12-374553-8.00172-6

Meyers, T.R. and McPherson, B.P. (1985). Chronic glomerulonephritis in returning fall chinook salmon, Oncorhynchus tshawytscha (Walbaum), from the Rogue River, Oregon. *Journal of Fish Diseases*. 8(5), 407-416. https://doi.org/10.1111/j.1365-2761.1985.tb0 1274.x

Magi, G.E., Lopez-Romalde, S., Magariños, G.E., Lamas, J., Toranzo, A.E. and Romalde, L. (2009). Experimental Pseudomonas anguilliseptica infection in turbot Psetta maxima (L.): A histopathological and immunohistochemical study. *European journal of histochemistry*. 53(2), 73-80. https://doi.org/10.4081/ejh.2009.e9

Nuryati, S., Yanti, M., Rahman and Wahyuwardani, S. (2023). Kidney and liver histopathology of sea bass *Lates calcarifer* infected with black body syndrome-associated bacteria. *Jurnal Akuakultur Indonesia*. 22(2), 170-178. https://doi.org/10.19027/jai.22.2.170-1 78

Noga, E.J. (2010). *Fish disease: diagnosis and treatment*. John Wiley & Sons. pp 1-497.

Oidtmann, B., Steinbauer, P., Geiger, S. and Hoffmann, R.W. (2008). Experimental infection and detection of Aphanomyces invadans in European catfish, rainbow trout and European eel. *Disease of Aquatic Organisms*. 82, 195-207. https://doi.org/10.3354/dao01973

Palikova, M., Papezikova, I., Markova, Z., Navratil, S., Mares, J., Mares, L., Vojtek, L., Hyrsl, P., Jelinkova, E. and Schmidt-Posthaus, H. (2017). Proliferative kidney disease in rainbow trout (Oncorhynchus mykiss) under intensive breeding conditions: Pathogenesis and haematological and immune parameters, *Veterinary Parasitology*. 238, 5-16. http://dx.doi.org/10.1016/j.vet par.2017.03.003

Resende, A.D., Lobo-da-Cunha, A., Malhão, F., Franquinho, F., Monteiro, R.A.F. and Rocha, E. (2010). Histological and Stereological Characterization of Brown Trout (Salmo trutta f. fario) Trunk Kidney. *Microscopy and Microanalysis*. 16(6), 677-687. https://doi.org/10.1017/S1431927610093918

Rosidah, R., Yunita, M.D., Nurruhwati, I. and Rizal, A. (2020). Histopathological changes in goldfish (Carassius auratus (Linnaeus, 1758)) infected by Aeromonas hydrophila bacteria with various densities. *World Scientific News*. 142, 150-168.

Roberts, R.J. (2012). *Fish pathology*. John Wiley & Sons. pp 69-120.

Rastogi, V., Puri, N., Arora, S., Kaur, G., Yadav, L. and Sharma, R. (2013). Artifacts: A diagnostic dilemma—A review. *Journal of Clinical and Diagnostic Research*. 7(10), 2408-2413. https://doi.org/10.7860JCDR20136170.3541

Roy, A., Singha, J. and Abraham, T.J. (2018). Histopathology of Aeromonas caviae infection in challenged Nile tilapia Oreochromis niloticus (Linnaeus, 1758). *International Journal of Aquaculture*. 8(20), 151. https://doi.org/10.5376/ija.2018.08.0020

Rozi, R.; Rahway, K.; Daruti, D. N. and Stella, M. S. P. (2018). Study on characterization, pathogenicity and histopathology of disease caused by Aeromonas hydrophila in Gourami (Osphronemus gouramy). *IOP Conference Series: Earth and Environmental Science*. 137(1), 012003. https://doi.org/10.1088/1755-1315/137/1/01 2003.

Saraiva, A., Costa, J., Serrão, J., Cruz, C. and Eiras, J.C. (2015). A histology-based fish health assessment of farmed seabass (Dicentrarchus labrax L.). *Aquaculture*. 448, 375-381. https://doi.org/10.1016/j.aquaculture.2015.06.028

Saharia, P., Pokhrel, H., Hussain, I., Kalita, B., Yasmin, R. and Borah, G. (2018). Histopathological changes in Indian Major Carp, Labeo rohita (Hamilton), experimentally infected with Aeromonas hydrophila associated with hemorrhagic septicemia of Central Brahmaputra valley of Assam, India. *Journal of Entomology and Zoology Studies*. 6(5), 6-11. http://dx.doi.org/10.1111/are.14979

Su, Y.L., Feng, J., Liu, C., Li, W., Xie, Y.D. and Li, A.X. (2017). Dynamic bacterial colonization and microscopic lesions in multiple organs of tilapia infected with low and high pathogenic Streptococcus agalactiae strains. *Aquaculture*. 471, 190-203. http://dx.doi.org/10.1016/j.aquaculture.2017.01.013

Soto-Rodriguez, S.A., Lozano-Olvera, R., Garcia-Gasca, M.T., Abad-Rosales, S.M., Gomez-Gil, B. and Ayala-Arellano, J. (2018). Virulence of the fish pathogen Aeromonas dhakensis: genes involved, characterization and histopathology of experimentally infected hybrid tilapia. *Diseases of aquatic organisms*. 129(2), 107-116. https://doi.org/10.3354/dao03247

Thapa, G.B. and Pal, J. (2022). Histopathology of the fish infected with

the epizootic ulcerative syndrome in Eastern Nepal. *Nepalese Journal of Zoology*. 6(1), 20-29. https://doi.org/10.3126/njz.v6i1.46750

Taqi, S.A., Sami, S.A., Sami, L.B. and Zaki, S.A. (2018). A review of artifacts in histopathology. *Journal of Oral and Maxillofacial Pathology*. 22(2). 279. https://doi.org/10.4103%2Fjomfp.JOMFP_125_15

Velappan, M. and Munusamy, D. (2018). Pathological investigation of gill, intestine, liver and kidney of naturally infected *Streptococcosis* in ornamental fish, Tiger oscar, *Astronotus ocellatus*. *Research Journal of Pharmacy and Technology*. 11(6), 2549-2554. https://doi.org/10.5958/0974-360X.2018.00471.7

Wolf, K. (1988). *Fish virus and fish viral diseases*. Cornell University Press. pp 217.

Zhu, Z., Duan, C., Li, Y., Huang, C., Weng, S., He, J. and Dong, C. (2021). Pathogenicity and histopathology of infectious spleen and kidney necrosis virus genotype II (ISKNV-II) recovering from mass mortality of farmed Asian seabass, *Lates calcarifer*, in Southern China. *Aquaculture*. 534, 736326. https://doi.org/10.1016/j.aquaculture.2020.736326