Mapping and research analysis on freshwater fish vaccines in Indonesia of the last decade (2013-2023), in reference to Streptococcus sp.

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Abstract. Streptococcosis caused by Streptococcus sp. in freshwater fish in Indonesia leads to serious diseases, massive fish mortality, and significant economic losses. A preventive measure through fish vaccination can help to stop the spread of Streptococcosis. This study conducted research mapping and clustering on vaccines for Streptococcus sp. in freshwater fish in Indonesia (VSFI) over the last decade. The aim was to identify trends in the research and recommend future research topics. Relevant documents from 2013-2023 were retrieved using Scopus, Semantic Scholar, and Google Scholar search engines in July 2023, resulting in 61 docs, which then declined to 31 docs after final refinement. The metadata was organized using Mendeley before being submitted to VOSviewer software (Vv). An Open Knowledge Map (OKM) was used to plot the VSFI research clusters. Vv showed eight clusters, while OKM showed five. Both analyses suggest that future research can be directed toward candidate vaccines against Streptococcosis, especially which is caused by S. agalactiae. Nile tilapia was the most used fish in the related research. The results of this study could assist other scientists in identifying research clusters and expanding their investigation into fish vaccine development against Streptococcus sp.

1 Introduction

Freshwater fish production accounts for one-third of total aquaculture in Asia to date [1]. The aquaculture industry in some countries has been significantly affected by fish diseases [2], and aquaculture practices are suffering considerable setbacks because of various infectious organisms that are responsible for high mortality and morbidity in all farmed freshwater fish species, resulting in severe economic losses [3].

Fish farmers have long used antibiotics and synthetic chemicals to combat fish diseases [4], which has resulted in a concomitant increase in the irrational and inappropriate use of antibiotics [5] and in turn, led to drug-resistant fish pathogens that have become serious threat to the industrial aquaculture [6]. The detrimental effects of antibiotics have

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necessitated the development of alternate prophylaxis measures, such as vaccination for better protection against pathogens because vaccine(s) have proved to be an effective strategy against pathogens to improve fish production [3].

Streptococcus is among the 13 genera of pathogenic bacteria that can infect fish [7] and \textit{Streptococcus} sp. is the major bacterial pathogen in tilapia that can cause mortality in fish up to 70% (risk of financial loss up to 70%). The two most known species isolated from freshwater fish are \textit{Streptococcus agalactiae} and \textit{S. iniae} which can cause streptococcosis or streptococciasis [8, 9].

Vaccination can increase fish resistance and protect against certain diseases [10]. Recent findings summarized by Kayasamruaj et al. [1] provided novel insight into the future development of suitable vaccines and vaccination regimes against bacterial infection in the Southeast Asia region. Another report confirmed that different studies have been conducted to enhance the development of freshwater fish vaccines [11].

The primary objective of this study is to conduct a comprehensive bibliometric analysis of research themes pertaining to vaccination against \textit{Streptococcus} sp. in freshwater fish within the last decade. This analysis aims to delineate the trajectory of vaccine-related studies in the aquaculture industry, specifically in addressing bacterial infections such as streptococcosis or streptococciasis, which have inflicted significant economic losses. By offering insights into the trends in the research and development of fish vaccines, this study serves as a pivotal reference for future investigations in this domain. Furthermore, it aims to aid scientists in augmenting the efficacy of vaccination strategies against \textit{Streptococcus} sp. in freshwater fish. Despite recent reviews, no prior bibliometric analysis has been undertaken on the chosen themes, rendering this study a pioneering effort in mapping and evaluating the progress of VSFI-related studies over the past decade. The findings of this research are anticipated to facilitate the identification of emerging trends and foster further exploration in the development of fish vaccines against \textit{Streptococcus} sp.

2 Methods

2.1 Research questions

Three research questions addressed in this present study are:

\begin{itemize}
  \item RQ1. How is the last decade's VSFI research clustered?
  \item RQ2. What is the current state of VSFI research?
  \item RQ3. What is the future topic that will provide the opportunity for more research?
\end{itemize}

2.2 Metadata collection

Relevant documents from 2013-2023 were retrieved using Google, Semantic, and Scopus search engines in July 2023, as shown in Table. 1 Google Scholar and Semantic Scholar were used in this study to collect metadata, as it was suggested that most of the VSFI’s papers had been published in national-scale indexed journals in Bahasa within the last ten years. Meanwhile, the Scopus database was also used to expand the search for more references to find Scopus-indexed VSFI papers during the period.
Table 1. Metadata collection procedures in this study

<table>
<thead>
<tr>
<th>No</th>
<th>Databases</th>
<th>Queries</th>
<th>Number of docs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Google Scholar</td>
<td>“Vaksin Streptococcus agalactiae iniae” (in Indonesian) year limited 2013-2023; “vaksin streptococcus” within the title</td>
<td>140 → 132 → 32</td>
</tr>
<tr>
<td></td>
<td>Final number of retrieved docs</td>
<td></td>
<td>18 docs</td>
</tr>
<tr>
<td>2</td>
<td>Semantic Scholar</td>
<td>“Vaksin streptococcus ikan” 10 years (2013-2023), has pdf, publication types: journals and conference papers, most relevant</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Final number of retrieved docs</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>Scopus</td>
<td>“vaccine*” AND “streptococcus” AND “fish” AND “tilapia. Most relevant; year (2013-2023)</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Final number of retrieved docs</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Final number of docs from the 3 databases</td>
<td></td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Final numbers of docs after removing duplicates</td>
<td></td>
<td>31</td>
</tr>
</tbody>
</table>

2.3 Data analyses

The metadata from three databases (31 docs) (see Table 1) was exported into Mendeley software before being analyzed. The research method is designed by combining between the Open Knowledge Map (OKM) application and VOSviewer software (Vv). OKM [12] was used to plot the VSFI research cluster. The collection metadata(.ris) was subjected to visualization using VOSviewer [13] from three types of mapping produced, namely network visualization (Nv), overlay visualization (Ov), and density visualization (Dv).

3 Results

The mapping results from the OKM and Vv applications are in visual form and equipped with tabulations of the data obtained, which are then grouped to facilitate the analysis process. OKM results can be seen in Figure 1 and Table 1, while Vv results can be seen in Figure 2-4 and Table 2.

![Fig. 1. Visualization from Open Knowledge Map [12]](image-url)
Table 2. Cluster analysis from Open Knowledge Map

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Items</th>
<th>Number of sources [refs]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster-1</td>
<td>DNA vaccines</td>
<td>5 [14, 15, 16, 17, 18]</td>
</tr>
<tr>
<td>Cluster-2</td>
<td>Vaccine effectivity against <em>Streptococcus</em> sp.</td>
<td>4 [19, 20, 21, 22]</td>
</tr>
<tr>
<td>Cluster-3</td>
<td>Vaccines against <em>S. agalactiae</em></td>
<td>4 [23, 24, 25, 26]</td>
</tr>
<tr>
<td>Cluster-4</td>
<td>The effect of booster on immunity</td>
<td>3 [27, 28, 29]</td>
</tr>
<tr>
<td>Cluster-5</td>
<td>Vaccine ingredients</td>
<td>1 [30]</td>
</tr>
</tbody>
</table>

Table 3. Cluster analysis from VOSviewer

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Items</th>
<th>Number of sources [refs]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster-1</td>
<td>Post-release evaluation, hydrovac, motile <em>Aeromonas septicamia</em>, bacterial disease, streptovac, vaccine, inactivated vaccine</td>
<td>8 ([31]–[38])</td>
</tr>
<tr>
<td>Cluster-3</td>
<td>Vaccine effectivités, immersion, tilapia immunity, vaccine coating, <em>soaking Artemia</em> sp., <em>S. agalatiae</em> time of vaccine administration</td>
<td>8 [8, 20, 36, 40, 42, 46]</td>
</tr>
<tr>
<td>Cluster-4</td>
<td><em>S. agalactiae</em> antigen, protection duration, ECP, vaccine candidate, indigo, whole cells, streptococcosis, <em>S. agalactiae</em> vaccine</td>
<td>8 [36, 37, 38, 47, 48, 49, 50]</td>
</tr>
<tr>
<td>Cluster-5</td>
<td>Tilapia seeds, vaccine efficacy, maternal immunity, tilapia brood, booster vaccine, vitamin C</td>
<td>6 [35, 42, 51, 52, 53, 54]</td>
</tr>
<tr>
<td>Cluster-6</td>
<td>Different vaccine doses, hematological parameters, <em>Streptococcus iniae</em>, DNA vaccines</td>
<td>4 [36, 43, 52, 54]</td>
</tr>
<tr>
<td>Cluster-7</td>
<td>Immunity, vaccine through feed</td>
<td>2 [8, 48]</td>
</tr>
<tr>
<td>Cluster-8</td>
<td>Hyperosmotic infiltration</td>
<td>1 [55]</td>
</tr>
</tbody>
</table>

Fig. 2. Network Visualization from VOSviewer. Arrows : major focuses related to VSFI
4 Discussion

Bibliometrics has become an indispensable instrument for monitoring and analyzing scientific output, university collaboration, the impact of state-owned science financing on national research and development performance, and educational efficiency, among other applications. Google Scholar and Semantic Scholar search engines initially captured literature about VSFI in Bahasa. The Scopus database also captures VSFI-related publications in English-language journals indexed by Scopus. The combined results of the three websites are 61 articles. After the final shortlisting and removal of duplicate papers, the final number of articles was 31 (Table 1), and they were subjected to VOSviewer analysis. VOSviewer has a fantastic visualization and can load and export information from many sources [13]. In contrast, knowledge map technology provides a means to extract structured knowledge from massive texts and images, thus having broad application prospects [12] of the five clusters formed from OKM (Figure 1), there are four main clusters and one small cluster. The DNA vaccine theme is the largest cluster with six sources. This cluster intersects with the second largest cluster, namely the effectiveness of the *Streptococcus vaccine*. The third largest cluster is the *Streptococcus agalactiae* vaccine
Furthermore, the cluster of the effect of booster vaccines on immunity (three items) and the last cluster of vaccine basic ingredients, which only has one item.

The OKM resulted in several analyses being produced. First, in the last ten years (2013–2023), VSFI research has focused the most on the development of DNA vaccines. Previous reports suggested that DNA vaccines have been developed in Indonesia since 2010 and have succeeded in increasing tilapia immunity against *S. iniae* with 100 percent fish survival [56]. DNA vaccines can be used as alternative vaccines because of their advantages, which can improve some weaknesses of traditional vaccines (live and dead vaccines), such as the risk of infection [46]. After vaccination, tilapia is expected to be automatically resistant to this type of disease.

The second analysis is that VSFI research is close to the topic of vaccine effectiveness. The research on the effectiveness of vaccines and the *S. agalactiae* vaccine has attracted high interest. The research of this bacteria strain is getting more attention in Indonesia because 85% of streptococcosis in tilapia was caused by *S. agalactiae* and the infection can cause mass death of >50% within 3-7 days [57, 58]. A previous study found that a freeze-dried vaccine with 1% coated chitosan effectively improves the immunity system of Nile tilapia [17]. The third analysis, based on the map from OKM (Figure 1), indicated that the topic of aquaculture is less desirable in VSFI-related research.

Eight clusters related to VSFI research were produced in the analysis of Vv mapping in network visualization. Regarding the OKM analysis (Figure 2), the results in network visualization Vv, where the nodes displayed have different colors and sizes related to VSFI, are strong. The three largest VSFI-related nodes are *S. agalactiae*, tilapia, and streptococcosis. Therefore, the results of this Vv mapping strengthen OKM's analysis of the justification of the relationships between clusters that have been described.

VOSviewer analysis can clarify the historical year related to VSFI research over a decade (2013–2023) in overlay visualization (Figure 3). The dominant tosca (Turquoise) colour shows that VSFI research was conducted between 2013 and 2018, which focused a lot on *Streptococcus agalactiae*, tilapia, *Streptococcosis*, and vaccine effectiveness. Then the yellow nodes indicate that VSFI research began to turn to perendaman *Artemia* sp., imunitas maternal, and imunitas (in Bahasa) or immersion of *Artemia* sp., maternal immunity, and immunity, respectively.

Density visualization from VOSviewer (Figure 4) demonstrates that the nodes related to VSFI are divided based on the different colors, which the brightness of the nodes can justify. The three largest nodes with the highest brightness were seen in the focus of research related to *Streptococcus agalactiae*, streptococcosis and tilapia. This further emphasizes that these three items have been the main research focus on VSFI over the past decade. Meanwhile, a node for perbedaan dosis vaksin (in Bahasa) or different vaccine doses showed that within the last decade, it was less desirable in VSFI research.

Research on vaccines against *S. agalactiae* has been the first concern in Indonesia over the last ten years, possibly due to high public health priorities, adequate resource availability, a high incidence of *S. agalactiae* infections, and supportive research collaborations. These factors have driven research on vaccination against this bacterial pathogen, although research priorities may change over time.

Vaccines become an alternative to antibiotics for treating bacterial infections because vaccines can enhance fish disease resistance and specific and non-specific immunity, increasing fish survival. Only one or two vaccine doses are needed to provide immunity to fish during the healing period. Unlike antibiotics, which negatively affect fish, vaccination has the additional benefit of not causing negative side effects for fish [33, 59].

Over the past decade (2013–2023), various research endeavors in Indonesia have focused on developing fish vaccines to combat *Streptococcus*, yielding diverse methods and outcomes. In the context of creating *S. agalactiae* vaccines for freshwater fish in the
country, it appears that a "trivalent" vaccine holds promise as a viable immunization method against freshwater fish diseases resulting from the simultaneous presence of multiple pathogenic bacteria [60]. This aligns with findings from a literature review by Lusiastuti et. al. [61], suggesting that future efforts in Indonesian aquaculture should prioritize the ongoing development of polyvalent vaccines utilizing local pathogen strains to enhance coverage against a range of pathogens and foster cross-reactivity responses.

5 Conclusion

This study shows that research related to vaccines for *Streptococcus* sp. in freshwater fish in Indonesia (VSFI) spread across different focusses. The results of open knowledge map (OKM) produce several publication clusters related to VSFI research that are different from those of VOSViewer (Vv). OKM ranks the topic of *S. agalactiae* vaccines as the second largest cluster after DNA vaccine. While Vv placed VSFI publications related to the *S. agalactiae* vaccine in the third and fourth clusters with eight sources, semilar with those of the first and seconds clusters. However, both of the mapping results seem to agree that the main focus of study related to VSFI within ten years (2013-2023) is vaccines related to *S. agalactiae*, and the fish studied are tilapia. Therefore, the future topic for more research is vaccine development against *S. agalactiae* in nile tilapia, especially polyvalent vaccines.

We would like to express our great thanks to the National Research and Innovation Agency, Indonesia, which has provided free access to the Scopus database.

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