Surveillance of infectious salmon anaemia virus in farmed and wild salmon: protocol for scoping review

Registration:

The protocol will be made available at Systematic Reviews for Animals and Food (SYREAF) (http://www.syreaf.org).

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Amendments:

None to report.

Support: Source, sponsor, and role of funder:

Funding was received from the Atlantic Fisheries Fund (AFF). The funding agency will not influence the design, implementation, analysis of the work, review, or development of the manuscript prior to submission.

Conduct and reporting guidelines:

This protocol was established in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Scoping Reviews (PRISMA-ScR) reporting guidelines (Tricco et al. 2018).

Abstract

Background: Infectious salmon anemia (ISA) is a disease condition that is caused by infectious salmon anemia virus (ISAV) and can lead to devastating outcomes in Atlantic salmon *(Salmo salar*), causing elevated mortality along with substantial financial losses. Notwithstanding the surveillance initiatives that are currently in place, outbreaks of ISA continue to pose significant challenges for salmon producers and policymakers. Therefore, it is essential to conduct a comprehensive study to fill the existing gaps in the literature regarding ISAV surveillance methodologies.

Objectives: The aim of this scoping review is to present a comprehensive overview of optimal ISAV surveillance procedures in both farmed and wild salmon.

Eligibility criteria: Observational, experimental studies and review articles from peer-reviewed journals, government reports, and grey literature outlining various ISAV surveillance practices will be included. However, case reports and case series will not be considered.

Sources of evidence: A Boolean search will be conducted utilizing CAB abstracts (through EBSCO host), PubMed, Scopus, and the Earth, Atmospheric & Aquatic Science Collection (through ProQuest) on the same day.

Charting methods: Data charting will include study characteristics, variables related to population of interest (farmed and wild salmon) and different surveillance practices.

Conclusion: The findings of this review will offer valuable guidance for fish farmers, researchers, and policymakers to pinpoint the most effective strategies for early detection of ISAV in both farmed and wild salmon populations.

Introduction

1.1. Rationale

Infectious salmon anemia (ISA) is an internationally notifiable, viral disease of salmon with great potential for virulence and transmissibility (Polinski et al., 2024). ISA is a multisystemic disease that causes severe anemia and circulatory abnormalities, and it can in certain cases lead to significant mortality (Aamelfot et al., 2014). The disease can cause serious fish health and welfare problems and lead to large financial losses for the aquaculture industry (Spilsberg et al., 2024).

There is no treatment for the infection. As a result, the only available control measures are vaccination and early detection to enable depopulation, which is most effective before mortality rates increase (Romero et al., 2022). The cumulative production losses, due primarily to depopulation measures, in impacted countries such as Norway, Canada, the United Kingdom, the Faroe Islands, and Chile over the years can be conservatively calculated in the billions of USD (Polinski et al., 2024).

ISA is caused by the infectious salmon anaemia virus (ISAV), which belongs to the family Orthomyxoviridae (Kawaoka et al., 2005). Its genome consists of eight single-stranded, negative-polarity RNA segments encoding at least 10 proteins (Christiansen et al., 2017). Key structural proteins include nucleoprotein (NP), matrix protein (M), hemagglutinin-esterase (HE), and fusion (F) protein (Falk, 2014).

The HE and F proteins, encoded by segments 6 and 5 respectively, are surface proteins. HE mediates receptor binding and destruction, while F facilitates viral-cell membrane

fusion (Aspehaug et al., 2005; Romero et al., 2022). Phylogenetic analysis of the HE gene identifies two major ISAV clades: European and North American (Devold et al., 2001).

Virulence of ISAV is associated with deletions in the hypervariable region / highly polymorphic region (HPR) of the HE protein and mutations or insertions near the F protein's cleavage site (Markussen et al., 2008; Fourrier et al., 2015). Consequently, each clade contains variants with differing virulence, including the virulent ISAV HPR-deleted (ISAV HPRdel) and the nonvirulent ISAV-HPR0.

Since ISA poses a threat to the global salmon aquaculture industry (Godoy et al., 2008) and has been recognized as a notifiable disease by the World Organization for Animal Health (OIE, 2009), it is crucial that regions implement comprehensive surveillance programs for early detection of ISAV infection. This approach facilitates effective depopulation decisions prior to high mortality events and reduces the probability of spread to other cages and neighboring production sites, thereby mitigating subsequent economic losses for the industry.

Different surveillance programs are already implemented by the governments of the exposed countries including Scotland, Chile, US and Norway respectively (McBeath et al., 2009; Alvial et al., 2012; Bartlett, 2017; Gustafson et al., 2018; Jansen and Falk, 2019; Jansen and Silva de Oliveira, 2022).

Moreover, other countries are adopting more integrated national surveillance programs for aquatic animal diseases as Canada (National Surveillance for Aquatic Animal Diseases - inspection.canada.ca) and Iceland (https://www.mast.is/static/files/skyrslur/aquaculture-surveillance-program-disease-free-status-in-iceland-isa-vhs-ihn-bkd-2024.pdf.).

Typically, surveillance procedures reported in earlier studies / reports encompass conducting on-site inspections by certified veterinarians, collecting pertinent samples for laboratory testing, enforcing biosecurity regulations, and consistently reporting all monitoring activities to the appropriate authorities.

Despite the global importance of effective surveillance programs for managing infectious salmon anaemia, significant challenges remain. Variability in program design, implementation, and reporting standards across regions complicates efforts to assess their relative effectiveness. Many existing systems face differences in diagnostic capacity, sampling protocols, and data integration, leading to inconsistencies in disease detection and outbreak control (Nérette et al., 2008).

Additionally, factors such as geographic differences, environmental conditions, and the genetic diversity of the virus complicate the development of universally applicable protocols. Moreover, the economic and logistical constraints of implementing widespread surveillance across remote aquaculture regions, combined with the evolving nature of the infectious agent, further hinder the ability to achieve a one-size-fits-all approach that is comprehensive and reliable. Thus, a critical evaluation of current surveillance strategies and their shortcomings would inform the development of more standardized, efficient, and cost-effective surveillance models in the future.

On such a basis, this scoping review seeks to map and evaluate the diverse strategies employed in ISAV surveillance, identifying critical gaps in knowledge and practice that hinder the development of robust, globally applicable surveillance frameworks.

1.2.Objectives

The scoping review's objective is to answer the question "What are the best surveillance practices of the infectious salmon anaemia virus in farmed and wild salmon?".

2. Methods

2.1.Eligibility criteria

Observational studies (including cohort, case control, and cross-sectional studies), as well as experimental studies (including randomized control trials) will be considered in this review. Moreover, review articles and the available governmental reports and policies will be included. Search date will be from 1984 (when ISA was recorded for the first time in Norway, Thorud and Djupvik, 1988) until now. To allow comprehensive search, no limits will be placed on the language of the full text. Case reports and case series will not be included.

2.2. Information sources

Simultaneously, CAB abstracts (via EBSCO host), PubMed, Scopus and the Earth, Atmospheric & Aquatic Science Collection (via ProQuest) will be searched for eligible studies, using a Boolean search approach designed with the help of a librarian (KM). In addition to using Google Scholar to search the grey literature, the reference list of the articles that were obtained will be examined to find any pertinent references that were left out of the scoping review list.

146 *2.3. Search*

147 The search strategy used in the four databases is presented in Table 1.

148 **Table 1.** Scoping review search protocol

149 Preliminary search conducted in CAB abstracts (via EBSCO host). Date of search
150 19/09/2024

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#	Search	Results
1	(surveillance OR detection OR IFAT OR indirect fluorescent antibody technique OR direct immunofluorescent test OR immunohistochemistry OR immunochromatography OR rt-pcr OR qrt-pcr OR molecular testing OR sequencing OR genotyping OR isolation)	1,153,581
2	(salmo salar OR salmon)	31,008
3	(ISAV OR ISA virus OR ISA OR infectious salmon anemia virus OR infectious salmon anemia OR orthomyxoviridae OR orthomyxovirus)	39,730
4	1 and 2 and 3	260

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153 Preliminary search conducted in PubMed.

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#	Search	Results
1	(surveillance OR detection OR IFAT OR indirect fluorescent antibody technique OR direct immunofluorescent test OR immunohistochemistry OR immunochromatography OR rt-pcr OR qrt-pcr OR molecular testing OR sequencing OR genotyping OR isolation)	10,143,290
2	(salmo salar OR salmon)	31,030
3	(ISAV OR ISA virus OR ISA OR infectious salmon anemia virus OR infectious salmon anemia OR orthomyxoviridae OR orthomyxovirus)	82,071
4	1 and 2 and 3	342

155

156 Preliminary search conducted in Scopus.

#	Search	Results
1	TITLE-ABS-KEY(surveillance) OR TITLE-ABS-KEY(detection) OR TITLE-ABS-KEY(indirect AND fluorescent AND antibody AND technique) OR TITLE-ABS-KEY(direct AND immunofluorescent AND test) OR TITLE-ABS-KEY(immunohistochemistry) OR TITLE-ABS-KEY(immunochromatography) OR TITLE-ABS-KEY(rt-pcr) OR TITLE-ABS-KEY(qrt-pcr) OR TITLE-ABS-KEY(molecular AND testing) OR TITLE-ABS-KEY(sequencing) OR TITLE-ABS-KEY(genotyping) OR TITLE-ABS-KEY(isolation)	6,868,199
2	TITLE-ABS-KEY(salmon OR salmo salar)	13,771
3	(TITLE-ABS-KEY(isa) OR TITLE-ABS-KEY(isav) OR TITLE-ABS-KEY(isa AND virus) OR TITLE-ABS-KEY(infectious AND salmon AND anemia AND virus) OR TITLE-ABS-KEY(infectious AND salmon AND anemia) OR TITLE-ABS-KEY(orthomyxoviridae)) OR TITLE-ABS-KEY(orthomyxovirus))	45,384
4	1 and 2 and 3	201

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158 Preliminary search conducted in Earth, Atmospheric & Aquatic Science Collection via
159 ProQuest.

#	Search	Results
1	(surveillance OR detection OR IFAT OR indirect fluorescent antibody technique OR direct immunofluorescent test OR immunohistochemistry OR immunochromatography OR rt-pcr OR qrt-pcr OR molecular testing OR sequencing OR genotyping OR isolation)	860,486
2	(salmo salar OR salmon)	69,352
3	(ISAV OR ISA virus OR ISA OR infectious salmon anemia virus OR infectious salmon anemia OR Orthomyxoviridae OR orthomyxovirus)	14,017
4	1 and 2 and 3	689

2.4. Selection of sources of evidence

The search outcomes from every database, along with chosen articles from the grey literature search, will be uploaded to Covidence (Available at https://www.covidence.org/). Covidence is an online software created to simplify the systematic/scoping review procedure frequently utilized in research within health and social sciences (Kellermeyer et al., 2018).

A primary screening round at the titles and abstracts level will be conducted by two independent authors (AA and PCT). The second round will be for screening of full articles. At any screening level, discrepancies will be resolved by offering the selected articles to co-authors (KT and KLH) to get a consensual decision either to include or exclude those articles. At the title and abstract screening phase, KT and KLH will conduct a blind screening of randomly selected 10% of the included and irrelevant articles identified at this stage by AA and PCT to ensure reliability and precision throughout the screening procedure (Frampton et al., 2017). A kappa score of 0.8 "substantial agreement" will be used as a cut-off point to assess the inter-reviewer reliability (Hanegraaf et al. 2024).

2.5. Data charting process

The procedure of charting the data will be carried out independently by AA and PCT using Microsoft Excel. If there is disagreement, resolution will first involve discussion among the two authors. When a collective agreement cannot be reached, a third author (KT) will be consulted. A pre-test of the data charting form will be conducted with a random selection of studies, and any modifications that are deemed essential will be implemented based on the input received. AA will compile the charted data for synthesis.

2.6. Data items

The following data elements are recommended for extraction from the literature, but they may be adjusted as the study progresses to accommodate new or modified requirements. We will record the following study characteristics: study ID, year, season, country, study design, and study duration. We will then extract the following population characteristics: numbers of infected fish / net pens and or farms, and the stage of infection (pre-smolt, smolt or adult). The following surveillance procedures will be described:

- Frequency of farms' visiting - sampling
- Number of sampled fish and types of the collected samples
- Types of tests applied to the collected samples
- Case definition
- Biosecurity measures applied
- The reported key performance measures to assess the effectiveness of a surveillance program.
- ISA incidence rate (or any other measures).

2.7. Critical appraisal

As this is a scoping review, no in-depth critical appraisal of the literature will be conducted.

2.8. Synthesis of results

Descriptive statistics will be employed to deliver a succinct summary of the findings. The statistics will be presented as tables, figures, and descriptive text. To address the gaps in the current research, we will summarize the range of ISAV infection surveillance strategies for practical application in the field.

2.9. Discussion

This scoping review aims to provide a comprehensive and detailed overview of the current state of knowledge, research advancements, and existing methodologies related to the surveillance of ISAV. This study will systematically analyze and synthesize existing literature to offer valuable qualitative information on the most effective and reliable surveillance methods for identifying and monitoring ISAV in both farmed and wild salmon populations.

The findings of this scoping review will serve as a significant resource for fish farmers, aquaculture sector stakeholders, researchers, and policymakers by presenting well-founded suggestions on the ideal surveillance measures for earlier detection of ISA outbreaks that will help to mitigate its impact on salmon population.

Funding

Funding was received from the Atlantic Fisheries Fund (AFF).

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