

What Happened Over the Last 10 Years (2012 to 2021): A Bibliometric Analysis of Acute Hepatopancreatic Necrosis Disease (AHPND) Research in Southeast Asia

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Abstract: This paper described the research landscape in Southeast Asia over the last 10 years (2012 to 2021) in terms of Acute Hepatopancreatic Necrosis Disease (AHPND), a shrimp disease prevalent in the region. Three hundred and ninety-six (396) records from Scopus database were screened for duplication and eligibility, to come up with a total of 155 papers used in the bibliometric analysis. Among all countries, Thailand produced the most publications, total citations, and the highest *h*-index. No papers from Brunei, Cambodia, Lao PDR, Myanmar, and Timor Leste on AHPND were obtained. Southeast Asian countries had strong linkages within the region and beyond. Overlay visualization of keywords used in publications over the last 10 years showed that there was a shift in focus from the diagnosis and characterization of the disease to treatments. Interestingly, there were no significant correlations between a country's research investments and productivity, possibly because of issues on allocation. However, there was a positive correlation between the region's research outputs and crustacean production. Limitations of the study include the use of a single database and the exclusion of non-peer reviewed papers. Nonetheless, these results may serve as basis on policymaking on AHPND research investments, prioritization, and allocation in Southeast Asia.

Keywords: *Acute hepatopancreatic necrosis diseases; bibliometric analysis; shrimp early mortality syndrome, Southeast Asia*

Introduction

In 2009, the first report of a shrimp disease called acute hepatopancreatic necrosis disease (AHPND) was in China. The pathology of this disease was, at first, primarily based on the gross examination of the shrimp hepatopancreas. Some of the gross signs of AHPND include the discoloration of the hepatopancreas due to pigment loss and degeneration of the hepatopancreas. This disease was initially observed to be caused by *Vibrio parahaemolyticus* (Tran *et al.*, 2013). It is characterized by collapsed epithelial lining of the hepatopancreas, lethargy, and empty gut (Soto-Rodriguez *et al.*, 2015). After this initial report, it has since plagued Southeast Asian countries including Vietnam, Malaysia, Indonesia, Thailand, and the Philippines (De La Peña *et al.*, 2015; Flegel, 2012; Hastuti & Desrina, 2016). Such as in the case of the Philippines, wherein between 2014 and 2015, disease outbreaks caused by *Vibrio* spp. in shrimp farms were recorded and confirmed to be the first report of AHPND in the country (Dabu *et al.*, 2017; De La Peña *et al.*, 2015).

Because of these outbreaks, a decline in shrimp production was recorded (Figure 1) which caused the country huge economic loss (Figure 2) (Philippine Statistics Authority [PSA, 2013, 2015, 2017, 2019]). In Thailand, total shrimp production decreased from around 611, 194 tonnes to 200,000 tonnes due to AHPND – costing the country around US\$11.58 billion in total monetary value. Similarly, Vietnam reported a loss of around US\$ 97.96 million due to AHPND (Shinn *et al.*, 2018). Reports of AHPND in other parts of the world were also published in recent years, indicating its impact not just in Southeast Asia, but also worldwide (Dhar *et al.*, 2019; Soto-Rodriguez *et al.*, 2015).

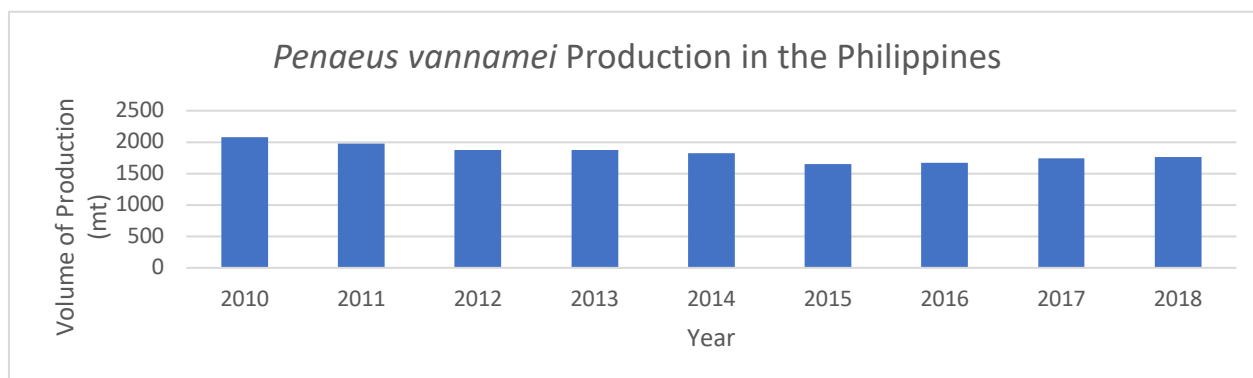


Figure 1: Total *Penaeus vannamei* production (in metric tons) in the Philippines from Year 2010 to 2018 based on PSA statistics (PSA, 2013, 2015, 2017, 2019).

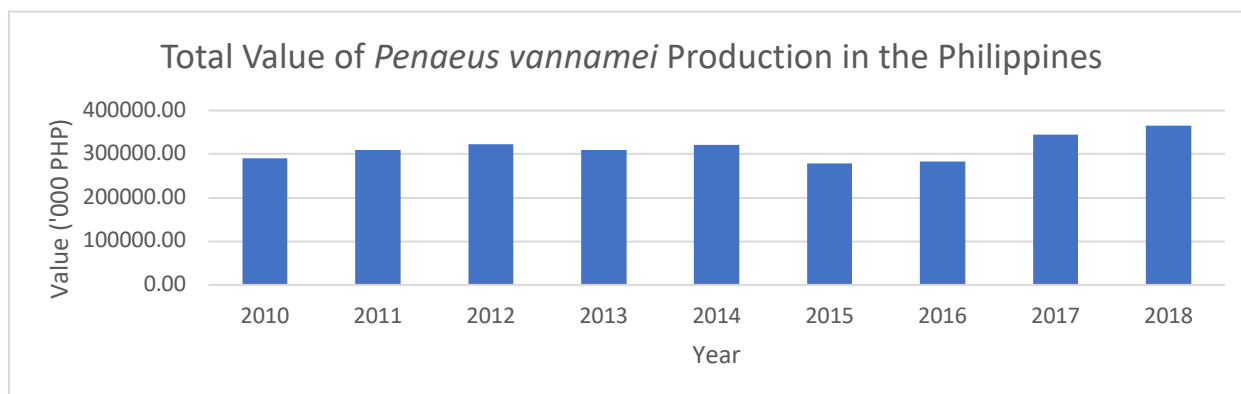


Figure 2: Value of the total *Penaeus vannamei* production (in Philippine Peso) in the Philippines from Year 2010 to 2018 based on PSA statistics (PSA, 2013, 2015, 2017, 2019).

Because of the importance of shrimp aquaculture in the Southeast Asian region – contributing much to their economy, as well as the region's role in the global shrimp production (FAO, 2020; GLOBEFISH, 2019), disease outbreaks cause huge economic losses to Southeast Asia (Shinn *et al.*, 2018). Thus, AHPND has been highlighted as one of the major shrimp diseases which needs to be addressed (Kumar *et al.*, 2021). Several approaches on mitigating this issue hampering the development of the Southeast Asian shrimp industry were proposed in the past (Santos *et al.*, 2020). But the question is this: where does Southeast Asia stand now on AHPND research?

In this paper, literature discussing AHPND were analyzed through bibliometric analysis. This approach is used to assess the current status of research on a particular topic by measuring the research outputs on different levels, including countries, institutions, and

authors (Tantengco *et al.*, 2021). It provides guidance to policymaking, especially on research investments and outcomes (Junquera & Mitre, 2007).

Previous bibliometric analyses on aquaculture showed that scientific literature focused much on the themes of genetics and reproduction, growth and physiology, farming systems and environment, nutrition, water quality, and health (Natale *et al.*, 2012). There were also bibliometric analyses looking at researches on specific commodities (Cantillo *et al.*, 2021) and practical aquaculture efficiency (See *et al.*, 2021). A bibliometric analyses on shrimp diseases was also performed ten years ago (Dastidar *et al.*, 2013). But where are we on the topic of AHPND, especially in the case of Southeast Asia, a region contributing much on the global shrimp production? This question was aimed to be answered by this paper, with the goal of contributing to research policy via bibliometric analysis (Allen *et al.*, 2009). Research trends over the last 10 years, as well as linkages between countries in and outside of the region were also visualized.

Additionally, research productivity on AHPND in Southeast Asia was also correlated in this paper with socioeconomic factors of each country and the region as a whole to have a glimpse of the research atmosphere and its impact to the region's progress, and vice versa (Sokolov-Mladenović *et al.*, 2016; Tantengco *et al.*, 2021; Tuna *et al.*, 2015).

Materials and Methods

Selection of publications

Literature search for publications in the last 10 years (2012-2021) was performed using the Scopus database. The following terms were used: "Acute hepatopancreatic necrosis disease" or "AHPND" or "shrimp early mortality syndrome" or "shrimp EMS." Affiliations of the authors were limited to Southeast Asian countries – Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, The Philippines, Singapore, Thailand, Timor Leste, and Vietnam (Tantengco *et al.*, 2021). The literature search was performed on 01 November 2021, and papers which were published in 2021 but were included in the 2022 issues of the journals were included (Figure 3).

Data collection and visualization

A total of 396 records were gathered through the literature search described above. After removing the duplications (171) and papers which were irrelevant to the topic, 155 papers were included in the bibliometric analysis (Page *et al.*, 2021). Information such as the title of the publication, year of publication, journal, names of the authors, affiliations, country of affiliations, keywords, citations, and funding source were collected.

Furthermore, country-specific data such as total population, gross domestic product (GDP), GDP *per capita*, research and development expenditure share in GDP, researcher-to-population ratio, and total aquaculture production were obtained from the World Bank Open Data (The World Bank, 2021). The total crustacean production was also obtained from the 2020 Food and Agriculture Organization of the United Nations (FAO) report (FAO, 2020).

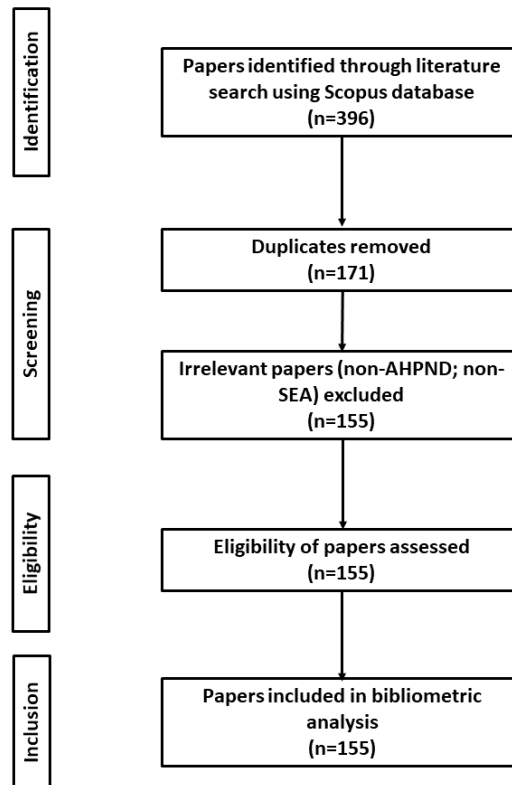


Figure 3: Flow chart illustrating the steps taken in the selection of AHPND papers for bibliometric analysis based on PRISMA Guidelines (Page et al., 2021).

Using VOSviewer version 1.6.17 (van Eck & Waltman, 2010), collaboration networks between countries of affiliations and linkages between keywords used in publications were visualized.

Statistical Analysis

Statistical analysis was performed using IBM SPSS 2.0 software. Correlations between the country-specific data and the bibliometric indices were determined using Pearson's correlation test.

Results and discussion

Publications on AHPND over the last ten years showed a steady increase

In 2012, Dr. Timothy Flegel published a paper looking at the current status of shrimp pathogens in Asia. In the same paper, AHPND was cited as one of the emerging diseases whose causative agent is still unknown at that time (Flegel, 2012). Two years after this publication, reports of genome sequences of *Vibrio parahaemolyticus* causing AHPND were published (Kondo et al., 2014). Thereafter, in 2017, the number of papers discussing AHPND steadily increased (Figure 4). The highest number of papers on AHPND published in the region was in 2020 (n=33). So far, three papers are now published in 2021 but was included in the 2022 issues of the journals.

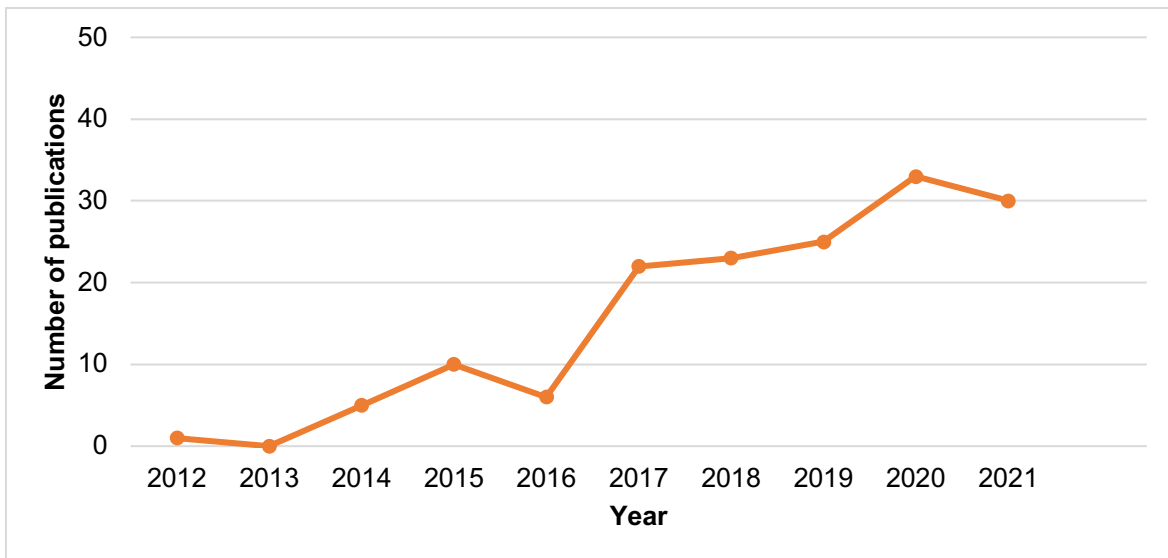


Figure 4: Total number of publications from 2012 to 2021. Publications which were available in 2021 but were included in the 2022 issues of journals were still considered.

Thailand leads the region in terms of publications on AHPND

Among all Southeast Asian countries, Brunei, Cambodia, Lao PDR, Myanmar, and Timor Leste did not produce a paper on AHPND in the last 10 years based on literature search in Scopus database. On the other hand, Thailand leads the region in terms of the number of publications on AHPND (n=94) (Figure 5). Papers from Thai researchers accounted for around 61% of the total number of papers on AHPND in Southeast Asia. Behind Thailand is Vietnam with 33 papers, Malaysia with 25, and the Philippines with 15. Despite its archipelagic geography, meanwhile, Indonesia only published four papers and Singapore comes last with only a single paper on AHPND.

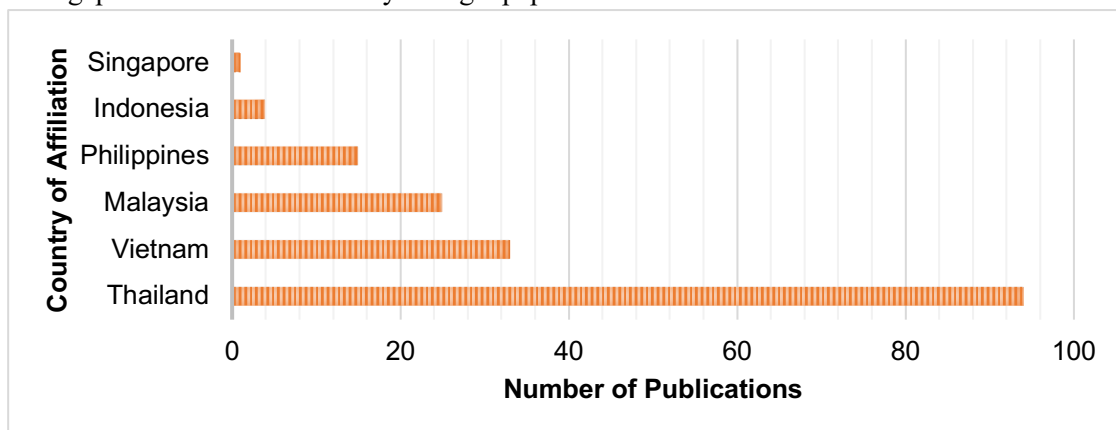


Figure 5: Total number of publications on AHPND of Southeast Asian countries for the last 10 years (2012 to 2021).

Seven of the top 10 institutions in Southeast Asia in terms of research outputs on AHPND were from Thailand (Table 1). Most of these papers were published by authors from the National Center for Genetic Engineering and Biotechnology, Mahidol University, and the National Science and Technology Development Agency. Despite placing third in terms of number of publications, two Malaysian institutions, the University Putra Malaysia

and the Universiti Malaya, were part of the 10 most published institutions in Southeast Asia on AHPND research. Lastly, Can Tho University in Vietnam was the only Vietnamese institution in the top 10 despite ranking second behind Thailand in terms of number of research publications.

The total number of publications from Thailand and Vietnam translated to the number of total citations (Figure 6) and h -index (Figure 7). However, papers from the Philippines were cited more than Malaysia despite the latter having ten more publications. Despite this, though, Malaysia had a higher h -index.

Table 1: Top 10 institutions in Southeast Asia based on the number of publications on AHPND.

Institution	Number of Publications	Total Citations	h -index
National Center for Genetic Engineering and Biotechnology (Thailand)	37	1382	14
Mahidol University (Thailand)	35	1321	14
National Science and Technology Development Agency (Thailand)	33	1362	14
Chulalongkorn University (Thailand)	20	267	11
Prince of Songkla University (Thailand)	16	204	9
Kasetsart University (Thailand)	10	168	4
University Putra Malaysia (Malaysia)	9	80	5
Universiti Malaya (Malaysia)	8	51	4
Srinakharinwirot University (Thailand)	6	112	5
Can Tho University (Vietnam)	6	15	3

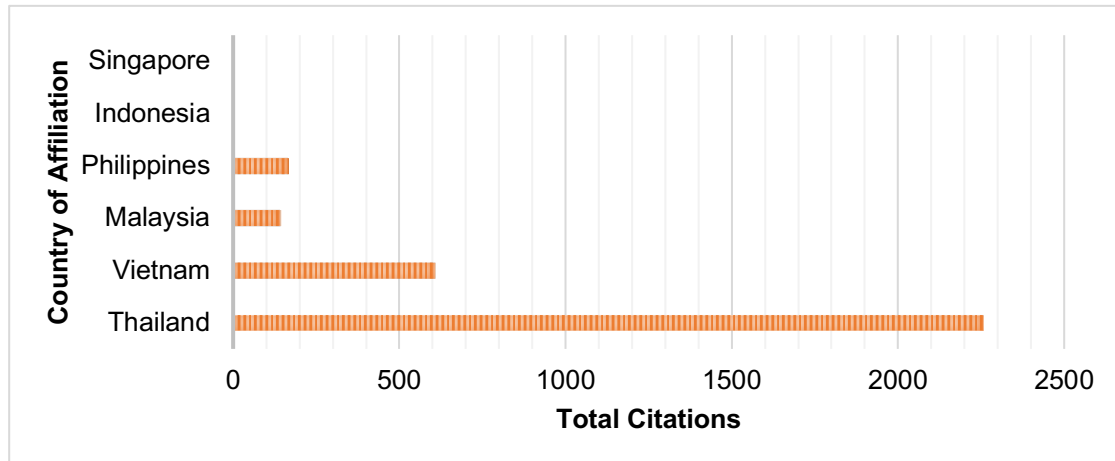


Figure 6: Total number of citations of papers on AHPND from Southeast Asian countries for the last 10 years (2012 to 2021).

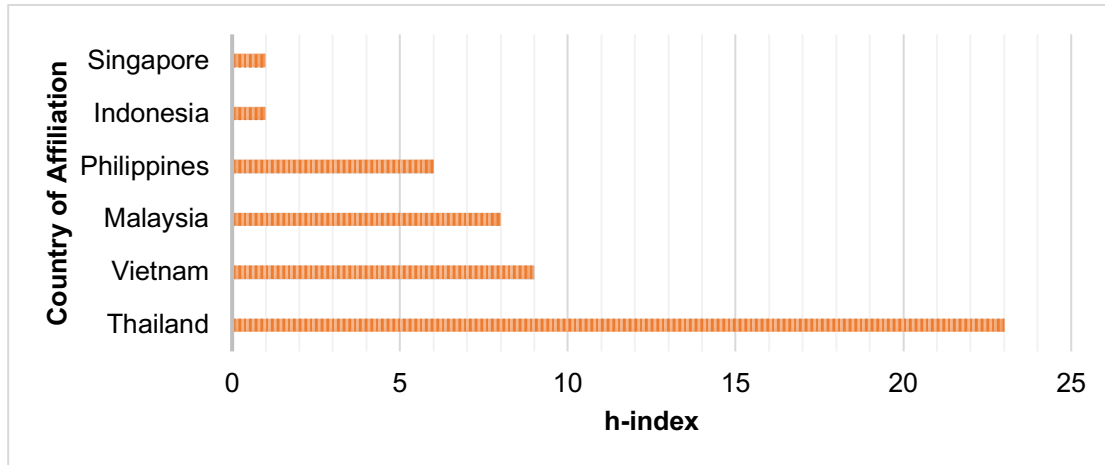


Figure 7: h-index of Southeast Asian countries based on papers on AHPND published in the last 10 years (2012 to 2021).

Most of the papers were original research articles, accounting to around 93% of the total publications (Figure 8). There were only six review papers on AHPND published in the last 10 years, yet, 18% of the total citations were from these publications (Table 2).

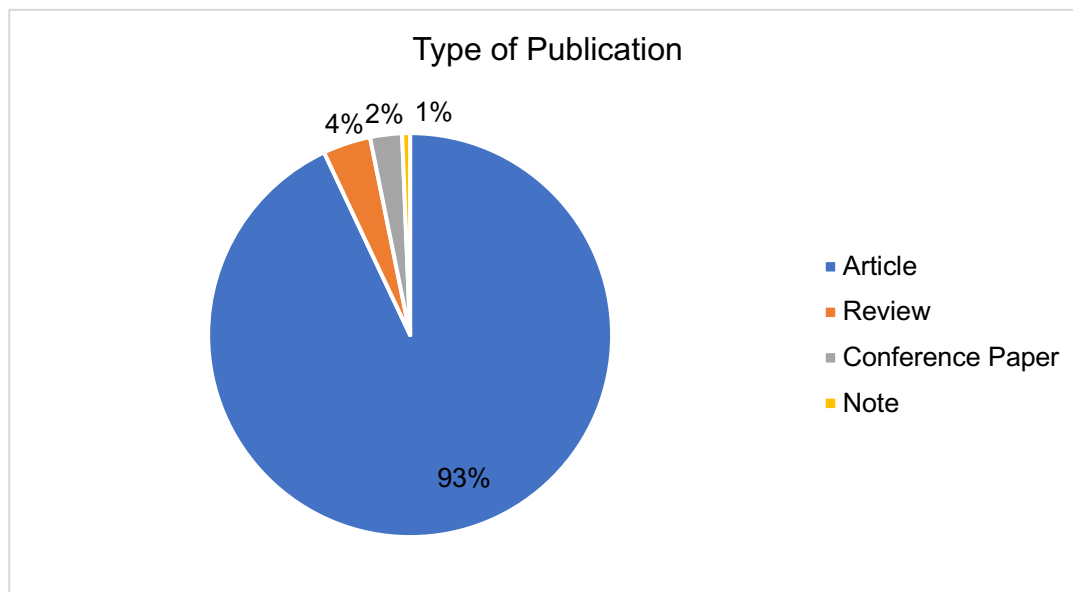


Figure 8: Types of publication of papers on AHPND published in Southeast Asia in the last 10 years (2012 to 2021).

Among the top 10 journals where AHPND researches were published, only two were not specializing on aquaculture: Developmental and Comparative Immunology (n=5), and Scientific Reports (n=5). The rest of which are from Asian Fisheries Science (n=10), Fish and Shellfish Immunology (n=10), Journal of Fish Diseases (n=7), Diseases of Aquatic Organisms (n=6), Aquaculture International (n=5), Aquaculture Research (n=5), and Aquaculture Reports (n=4). Meanwhile, around 19% of the papers on AHPND were published in Aquaculture (n=29).

The work by Flegel in 2012 was the most cited paper on AHPND. This was followed by the updates on emerging shrimp diseases in 2016 by Thitamadee *et al.* The remaining papers in the list of the 10 most cited publications were about the variations in the phenotypes and genomic sequences of *V. parahaemolyticus*, as well as the characterization of its pathogenesis, particularly, the role of pir toxins (Table 2). Beyond Southeast Asia, other parts of the world are also looking into the same topics on AHPND around the same time (Soto-Rodriguez *et al.*, 2015).

Table 2: Most cited publications on AHPND published in the last 10 years (2012 to 2021) in Southeast Asia.

Authors	Title	Year	Journal	Total Citations
Flegel T.W.	Historic emergence, impact and current status of shrimp pathogens in Asia	2012	Journal of Invertebrate Pathology	2855
Thitamadee <i>et al.</i>	Review of current disease threats for cultivated penaeid shrimp in Asia	2016	Aquaculture	300
Joshi <i>et al.</i>	Variation in <i>Vibrio parahaemolyticus</i> isolates from a single Thai shrimp farm experiencing an outbreak of acute hepatopancreatic necrosis disease (AHPND)	2014	Aquaculture	251
Han <i>et al.</i>	Phototransducing insect-related (Pir) toxin-like genes in a plasmid of <i>Vibrio parahaemolyticus</i> , the causative agent of acute hepatopancreatic necrosis disease (AHPND) of shrimp	2015	Diseases of Aquatic Organisms	183
Sirikharin <i>et al.</i>	Characterization and PCR detection of binary, pir-like toxins from <i>Vibrio parahaemolyticus</i> isolates that cause acute hepatopancreatic necrosis disease (AHPND) in shrimp	2015	PLoS ONE	175
Lai <i>et al.</i>	Pathogenesis of acute hepatopancreatic necrosis disease (AHPND) in shrimp	2015	Fish and Shellfish Immunology	130
Yang <i>et al.</i>	Draft genome sequences of four strains of <i>Vibrio parahaemolyticus</i> , three of which cause early mortality syndrome/acute hepatopancreatic necrosis disease in shrimp in China and Thailand	2014	Genome Announcements	124
Kondo <i>et al.</i>	Draft genome sequence of non- <i>Vibrio parahaemolyticus</i> acute hepatopancreatic necrosis disease strain KC13.17.5, isolated from diseased shrimp in Vietnam	2015	Genome Announcements	95
Kondo <i>et al.</i>	Draft genome sequences of six strains of <i>Vibrio parahaemolyticus</i> isolated from early mortality syndrome/acute hepatopancreatic necrosis disease shrimp in Thailand	2014	Genome Announcements	94

This is in agreement with the results of the overlay visualization of keywords performed via VOSviewer version 1.6.17 (Figure 9) wherein early researches on AHPND focused on the characterization of the bacterial causative agent and its plasmid, development of detection protocols via polymerase chain reaction (PCR), loop-mediated isothermal amplification (LAMP), and histopathological analyses. As shown in Figure 9, recent advances in AHPND research in Southeast Asia include the characterization of non-*Vibrio parahaemolyticus* species as causative agents of AHPND (De Guia *et al.*, 2020; Dong *et al.*, 2017; Muthukrishnan *et al.*, 2019). As time progressed, research on AHPND focused on combating the disease (Santos *et al.*, 2020), immune response of shrimp against AHPND upon supplementation with immunostimulants (Alonzo *et al.*, 2017; Arabit *et al.*, 2017), generation of polyclonal antibodies (Nguyen-Phuoc *et al.*, 2021), the role of quorum sensing (Paopradit *et al.*, 2021), and the use of bioactive compounds to target the mechanisms involved in the pathogenesis of AHPND (Dadi *et al.*, 2021; Guzman *et al.*, 2021; Karnjana *et al.*, 2019, 2020; Nguyen Thi Truc *et al.*, 2019; Soowannayan, Boonmee, *et al.*, 2019; Soowannayan, Chandra Teja, *et al.*, 2019; Yatip *et al.*, 2018).

Thailand collaborates most frequently with Vietnam, Japan, the Philippines, and Taiwan in Asia. It also has several linkages with countries in and outside of Asia. Meanwhile, Vietnam had strong collaborations with Thailand and Malaysia in the region, and Taiwan and Japan in East Asia. It also had networks with European and South American countries. Among Southeast Asian countries, Malaysia collaborated with Thailand, Vietnam, and the Philippines. On the other hand, the Philippines frequently collaborated with Thailand and Malaysia. Outside the region, it had collaborations with Japan, Taiwan, the United States, Germany, and the United Kingdom. Interestingly, Indonesia only had collaborations on AHPND research with European countries such as Sweden, Netherlands, France, and Belgium over the last 10 years (Figure 10).

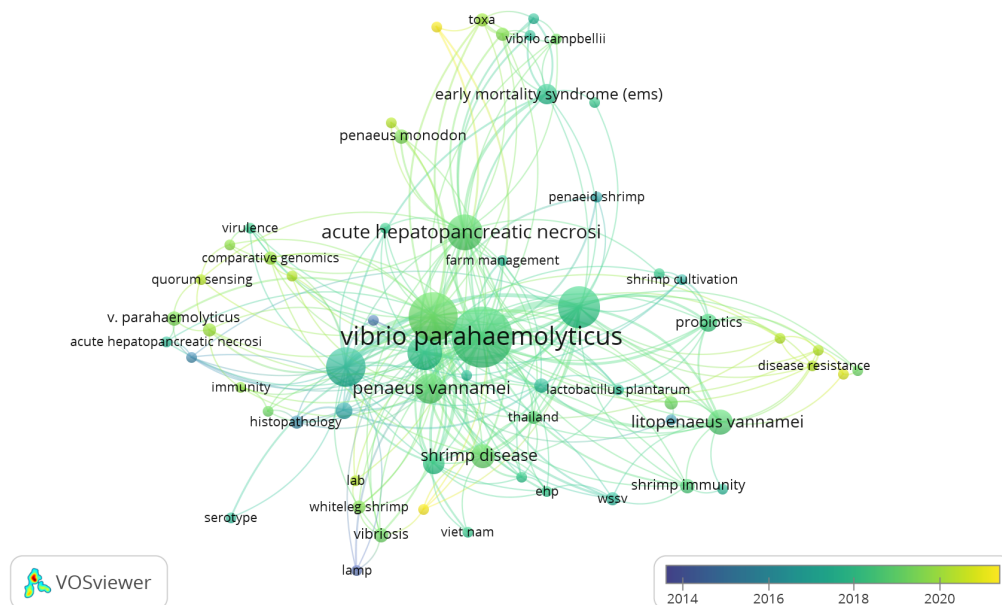


Figure 9: Visualization of linkages between keywords used in the publications on AHPND in Southeast Asia in the last 10 years (2012 to 2021). The size of the circles indicates the number of publications where the keyword was included. The thickness of the lines signifies the weight of the linkages between the keywords. The color of the circles and the lines indicate the year when the keyword occurred more frequently.

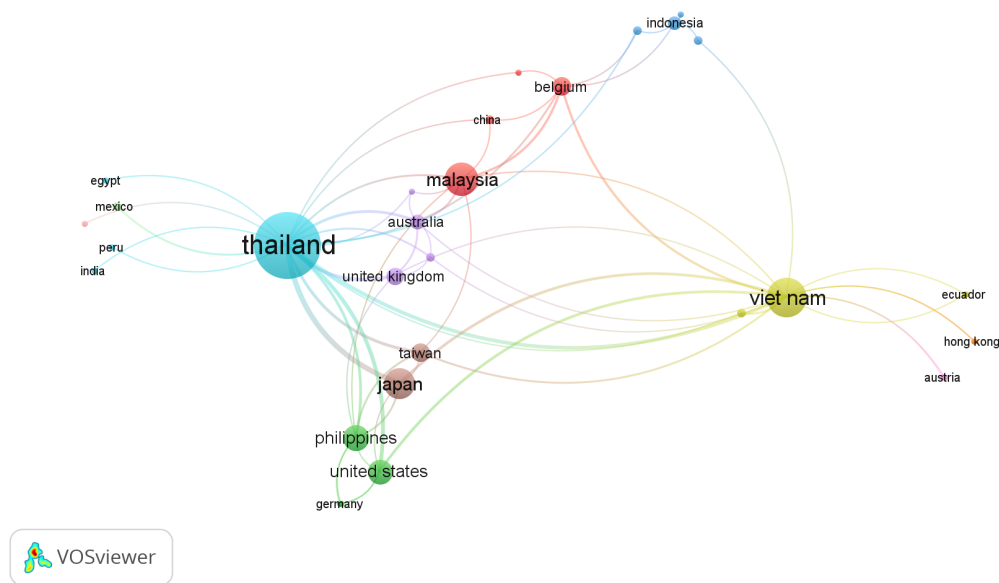


Figure 10: Visualization of collaboration between Southeast Asia and other countries. The size of the circles indicates the number of publications of each country. The thickness of the lines signifies the strength of the linkages between countries.

Thailand, having the most publications in Southeast Asia, also funded most of the research on AHPND in the region, based on the number of research funded by its institutions. Interestingly, though they are not part of Southeast Asia, Japan and Taiwan funded several AHPND research conducted in the region (Figure 11).

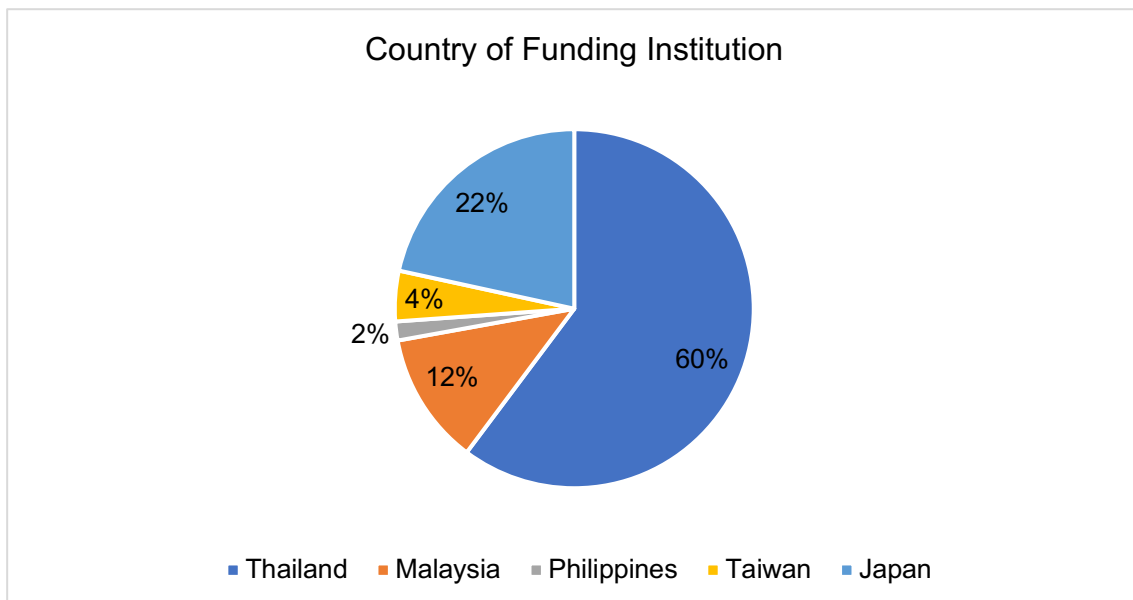


Figure 11: Countries where most of the funding for AHPND papers published in Southeast Asia came from.

Correlations between research publications and the economy

Gross domestic product (GDP), percent share on GDP of research and development (R&D) expenditure, and researcher-to-population ratio were previously reported to have positive correlation to research outcomes in Southeast Asia (Tantengco *et al.*, 2021). The same was observed for countries outside the region (Sokolov-Mladenović *et al.*, 2016). However, that is not the case for research on AHPND in Southeast Asia (Supplementary Table 1). No significant correlations were observed between different country-specific data and research publications (Table 3). Similar results were reported in a number of OECD countries and Turkey (Ntuli *et al.*, 2014). This is probably because of the allocations of research funds on a variety of fields (Manners & van Etten, 2018; Tuna *et al.*, 2015). It is possible that, though there is an increase in %GDP share for R&D expenditure, research funds were allocated elsewhere.

Table 3. *Correlations between country-specific data and bibliometric indices.*

Country data	Bibliometric indices	ρ	p-value
Total Population*	Publications	-0.218	0.679
	Citation	-0.173	0.744
	h-index	-0.269	0.606
Gross Domestic Product (GDP)*	Publications	0.149	0.778
	Citation	-0.086	0.871
	h-index	-0.228	0.664
GDP per capita*	Publications	-0.349	0.497
	Citation	-0.269	0.607
	h-index	-0.377	0.461
%GDP Share for Research Expenditure*	Publications	0.028	0.958
	Citation	0.06	0.911
	h-index	0.006	0.991
Researchers in R&D (per million people)*	Publications	-0.255	0.625
	Citation	-0.2	0.704
	h-index	-0.278	0.594
Total Aquaculture Production**	Publications	-0.333	0.625
	Citation	-0.282	0.704
	h-index	-0.399	0.594
Total Crustacean Production**	Publications	-0.149	0.811
	Citation	-0.043	0.945
	h-index	-0.252	0.683

*Based on figures for East Asia and the Pacific (excluding high-income economies) aggregates (The World Bank, 2021)

**Based on figures for Asia, excluding China (FAO, 2020).

Nonetheless, based on annual data aggregating the values from the region, it was found that there is a positive correlation between the total publications and citations of papers published in Southeast Asia and the total crustacean production (Table 4). While it is expected that the impact of research outputs take time before it is reflected in various economic factors (Tuna *et al.*, 2015), it is possible that the changes in the data were at least partially affected by policies implemented as a result of novel information coming out of these research papers (Bertoni *et al.*, 2018). While this study provides an overview of the current status of research on AHPND in Southeast Asia, it is important to consider its limitations, including the use of other databases and other non-peer reviewed papers (Palcullo *et al.*, 2019), and the impact of other socioeconomic factors which were not included in the analyses.

Finally, while research outputs (Figure 4) and research expenditure (Supplementary Table 2) in Southeast Asia are steadily increasing, it is necessary to ensure its continuity, and to evaluate the allocation of research investments to trigger further development of different industries (Stads *et al.*, 2020), including shrimp aquaculture.

Table 4: Correlations between regional annual data and bibliometric indices.

Annual data	Bibliometric indices	ρ	p-value
%GDP Share for Research Expenditure*	Publications	.887	.113
	Citation	.829	.171
Researchers in R&D (per million people)*	Publications	.889	.111
	Citation	.833	.167
Crustacean Production**	Publications	.957	.043
	Citation	.967	.033

*Based on figures for East Asia and the Pacific (excluding high-income economies) aggregates (The World Bank, 2021)

**Based on figures for Asia, excluding China (FAO, 2020).

Future Directions

With the information gathered from this bibliometric analysis, Southeast Asia is seen to move towards researches looking at the finding solutions against AHPND by using bioactive compounds, extracts, and probiotics against AHPND-causing bacterial species. Particularly, investigating different mechanisms vital to the survival of the pathogen such as, but not limited to, quorum sensing and biofilm formation. Similarly, researches on characterizing and enhancing the immune response of the shrimp against pathogens were gaining ground in the recent years. There was also a recent trend in the characterization of the genomes of AHPND-causing isolates, as horizontal gene transfer was found to occur for plasmids carrying the gene for the toxin responsible for AHPND. Continuous investigation of these topics is essential towards addressing the issues rooting from AHPND.

Furthermore, in terms of research outputs, other Southeast Asian countries such as the Philippines, Indonesia, and Malaysia need to step up their conduct of AHPND research to keep pace with leading neighboring countries, especially Thailand and Vietnam. Though in this study, socioeconomic factors of individual countries were found not to be significantly correlated with AHPND research outputs, increasing R&D investments, especially those allocated for AHPND research is of great importance. Being some of the top global shrimp producers, their research on AHPND considering their local settings would provide the necessary and more appropriate information in addressing this issue. Collaborations among Southeast Asian countries, as well as between them and countries beyond the region were proven to be fruitful, and is best if continued.

Conclusions

This bibliometric analysis showed that there was an exponential increase in AHPND research outputs in Southeast Asia over the last 10 years. Among the Southeast Asian countries, Thailand produced most of the papers on AHPND in the region, followed by Vietnam, Malaysia, and the Philippines. Meanwhile, Indonesia and Singapore shared the least. No research publications on AHPND from Brunei, Cambodia, Lao PDR, Myanmar, and Timor Leste were collected from the database. Over the last 10 years, there was also a change in priority research topics on AHPND based on visualization of keywords. Furthermore, Southeast Asian countries sourced a significant amount of its research funds

from institutions outside the region. They also maintained strong linkages with each other and with non-Southeast Asian countries. Finally, while there were no correlations between research investments and research outputs on AHPND research, it is recommended that resource allocations be revisited to determine whether this has impact on AHPND research and the shrimp industry.

Ethical Statement

No animals were used in this study; thus, no ethical approval is required.

Funding

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Declaration of Conflict of Interest

The author declares no conflict of interest.

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ANNEXES

Supplementary Table 1. Country-specific information on economy and research

Southeast Asian Countries	Population (in millions)	GDP, current US\$ (in billions)	GDP per capita (current US\$)	% GDP Share for Research Expenditure	Researchers in R&D (per million people)	Aquaculture production (in metric tons)	Crustacean Production (in tonnes)**
Indonesia	273.52	1058.42	3869.59	0.23	216	14,772,104	900,000
Vietnam	97.34	271.16	2785.72	0.53	708	4,153,323	800,000
Thailand	69.8	501.79	7189.04	1	1350	890,864	363,000
Philippines	109.58	361.49	3298.83	0.16	106	2,304,361	80,400
Malaysia	32.37	336.66	10401.79	1.04	2185	391,977	45,900
Singapore	5.69	340.00	59797.75	1.92	6803	5,702	No data

*Based on figures for individual countries (The World Bank, 2021)

**Based on figures for individual countries (FAO, 2020).

Supplementary Table 2. Annual regional data on economy and bibliometric indices

Year	Total Publications*	Total Citations*	% GDP Share for Research Expenditure**	Researchers in R&D (per million people)**	Crustacean Production (in thousand tonnes)***
2012	1	2	1.881	1030.668	6016
2014	5	33	1.942	1103.037	6748.3
2016	6	92	1.903	1060.434	7676.1
2018	23	357	1.983	1150.854	9386.5

*Based on aggregates of figures from Thailand, Vietnam, Malaysia, Philippines, Indonesia and Singapore

**Based on figures for East Asia and the Pacific (excluding high-income economies) aggregates (The World Bank, 2021)

***Based on figures for Asia, excluding China (FAO, 2020).

