Pertanika J. Trop. Agric. Sc. 42 (3): 1023 - 1047 (2019)

TROPICAL AGRICULTURAL SCIENCE

Journal homepage: http://www.pertanika.upm.edu.my/

Review article

The Significance of Major Viral and Bacterial Diseases in Malaysian Aquaculture Industry

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ABSTRACT

Aquaculture is an upcoming industry in Malaysia as sustainable fish production with total production of 407,387 tonnes in 2016. As a growing industry, current practices have led to disease outbreaks which are highlighted as one of the major issues faced in aquaculture farms. Throughout the 20 years of disease reporting in Malaysia, several bacterial and viral diseases were found to persist in farms. In addition, emerging global diseases have also been detected in several farms. The consequence of these diseases were outbreaks led to huge economic losses. Eventually, the combination of persistent and emerging diseases creates a potential threat for the aquaculture industry and hence requires immediate attention. Therefore, this review summarises the major viral and bacterial pathogens of fish and crustaceans in the context of Malaysian aquaculture. It also considers the characteristics of disease and their impacts as well as the potential for future disease emergence in these aquatic animals as aquaculture industry continues to expand. This review serves as a platform for future directions in research in improved monitoring, detection and prevention as a step towards increasing biosecurity in Malaysian aquaculture.

Keywords: Aquaculture, bacterial, disease, Malaysia, viral

ARTICLE INFO

Article history:
Received: 29 November 2018
Accepted: 11 February 2019
Published: 19 August 2019

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ISSN: 1511-3701
e-ISSN: 2231-8542

INTRODUCTION

The Malaysian government has identified aquaculture as a major source for increasing fish production to meet domestic demand, accounting for 520,513 tonnes of total fish production in 2014. Increasing at a rate of 8% per annum, the aquaculture production target under National Agro-Food Policy (NAFP) was set at 794,000 tonnes by the end of 2020 (Department of Fisheries Malaysia [DOF], 2017). However, several problems arise from current aquaculture practices, such as the occurrence of diseases in the farms and environmental concerns (Ashley, 2007; Cao et al., 2007).

Disease occurrence and outbreaks gain precedence due to the potential to eradicate fish stocks within the farm, assisted by the ease of disease transmission through the water (Leung & Bates, 2013). Additionally, the combination of stressful conditions from high stocking density in farms and deteriorating environmental conditions further aggravate the occurrence and severity of diseases (Bowden, 2008). If diseases remain unresolved, farms are expected to incur loss of stocks, potentially disrupting operations of the facility and limiting growth in the aquaculture sector (Stentiford et al., 2012). Thus, disease management and biosecurity are key issues to be addressed by the aquaculture industry today (Tan et al., 2008). This paper aimed to review major viral and bacterial diseases in Malaysian aquaculture industry and propose directions for future studies and efforts on their prevention.

DISEASE MONITORING IN MALAYSIAN AQUACULTURE INDUSTRY

While disease outbreaks are common throughout the world, regions in Asia are often highlighted due to higher relative aquaculture production plus tropical conditions which increases risk of outbreaks (Leung & Bates, 2013). In many countries, awareness of aquaculture disease has increased investment in research and disease control programs, including Malaysia (Bondad-Reantaso et al., 2005).

In Malaysia, disease monitoring is conducted by the Fisheries Research Institute under the Department of Fisheries, as part of the Fish Health Surveillance Program. Reports are compiled by the National Fish Health Research Centre (NaFisH), which are then compiled by the Network of Aquaculture Centres in Asia-Pacific (NACA) and the Food and Agriculture Organisation of the United Nations (FAO) as active disease monitoring of aquaculture in the Southeast Asian region (Network for Aquaculture Centres in Asia-Pacific [NACA], 2018). In this review, the disease have been categorised as finfish viral diseases, crustacean viral diseases and bacterial diseases.

FINFISH VIRAL DISEASES

Herpesvirus Diseases

Herpesviruses in the family of *Alloherpesviridae* are predominantly pathogens of fish and amphibians. Key features of herpesviruses include a high level of host specificity and the ability to establish long term latency while interacting intricately with host defences (Hanson et al., 2011). Fish species affected by herpesviruses include koi (*Cyprinus carpio*), eels (*Anguilla* sp.), sturgeons (*Acipenser* sp.) and cod (*Gadus* sp.) (Hanson et al., 2011; Lepa & Siwicki, 2013). The koi herpesvirus and channel catfish virus were also detected in Malaysian aquaculture industry.

Koi Herpesvirus (KHV). KHV currently recognised as *Cyprinid herpesvirus 3* (CyHV3), is a major economic threat to common carp (*Cyprinus carpio*) and koi rearing industries worldwide. The key clinical signs include lethargy, loss of appetite and gill necrosis, usually resulting in death within two days of the onset of symptoms (Hedrick et al., 2000). Internally, severe inflammation can be observed in the gill, skin, kidney, liver, spleen, gastrointestinal system and brain of diseased fish (Pikarsky et al., 2004).

Up to date, KHV has been persistently detected in koi and common carp farms located in Perak, Negeri Sembilan and Selangor (NACA, 2018). However, no studies have been published detailing disease outbreaks attributed to the virus in Malaysia. Azila et al. (2012) detected CyHV3 in apparent healthy Malaysian koi stocks using ELISA-based techniques. This observation illustrates the importance of further surveillance of fish stocks to verify the status of the CyHV3 infection in Malaysian koi carps. In addition, KHV can remain latent in the leucocytes of healthy fish and act as a reservoir until rearing waters achieve a temperature range of 15-28°C, activating viral expression (Uchii et al., 2009). As such temperatures are prevalent across Malaysia, the carp aquaculture industry may be susceptible to disease outbreaks, especially in the event of temperature fluctuations (Azila et al., 2012).

Channel Catfish Virus (CCV). CCV also known as *Ictalurid herpesvirus 1*, is a cytopathic herpesvirus which mainly infects catfish and causes severe haemorrhageespecially in young fingerlings (Lepa & Siwicki, 2013). Other clinical symptoms include erratic swimming, exophthalmia, distended abdomen and haemorrhages at the base of fins (Camus, 2004). This disease was thought to be specific to the channel catfish (*Ictalurus punctatus*), but has been recently reported in striped catfish as well (Siti-Zahrah et al., 2013). Meanwhile, very few studies were conducted on the diseases affecting other catfishes cultured in Malaysia, including the African catfish (*Clarias gariepinus*), bagrid catfish (*Hemibagrus gracilis*) and striped catfish (*Pangasius hypophthalmu*s) (DOF, 2016).

Detection of CCV in Malaysian catfish was first reported by Siti-Zahrah et al. (2013) who detected the virus in cage-cultured striped catfish, “ikan patin”, resulting in 30-40% mortality rates throughout a two-year epidemiological study. However, CCV was not confirmed to be the cause of mortality due to the presence of bacterial-like lesions, which may have been as a result of *Aeromonas hydrophila* and *Flexibacter columnaris* infection.

Iridovirus Diseases

The family of *Iridoviridae* represent a group of large icosahedral viruses (120-200 nm in diameter) that have the ability to remain infectious without the viral envelope and may be released as naked particles following cell lysis (Chinchar et al., 2009). It was suggested that only genera *Lymphocystivirus*, *Ranavirus* and *Megalocytivirus* contribute to mortalities in fish with differing clinical symptoms. *Lymphocystiviruses* cause non-fatal, superficial dermal infections, while *Ranaviruses* and *Megalocytiviruses* cause serious systemic diseases with high mortality rates (Leu et al., 2013). Infection from *Ranaviruses* and *Megalocytiviruses* produce similar symptoms, such as dark skin colouration, abnormal swimming behaviour, skin lesion, haemorrhage and fin erosion (Whittington et al., 2010). While, *Megalocytiviruses* produce unique symptoms include the formation of hypertrophy in cells, which can lead to organ enlargement (Yanong & Waltzek, 2010).

Disease outbreaks caused by *Iridovirus* were first reported in 2009, which resulted in a cumulative mortality of 100% and loss of approximately RM 50,000 (NACA, 2018). An iridovirid disease outbreak was reported in grouper (*Epinephelus* sp.) cultures in Sabah, Malaysia, where *Megalocytivirus* was revealed to be the cause of mortality via phylogeny analysis and evidence of organ enlargement. While the actual cause of the outbreak was not verified, high water temperatures of approximately 28°C to 30°C had been reported to stimulate virus replication and were reported in the affected waters, possibly contributing to the outbreak (Razak et al., 2014).

Betanodavirus Diseases

Betanodavirus from the family of *Nodaviridae* are composed of a non-enveloped and icosahedral particle size of between 25 to 30 nm. This virus causes a major disease termed Viral Nervous Necrosis (VNN) or Viral Encephalopathy and Retinopathy (VER), present mainly in groupers and seabass, but has also been reported in farmed cod (Hellberg et al., 2010). Clinical signs include loss of swimming orientation, lethargy, loss of appetite and bloated bellies. In addition, histological lesions also include cellular vacuolation, necrosis and neuronal degradation in the central nervous system (Vendramin et al., 2013). In Malaysia, *Betanodavirus* outbreaks have been reported in groupers, golden pompanos (*Trachinotus blochii*) and Asian seabass (*Lates calcarifer*).

Grouper. Groupers represent a major aquaculture species that can be threatened by the occurrence of VNN while also acting as a natural reservoir for the virus (Ma et al., 2012). Outbreaks have been studied across various countries and revealed high rates of mortality within a few days post infection (Kara et al., 2014; Vendramin et al., 2013).

Only one VNN outbreak occuring in Langkawi, Kedah has been reported by NACA (2018). The outbreak led to high mortalities of brown marbled groupers (*Epinephelus fuscoguttatus*) and giant groupers (*Epinephelus lanceolatus*), resulting in a loss of RM 131,400. The disease was identified via molecular methods by the NaFisH, Penang. A study by Ransangan et al. (2013) found that *Betanodavirus*-related mortalities might occur without displaying clinical symptoms in groupers which may result in fewer outbreaks categorised under VNN. In addition, persistence of *Betanodavirus* in the environment may also contribute to reoccurrence of outbreaks.

Asian Seabass. VNN is one of the key diseases which affects the Asian seabass aquaculture in Malaysia and is capable of vertical transmission. However, only one report of a disease outbreak in Malaysia has been published (Ransangan & Manin, 2010). Earlier studies of suspected outbreaks have been published, however, authors were unable to confirm whether the mortalities were a direct result of VNN or other causal agents (Ransangan et al., 1999).

A number of potential outbreaks have also occurred in Sabah, Malaysia but again have not been confirmed due to the lack of diagnostic facilities and expertise (Ransangan & Manin, 2010). An outbreak between July to October 2008 was confirmed to be caused by *Betanodavirus* using PCR, in addition to matching VNN clinical symptoms. Apart from that, the disease did not resurface in farms in recent years (NACA, 2018). On the other hand, larvae up to 50 days post-hatching were found to be more vulnerable, after which mortality rates reduced significantly (Hick et al., 2011). However, mortalities do not occur in older fishes and they remain as carriers for the virus and can potentially spread it via horizontal transmission (Gomez et al., 2004).

Golden Pompano. Golden pompano are cultured in Malaysian aquaculture on a small scale due to limitations in availability of seed and fingerlings (Food and Agriculture Organisation [FAO], 2007). Nevertheless, an outbreak of VNN on a golden pompano farm has been reported in Langkawi, which utilises deep-sea cages and suffered approximately 60% mortality rates within a week (Ransangan et al., 2011). However, the origin of infection could not be identified due to common reports of the virus in other Southeast Asian regions. Apart from that, no further outbreak was reported recently (NACA, 2018).

Tilapia Lake Virus Disease

The Tilapia Lake Virus Disease (TiLVD), also known as the syncytial hepatitis of tilapia (SHT) is a recently emerging disease which targets tilapias (*Oreochromis* sp.) and was first recognised in a freshwater lake in Israel (Dong et al., 2017). The causal agent is a novel segmented RNA virus called the Tilapia Lake Virus (TiLV) which was clasified as an Orthomyxo-like virus with negative-sense RNA but differs with the formation of syncytia, which is not a feature of orthomyxoviral infections (del-Pozo et al., 2017). Clinical symptoms include lethargy, skin erosion, hemorrhage and abdominal distension, which usually result in mortality within 10 days (Tattiyaponga et al., 2017). Meanwhile, histopathological symptoms show lesions found in multiple organs (Senapin et al., 2018; Tattiyapong et al., 2017). Although slight variations exists in the symptoms observed, such as necrosis of gastric glands (Ferguson et al., 2014), ocular lesions (Eyngor et al., 2014) and necrotic foci in kidney (Fathi et al., 2017), hepatitis was the most common histopathological feature found in TiLV outbreaks (Jansen et al., 2018).

Currently, TiLV is highlighted as an upcoming disease with its presence confirmed in Ecuador, Israel, Colombia, Egypt, Uganda, Tanzanian, India, Malaysia, and Thailand (Amal et al., 2018; Behera et al., 2018; Jansen et al., 2018; Mugimba et al., 2018; Senapin et al., 2018),while many other countries have also been listed to be at high risk of TiLVD (Dong et al., 2017). Several studies have developed methods of analysis, including suitable cell lines and virus detection with reverse-transcriptase PCR (Tsofack et al., 2017), as well as non-lethal methods for sampling (Liamnimitr et al., 2018).

Up to date, two outbreaks were reported in Malaysia occuring in tilapia farms in Kedah and Perlis (NACA, 2018). Meanwhile, an outbreak occuring in Selangor was reported by Amal et al. (2018), describing mass mortality occuring in a tilapia farm as a result of a co-infection of TiLV and *Aeromonas veronii*. The disease was confirmed via PCR sequencing analysis and histopathological detection of syncytial hepatitis cells suggesting potential synergystic co-infection of TiLV with other bacteria. Lastly, TiLV was also detected in wild tinfoil barb (*Barbonymus schwanenfeldii*) in Perlis (Abdullah et al., 2018). However, it was unconfirmed if the virus is infectious in tinfoil barb as virus culture was not performed. Nevertheless, the authors highlight potential risks of TiLV occuring in other freshwater fish, especially in the barbs family.

CRUSTACEANS VIRAL DISEASES

White Spot Syndrome

White spot syndrome (WSS) is a key disease in farmed prawns and shrimps, caused by the white spot syndrome virus (WSSV). WSSV is a non-occluded enveloped, rod-shaped double-stranded DNA virus with a tail-like appendage and can cause cumulative mortalities of 100% within two to seven days (Escobedo-Bonilla et al., 2008). The virus belongs to the genus *Whispovirus* in the family *Nimaviridae* (Sánchez-Paz, 2010). WSS was first reported in Malaysia in 1994 (Flegel, 1997) and has been observed in both tiger prawns (*Penaeus monodon*) and banana prawns (*Penaeus merguiensis*) in Malaysia (Wang et al., 2002).

A key symptom associated with WSS is the development of white spots on the exoskeleton and appendages, caused by the accumulation of cuticular substances on the inner surface of the cuticle following the destruction of cytoplasmic filaments post-infection (Rodríguez et al., 2003); however, this symptom is not diagnostic as it may also be caused by bacteria, high alkalinity and stress (Escobedo-Bonilla et al., 2008). Other symptoms include the pink-red colouration on the cephalothorax cuticle, reduction in feeding and increased lethargy, where infected shrimp swim slowly to the surface before sinking to the bottom to die (Sánchez-Martínez et al., 2007). Several internal organs also display destruction of tissue, accompanied by basophilic central inclusion bodies within the hypertrophied nuclei of cuticular epithelial and connective tissue cells (Escobedo-Bonilla et al., 2008). In addition, a yellow hypertrophied hepatopancreas may also develop due to haemolymph infiltration of the virus in the enlarged haemal sinuses and interstitial spaces (Sánchez-Martínez et al., 2007).

In Malaysia, several WSS outbreaks were investigated in a field study on shrimp farms from Penang, Kedah and Sarawak (Oseko, 2006). The author suggested that the poor environmental conditions on the farm led to the outbreak of this disease as previously reported in Thailand (Oseko, 2006). Two other studies also reported diseased tiger prawns obtained from farms along the coast of Peninsular Malaysia, indicating the occurrence of disease but this was not associated with any significant outbreak (Sahtout et al., 2001; Wang et al., 1995). While WSS has been commonly reported for tiger prawns, giant freshwater prawns (*Macrobrachium rosenbergii*), was found to be resistant to WSSV, possibly due to its innate immunity (Iwanaga & Lee, 2005).

White Tail Disease

White tail disease (WTD) is a common disease found in freshwater prawns and is caused by the *Macrobrachium rosenbergii* nodavirus (*Mr*NV) together with the extra small virus (XSV), where both are icosahedral and non-enveloped. The virus particles are commonly found in the cytoplasm of target cells and connective tissues, causing whitish colouration of the muscles starting from the tail to all prawn muscle. Eventually, the prawn shows abnormal behaviour, lethargy and anorexia, with mortality occuring within one to three days after the first clinical signs (Hameed & Bonami, 2012). Meanwhile, *Penaeus* prawns are not susceptible to this disease (Sudhakaran et al., 2006).

While outbreaks have not been reported, the *Mr*NV has been detected from the larvae of giant freshwater prawns randomly collected from hatcheries (Saedi et al., 2012). Detection of the virus was confirmed using RT-PCR and several samples were found to be positive for the virus despite showing no symptoms of WTD, which has also been reported previously (Widada et al., 2004). However, histological analysis of diseased prawns revealed progressive segmental myofibre degeneration of muscles and subsequent necrotic myopathy, both of which are associated with *Mr*NV infection (Saedi et al., 2012). As *Mr*NV has been detected in Malaysian freshwater prawns, future screening is vital to prevent the occurrence of outbreaks.

Infectious Hypodermal and Haematopoietic Necrosis Disease

Infectious hypodermal and haematopoietic necrosis disease (IHHNV) is a shrimp disease which causes high mortality rates in postlarvae and juvenile shrimps (Walker & Mohan, 2009). The causal agent, named after the disease, is a small icosahedral, non-enveloped virus from the family of *Parvoviridae* and contains a single-stranded linear DNA genome. Species affected by this disease includes blue shrimp (*Penaeus stylirostris*), whiteleg shrimp (*Penaeus vannamei*), tiger prawns, and giant freshwater prawns (Flegel, 2012).

The disease is fatal to blue shrimp and causes growth deformities in whiteleg shrimp and tiger prawn (Chayaburakul et al., 2005; Withyachumnarnkul et al., 2006). In larvae and juvenile giant freshwater prawns, high mortality rates occur while adults become carriers of the virus, which can be transmitted both horizontally and vertically (Hsieh et al., 2006). The clinical symptoms include large conspicuous eosinophilic intranuclear inclusions which occur in a range of organs, including the gills, nerve cords, stomach mucosa, antennal gland, and both hematopoietic and connective tissues. Infected prawns then become lethargic and swim on the surface before sinking to the bottom (Vega-Heredia et al., 2012).

In Malaysia, outbreaks of this disease has only been reported in recent years in farms located in Perak, Terengganu and Selangor, affecting giant freshwater prawn, tiger prawn and whiteleg shrimp (NACA, 2018). Prior to these outbreaks, several studies were conducted which detected the presence of IHHNV in wild prawn populations (Kua et al., 2011; Nita et al., 2012). In the study of Nita et al. (2012), wild giant freshwater prawns broodstocks from a river in Perak were screened and despite not displaying the usual symptoms, approximately 20% of the samples were found to be IHHNV positive. In contrast, another study from a river in Sarawak showed that, while clinical signs of disease were observed on giant freshwater prawns, but none of the samples were tested positive for IHHNV. The combination of these two studies suggest the presence of IHHNV in selected areas in Malaysia, highlighting the need for comprehensive screening of broodstocks before they are introduced into the hatchery (Nita et al., 2012).

FINFISH AND CRUSTACEAN BACTERIAL DISEASES

Vibriosis

Vibriosis is a major disease in aquaculture farms worldwide, caused by members from the genus *Vibrio*, which features Gram-negative, facultative anaerobic and rod shaped bacteria (Austin & Zhang, 2006). In addition to being an indigenous member of aquatic animals, *Vibrio* sp. also readily survive in the environment without being dependent on hosts, causing them to be a major issue in aquaculture (Ina-Salwany et al., 2018). Several notable species include *Vibrio harveyi*, *V. alginolyticus* and *V. anguillarum*. For Malaysian aquaculture, vibriosis has been reported in groupers, Asian seabass and crustaceans as described below:

Vibriosis in Fish. In fish, infection with *Vibrio* sp. commonly occurs in the intestinal epithelium when in contact with rearing water, potentially infecting and eliciting disease within a day (Verschuere et al., 2000). Penetration of host tissues is followed by the deployment of iron-sequestering systems and host cell damage via production of extra cellular products (Defoirdt, 2014). This leads to clinical symptoms such as septicaemia with haemorrhage at the base of fins, exophthalmia and cornea opacity in fishes. Fish exhibiting severe anaemia, as evidenced by pale gills, are at the moribund stage and are often anorexic. Oedematous lesions, predominantly centred on the hypodermis, were also often observed (Toranzo et al., 2005).

In the Malaysian aquaculture, vibriosis is a key disease faced by grouper farmers in Malaysia (Chuah, 2001). The disease was reported since the 1960s, where high mortality rates were observed in fish pens in Penang (Wong et al., 1979). Vibriosis was reported to occur mainly during the hatchery and grow-out phases; however, recent studies indicate that adults can also be affected (Nagasawa & Cruz-lacierda, 2004). Occurrence of vibriosis was also reported and found to be in combination with parasitic infections which occur at gills (Chuah, 2001). It is likely that the above correlates with the stress levels in groupers, such as higher temperatures which can lead to a reduction in immune responses and hence disease occurrence (Albert & Ransangan, 2013).

Meanwhile, for the Asian sea bass, an outbreak was reported in open net cages in Sabah, where the causal agent was identified as *V. harveyi* (Ransangan & Mustafa, 2009). The contributing cause of the outbreak was found to be the stressful conditions created from high stocking density of fish in net-cages. For adult fish, skin lesions, haemorrhage at the tips of fins and tails and eye opacity were the symptoms associated with vibriosis in Asian seabass. However, this is noted to be different from symptoms of vibriosis infection in other fish, which often present with gastroenteritis (Ransangan et al., 2012).

Vibriosis in Crustaceans. In crustaceans, infection with *Vibrio* sp. occurs mainly in the hepatopancreas - similar to other pathogenic bacteria. Infection of the digestive gland is eventually followed by the complete colonisation of the entire digestive tract. Clinical symptoms include severe damage to the hepatopancreas from inflammatory responses, leading to physiological imbalances and stress and eventually slower growth and mortality (Soonthornchai et al., 2015). Multiplication of bacteria on surfaces of shrimp, combined with poor nutritional and physiological conditions, may reduce the capacity of the shrimp to resist infection (Defoirdt et al., 2007). Luminous vibriosis is a form of the disease which occurs in high value crustaceans such as shrimps and tiger prawns. While this disease has been reported extensively in various countries practicing shrimp farming, very few studies report such outbreaks in Malaysia.

Acute Hepatopancreatic Necrosis Disease

Acute hepatopancreatic necrosis disease (AHPND) is a relatively new disease of shrimp, emerging in 2010 and was previously called 'early mortality syndrome' (EMS) due to mass mortality occurring within 10 days of post-stocking in a recently prepared pond (Tran et al., 2013). While the disease is generally caused by *Vibrio parahaemolyticus* carrying the toxin plasmids *PirA* and *PirB*, recent studies suggest *V. harveyi* strains may also elicit disease with the same plasmids. This disease has been reported to occur in shrimp farms worldwide, including Malaysia where the total economic loss from AHPND between 2011 to 2014 were estimated to reach US$ 0.49 billion (Kua et al., 2016).

A major clinical symptom of AHPND is the appearance of empty stomach and gut in tandem with a light-coloured, shrunken and atrophied hepatopancrease, which differs from a healthy dark-coloured brown hepatopancrease (Zorriehzahra & Banaederakhshan, 2015). Affected shrimp also often show soft shells, lethargy, muscle opacity and slow growth (Tran et al., 2013).

AHPND was first reported in Malaysia between late 2010 and early 2011, where several disease outbreaks occurring during the early stage of whiteleg shrimp culture due to *V. parahaemolyticus* infection (Kua et al., 2016). In 2011, high mortalities were reported to occur in shrimp farms throughout of Peninsular Malaysia, affecting the states of Perak, Penang, Kedah and Pahang. Eventually, samples from the states of Sabah, Sarawak, Terengganu, Johor and Melaka were also found positive for AHPND via histopathological analysis (Manan et al., 2015). While both whiteleg shrimp and tiger prawn were affected, infection rates were found to be higher in the former. High mortality rates were also documented in shrimp post larvae stages, juveniles and broodstocks. Nevertheless, prevalence of the disease has reduced throughout the years, from 50% in 2011 to 4% in 2015 (Kua et al., 2016).

Streptococcosis

Streptococcosis is a common disease which affects both Asian seabass, and hybrid tilapia and is caused by Gram-positive bacteria from the genus *Streptococcus*. *Streptococcus* sp. can also be found in the natural environment and a low bacteria load in water is sufficient to lead to mass mortality in fish (Agnew & Barnes, 2007). Major pathogens include *Streptococcus iniae* in Asian seabass and tilapia, and *S. agalactiae* in tilapia, which symptoms include erratic swimming, panophthalmitis, exophthalmos, corneal opacity and haemorrhage in the body cavity and ultimately resulted in mortality (Bromage & Owens, 2002). *Streptococcus* sp. have also been found to infect several organs, including the brain, blood, liver and kidney and liver of infected fishes (Abuseliana et al., 2011).

In Malaysia, streptococcosis has been reported only in tilapia and leading to 60-70% mortality in cage cultures located in Kenyir, Pedu and Pergau Lakes in 1997 (Siti-Zahrah et al., 2005). Several other studies have also reported on the mass mortalities and disease outbreaks caused by *S. agalactiae* (Abuseliana et al., 2011; Najiah et al., 2012). It was found that tilapia are more resistant towards water-based transmission of the pathogen when immersed in water containing 3 x 10^5

CFU/ml *S. agalactiae*, as no mortality was observed while clinical symptoms exhibited are limited to lethargy and loss of appetite (Abuseliana et al. 2011). Hence, it is unsure if this could lead to deterioration of health and ultimately susceptibility to the disease.

Meanwhile, Rahmatullah et al. (2017) reported on *S. iniae* isolated from tilapia cultured in Kenyir Lake. The fish showed abnormal swimming behaviour, haemorrhages were also found on pectoral, dorsal and caudal fins. The bacteria was isolated from brain, liver, kidney and eyeball. Experimental infection was also confirmed and the LD_{50} of the tilapia was 10^2 CFU/ml via IP injection, which was significantly lower bacteria concentration as opposed to other studies (Baums et al., 2013).

Overall, outbreaks of streptococcosis in the Malaysian aquaculture industry have been correlated with the intensification of tilapia aquaculture. Stressful conditions, including low water quality and high stocking density, can precipitate disease occurrence (Amal & Zamri-Saad, 2011). On the other hand, temperature fluctuations in the water due to dry seasons may also contribute to disease occurrence (Siti-Zahrah et al., 2004).

Motile Aeromonas Septicemia

Motile Aeromonas Septicaemia (MAS) is a disease linked to heavy mortalities in farmed and wild fishes globally (Harikrishnan & Balasundaram, 2005). The disease is caused by the genus *Aeromonas*, particularly *Aeromonas hydrophila* and *A. veronii* (Hamid et al., 2017). The virulence of Gram-negative *A. hydrophila* and *A. veronii* have been associated with virulence genes and haemolytic activity, allowing infections to occur when the host is under stress (Hamid et al., 2016). In Malaysia, *Aeromonas* sp. has been detected in giant freshwater prawns, tilapia and catfishes.

MAS is generally characterised by a wide range of symptoms caused by Aeronomad toxins (Laith & Najiah, 2013). Infected fish show abnormal swimming behaviour and aggregation on the water surface, with external symptoms including small surface lesions, local haemorrhages particularly in the gills and vent, ulcers, abscesses, exophthalmia, abdominal distensions (Hamid et al., 2017). Discolouration of catfish from normal gray to pinkish has also been associated as a symptom of infection from *Aeromonas* sp. (Anyanwu et al., 2015). Meanwhile, internal symptoms in fish include anemia, accumulation of ascitic fluid and ulcerative damage to the organs, notably the kidney and liver (Laith & Najiah, 2013).

Despite Aeromonas commonly reported as a major cause of mortality in the industry, only two cases of outbreaks were reported in Malaysia. The first case of mass mortality reported in a tilapia farm identified the causal agents to be a combination of *A. veronii* and the TiLV (Amal et al., 2018). The analysis of the symptoms, clinical signs and histopathological findings of affected fish also suggested that both pathogens acted synergistically, which has also been reported in Egypt and Thailand (Nicholson et al., 2017; Surachetpong et al., 2017). As TiLV is a major concern for the tilapia industry, the author cautions that such co-infections may further aggravate the issue and further studies should be conducted to understand the relationship of both pathogens (Amal et al., 2018).

Meanwhile, the second case reported the isolation and identification of *A. hydrophila* in diseased catfishes displaying common clinical and histological symptoms of MAS from a local farm (Laith & Najiah, 2013). The authors suggested that the virulence factor aerolysin and the presence of β-hemolysis in the bacteria may have played a role, which may have triggered the disease outbreak in addition to other factors including stress and changes in the environmental conditions (Laith & Najiah, 2013).

Piscine Tuberculosis

Piscine tuberculosis, also known as piscine mycobacteriosis, is caused by *Mycobacterium* sp., which are Gram-positive, pleomorphic, non-motile rod shaped bacterium found in soil and water. A wide range of species has been isolated from fishes, *Mycobacterium marinum*, *M. fortuitum* and *M. chelonae* are the only reported agents causing piscine mycobacteriosis (Gauthier & Rhodes, 2009).

As a chronic disease, piscine tuberculosis may not produce clinical symptoms, particularly in the early stages of infection. External clinical symptoms include scale loss and haemorrhagic lesions, abnormal behavior, spinal defects, emaciation, and ascites (Gauthier & Rhodes, 2009). Infected fish also show reduced food intake and weakened swimming one week prior to death (Swaim et al., 2006). Meanwhile, internal symptoms include enlargement of the spleen, kidney and liver, and characteristic grey or white nodules (granulomas) in internal organs (Toranzo et al., 2005). These granulomatous inflammation can be considered as a classic histopathological manifestation of chronic piscine mycobacteriosis, which are composed of concentric layers of epithelioid cells forming a discrete spherical lesions and is produced in multiple organs and tissues (Gauthier & Rhodes, 2009). While fish with chronic infections of mycobacteria may survive for up to eight weeks, acute infection usually leads to uncontrolled development of the pathogen and death of all fishes in within 16 days (van der Woude et al., 2014). Piscine tuberculosis outbreak has not been reported for aquaculture species in Malaysia despite being highlighted as a common bacterial disease in shrimp farms (Hashish et al., 2018).

Edwardsiellosis

Edwardsiellosis is a disease caused by genus of *Edwardsiella*, mainly *Edwardsiella tarda,* a Gram-negative, rod-shaped bacterium, which has been isolated from lakes, streams, seawater, mud and intestines of healthy aquatic animals (Choudhury et al., 2017; Mohanty & Sahoo, 2007). Edwardsiellosis causes spiralling movement and fish death with mouth agape and opercular flared, potentially due to anaemia and oxygen insufficiency. Other signs include lesions on skin, pale gills, tumefaction of the eye, excessive mucus secretion,scale erosion and ulcers (Xu & Zhang, 2014). Disease progression leads to the development of abscesses within the muscles of the flanks or caudal peduncle, which rapidly increases in size and further develops into large cavities filled with gas. Incission of these lesions lead to the emission of a foul odour from necrotic tissue remnants (Mohanty & Sahoo, 2007). Histologically, the lesions are characterised focal necrosis, often extending from muscle, haemopoietic tissue and liver parenchyma to perforate the abdominal wall (Choudhury et al., 2017).

So far, no reports have been published on *E. tarda* outbreaks in Malaysia. However, several studies report the isolation of *E. tarda* from fish. The first study reports bacteria isolation from diseased African catfish, tilapia, Asian swamp eel (*Monopterus albus*) and snakeskin gouramy (*Trichogaster pectoralis*) from commercial farms in Terengganu (Lee & Musa, 2008). The second study reports the isolation of *E. tarda* from an Asian seabass hatchery in Terengganu (Nadirah et al., 2012). Lastly, *E. tarda* was found to co-infect tilapia with *A. hydrophilla* in a farm in Kelantan, where fish displayed the symptoms of both MAS and edwardsiellosis (Lee & Wendy, 2017). Unfortunately, the specific cause of the disease was not investigated. One similarity shared between the studies reported heavy metal and antibiotic resistance in *E. tarda*, echoing concerns of the development of co-selection and cross-resistance in the bacteria community of the aquaculture environment in Malaysia (Lee & Wendy, 2017).

FUTURE DIRECTIONS AND PRIORITIES

Diseases continue to overwhelm the aquaculture industry, coupled with continuous intensification and expansion, eventually causing a constraint in economic and social developments in many countries, including Malaysia (Bondad-Reantaso et al., 2005). Several methods aimed at alleviating potential issues in the Malaysian aquaculture industry are proposed as follows:

Improving Disease Monitoring via Farmer Input

Farmers are ideal as a frontline for disease surveillance, especially via syndromic surveillance, which is described as "use of health-related information that may be indicative of a probability of change in the health of a population that merits further research or enables a timely impact assessment and action requirement" (Brugere et al., 2017). In brief, farmers can identify pending disease outbreaks via abnormal signs, such as patterns of swimming, poor growth and lack of food consumption (FAO, 2001). These signs could be verified with "point of care" surveillance tests which aspire to the ASSURED criteria, being affordable, sensitive, specific, user-friendly, robist, rapid, equipment-free and deliverable, which may be in forms of basic tests which can be used by untrained users while obtaining a robust result (Kettler et al., 2004). With immediate notification to authorities, action can be taken to remedy while also preventing disease outbreaks.

Improvement of Surveillance and Diagnostic Methods

Currently, the Malaysian Department of Fisheries carries out surveillance twice a year, while not much information is presented on diagnostics available (DOF, 2018). The development of risk-based surveillance (RBS), which emphasizes on the risk assessment methods and traditional design surveillance for appropriate and cost-effective data collection, could be applied in aquaculture (Stärk et al., 2006). An example for risk-assessment consideration is the identification of sources for pathogen exposure and transmission, such as via introduction of live fish directly onto farms or seasonal changes in temperature which contributes to disease spread. The identification of disease introduction and spread routes and subsequent allows biosecurity measures to be put in place to mitigate those risks (Oidtmann et al., 2013).

PCR is one of the most common methods applied for diagnostics of fish diseases in the Malaysian aquaculture industry. While its application in farms is a challenge due to the requirements of a thermocycler and technical knowledge. Several issues could be circumvented via use of loop mediated isothermal amplification (LAMP), which is similar to the PCR while being relatively equipment-free and robust (Adams & Thompson, 2011). Among the pathogens listed in this review, LAMP is currently shown to detect for CyHV-3, *Iridovirus*, *Betanodavirus*, WSSV, *Mr*NV and XSV, IHHNV, *V. parahaemolyticus, S. agalactiae,* and *E. tarda*. Alternatively, lateral flow devises (LFD) are also simple to use, cheap and rapid, which act via detection of specific antibodies of an infectious agent by its diffusion through porous substrate and the subsequent appearance of two coloured lines (Brugere et al., 2017). LFD are available for detection of WSSV and CyHV-3 (Sithigorngul et al., 2006; Vrancken et al., 2013).

Improvement and Enforcement of Biosecurity

In the Malaysian aquaculture industry, the biosecurity measures are categorised under the Official Analysis plan by the Department of Fisheries (DOF) which includes aquaculture farms, hatcheries, cages, ocean landings, export and import premises, as well as aquatic animal processing factories (DOF, 2018). The biosecurity plan aims to ensure that all farms operate in suitable locations while also adhering to biosecurity requirements. For aquatic animal health, surveillance is conducted bi-anually according to diseases outlined for that particular year according to the risk of diseases. The biosecurity plan can be improved further, such as through the development of contingency plans, and enforcement of record keeping and traceability.

Contingency plans reduce the impact of surprise as it includes familiarisation of the emergency situation through the assessment of risks, identification of uncertainties, definition of priorities and response strategies which may differ between aquaculture farms due to differences in equipment and management techniques, as well as the requirement of staff trained to act in an emergency (Georgiades et al., 2016). Such preparations ensure a farm's viability as they enable recovery from emergency situations while also reducing loss.

Enforcement of record keeping ensures product traceability, allowing identification of sources and input which led to disease, while also ensuring that other stock were not affected (Georgiades et al., 2016; Yanong, 2012). Additionally, the recording of environmental conditions and animal husbandry practices may also provide insights as to those conditions that lead to sub-optimal stock production or disease, forecasting potential issues and potentially preventing problems before they arise (Johansen, 2013; Meyers, 2010). While the degree of record keeping by individual farmers is uncertain, improving this practice as a form of biosecurity could benefit all farms in general with the information obtained.

CONCLUSION

In conclusion, this review has provided an overview of the types of viral and bacterial diseases detected in Malaysian aquaculture and their current status. Among the diseases highlighted, viral diseases are considered more significant due to persistence and the lack of means of recovery, whereas bacterial diseases are often a product of poor culture conditions. Instead of placing emphasis on the recovery from disease, prevention, through improved biosecurity measures, is highlighted as the key solution. These could also benefit environmental protection and provide sustainability if good aquaculture practices were implemented. Nevertheless, governing bodies could also play a role in the improvement of biosecurity, especially in smaller farms with lower capital. Ultimately, collective effort from all sides may effectively reduce the occurrences of disease, creating a long term benefit while preventing future economic losses to disease outbreaks.

ACKNOWLEDGEMENTS

We gratefully acknowledge Crops for Future (CFF) research centre for the PhD studentship (NCHB0004) and Dr Jonathan D. Wood for his advices on this work.

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