INPLASY PROTOCOL

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None declared.

Prevalence, risk factors, and antimicrobial resistance of Streptococcus suis and Campylobacter species in pigs: a systematic review

Mshelia, AB[1].

Review question / Objective: **What are the global frequency, attributable factors, and antimicrobial responsiveness of Streptococcus suis and Campylobacter species in pigs?/ To determine the rate of occurrence, predisposing factors, and antimicrobial susceptibility of the isolates of streptococcus suis and Campylobacter species of pigs, worldwide.**
Information sources: **The intended information sources are 20 electronic databases: MEDLINE® - (Mesh, Ovid Medline, Ovid PsycINFO, PubMed), Scopus®, ProQuest®, Google Scholar®, Web of Science® (ISI), EBSCO®, SciELO®, Wiley®, Compendex® - Engineering Village, Emerald®, Embase® - Emtree, Directory of Open Access Journals (DOAJ)®, Gale Academic OneFile®, DataCite®, J-STAGE®, SpringerLink Journals®, Journals Ovid complete®, BioMed Central Opens Access®, Nature®, Taylor & Francis®], 9 periodical titles (Journal of Veterinary Science, Antibiotics, BMC Veterinary Research, Canadian Journal of Veterinary Research, Journal of Veterinary Medical Science, Journal of Veterinary Medical Science B, PLoS One, Scientific Reports, Veterinary Microbiology), and the grey literature databases.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 March 2023 and was last updated on 20 March 2023 (registration number INPLASY202330053).

INTRODUCTION

Review question / Objective: **What are the global frequency, attributable factors, and antimicrobial responsiveness of Streptococcus suis and Campylobacter species in pigs?/ To determine the rate of occurrence, predisposing factors, and antimicrobial susceptibility of the isolates of streptococcus suis and Campylobacter species of pigs, worldwide.**

Rationale: **This systematic review aims to update the knowledge in the field of**

veterinary public health, providing a rigorous and accurate summary of all available primary and secondary research in response to research questions. In addition, it will provide information on what is unknown about the research area and topics and utilize the reviewed articles as a starting point for formulating veterinary public health requirements.

Condition being studied: Swine streptococcosis and campylobacteriosis are zoonotic diseases of pigs and humans. The natural habitat of Streptococcus suis is the upper respiratory tract of pigs, specifically the tonsils and nasal cavities, nevertheless, they can be found in the genital and digestive tracts. With nearly a hundred percent of pig farms globally having carrier animals, Streptococcus suis is one of the most important bacterial pig pathogens. The spreading of Streptococcus suis among animals is mainly through the respiratory route. Of the various manifestations of the disease, septicemia and meningitis are by far the most striking features, but endocarditis, pneumonia, and arthritis can also be observed. Nevertheless, in per acute cases of infection, pigs are often found dead with no premonitory signs of disease. A presumptive diagnosis of infection in pigs is usually based on clinical signs and macroscopic lesions. Confirmation of the infection is mandatory and must be achieved by isolation and characterization of the pathogen. Different from pigs, the main route of entry of Streptococcus suis in humans is thought to be through contact of cutaneous lesions, most usually on the hands and arms, with contaminated animals, carcasses, or meat. But this situation seems to be different in some Asian countries where the oral route is taken into consideration since many cases of infection have been reported after ingestion of contaminated raw pork products. In Western countries, infections in humans most usually occur sporadically. After an incubation period that ranges from a few hours to days, Streptococcus suis usually produces meningitis in humans. Nonetheless, it is also responsible for cases of endocarditis, pneumonia, peritonitis, arthritis, and other less common diseases usually related to generalized septicemia. Also, acute infections with shock and a high mortality rate have been described, particularly in the case of the streptococcal toxic shock-like syndrome (STSLS) closely associated with the 2005 Chinese epidemic, but also observed independently of this outbreak.
The Campylobacter infection, although it is usually subclinical, mainly affects piglets causing diarrhea; this does not exclude adult pigs. The alternative names are Campylobacter coli, Campylobacter jejuni, Campylobacter hyointestinalis, and Campylobacter mucosalis. Campylobacters are present in the small and large intestines of most mammals including pigs. Globally, Campylobacter coli is the most commonly present in pigs. Clinical signs are not always present but can cause watery diarrhea with mucous and occasional blood. Campylobacters (especially C. jejuni) are a particularly important and common cause of foodborne illness in humans. The predominant species of Campylobacter in pigs is Campylobacter coli. Most human infections in the United States are caused by Campylobacter jejuni, whereas in Europe, a high incidence of human infection with Campylobacter coli is reported. Apart from abortion in sheep, food animals that are colonized with Campylobacter usually do not have any clinical signs. A high percentage of animals at slaughter are infected and this is also an important phase in the farm-to-fork continuum where Campylobacters usually enters the food chain. Human foodborne Campylobacter infection most commonly comes from consuming food that is contaminated or cross-contaminated (i.e., uncontaminated foods that came in contact with contaminated sources) at the post-harvest level. Campylobacter infection is a major public health problem. The manifestations in humans are self-limiting after 3-5 days, but in an immuno-suppressed individual, it can progress to the bloodstream and become potentially deadly. Autoimmune disorders, cardiovascular disease, sepsis, and additional complications like Inflammatory Bowel Disease, Guillain-Barre syndrome, or

reactive arthritis have been noticed in infected persons. Nearly all individuals affected by campylobacteriosis displayed symptoms of watery or bloody diarrhea, vomiting, headache, fever, and abdominal pain.

METHODS

Search strategy: 20 related databases and 9 periodical titles will be thoroughly searched. Search terms are "Prevalence OR Frequency OR Occurrence" AND "Risk Factors OR Associated Factors OR Predisposing factors" AND "Antimicrobial Resistance" OR "Antimicrobial Susceptibility" OR "Antibiotic Resistance" OR "Antibiotic Susceptibility" OR "Drug resistance" OR "Multi-Drug Resistance" AND "Streptococcus suis" AND "Campylobacter species" AND "Pigs."

Participant or population: The population to be studied are pig populations as a source of meat protein worldwide. There are biotic and abiotic factors that can affect pig farming or productions. In addition to gender and age, epidemiological data like breed, body condition, herd size at the farm of origin, pig rearing system, source of drinking water, weather, altitude, cleanliness of cage floor, the slope of cage floor, and type of cage floor, as well as the level of pig cleanliness will be assessed for both swine streptococcosis and campylobacteriosis. At the retail markets, meat (raw pork), meat contact surfaces (chopping boards and knives, inner and outer surfaces of freezers), meat mincers' hands, and non-meat contact surfaces (walls, floors, and insects) will be assessed as risk factors.

Intervention: The intervention to be evaluated in this review is to know whether there are risk factors, whether these pathogens are susceptible to antimicrobials, and whether there are actions that have been taken to interrupt the occurrence of streptococcosis and campylobacteriosis in pigs. This will be done by determining the global prevalence, predisposing factors, and antimicrobial resistance of Streptococcus suis and Campylobacter species in pigs.

Comparator: The comparative intervention that will be applied to the target population are healthy carrier pigs, diseased pigs, convalescent pigs, and chronic carrier pigs.

Study designs to be included: The study designs to be included in this systematic review are observational studies.

Eligibility criteria: What to be included in this review are pigs of all ages (healthy carrier pigs, diseased pigs, convalescent pigs, and chronic carrier pigs); predisposing factors that are either attributable to the host, etiological agent, or environment which can lead to streptococcosis and campylobacteriosis in pigs; the language of publication will be English and non-English; published as full paper; and no restriction of publication year. Those to be excluded from this systematic review are publications that are not available as full texts and grey literature non-peer-reviewed.

Information sources: The intended information sources are 20 electronic databases: MEDLINE® - (Mesh, Ovid Medline, Ovid PsycINFO, PubMed), Scopus®, ProQuest®, Google Scholar®, Web of Science® (ISI), EBSCO®, SciELO®, Wiley®, Compendex® - Engineering Village, Emerald®, Embase® - Emtree, Directory of Open Access Journals (DOAJ)®, Gale Academic OneFile®, DataCite®, J-STAGE®, SpringerLink Journals®, Journals Ovid complete®, BioMed Central Opens Access®, Nature®, Taylor & Francis®], 9 periodical titles (Journal of Veterinary Science, Antibiotics, BMC Veterinary Research, Canadian Journal of Veterinary Research, Journal of Veterinary Medical Science, Journal of Veterinary Medical Science B, PLoS One, Scientific Reports, Veterinary Microbiology), and the grey literature non-peer-review.

Main outcome(s): High, low, or no prevalence of streptococcus suis and campylobacter species in pigs worldwide.
The various or no risk factors for Streptococcus suis and Campylobacter species in pigs worldwide.
The presence or absence of antimicrobial resistance to Streptococcus suis and Campylobacter species in pigs worldwide.

Additional outcome(s): There is no additional outcome.

Data management: Studies will be managed according to the PRISMA Statement. The PRISMA Statement consists of a 27-item checklist and a four-phase flow diagram. This will improve the reporting of this review. It is also useful for the critical appraisal of published systematic reviews.
The Endnote software version 20 will be used to organize the search studies into group structures [All, Not-Duplicate, Databases, Periodical titles, and Filters (Titles/Abstract/keywords; Available; Not-Available; and Not-Included)] prior to importing the studies. All imported studies will be added to the ALL-references group while in their appropriate groups (Databases). It will then be added to the Not-Duplicate group and the function of finding duplicates will be executed using the EndNote software. All the studies in the Not-Duplicate group will be added to the Filter group-Titles/Abstract/keywords. Then those Titles/Abstracts/Keywords that are not aligned with the research topic and area of this systematic review will be moved to the group Not-Included, and this is the first filter. To the group-Titles/ Abstracts/ Keywords, find full texts will be executed. If available, an icon clip format will appear. I will sort by clicking on the clip and selecting the available, i.e., those with the clip, and add them to the group-Available. For those articles that are not available, a follow-up will be done by clicking on the URL if available and trying to download or search for the article in Scholar Google®, Microsoft Academic Search®, Google®, Bing®, library portals, or by portal CAPES portals. After the end of the searches, I will perform the analysis of only those articles that are in the group Available.

Quality assessment / Risk of bias analysis: Cochrane risk-of-bias (RoB2) tool will be the tool for assessing quality and risk of bias in this systematic review. RoB 2 is structured into a fixed set of domains of bias, focusing on different aspects of the observational studies, conduct, and reporting. Within each domain, a series of questions ('signaling questions') aim to elicit information about features of the study that are relevant to the risk of bias. A proposed judgment about the risk of bias arising from each domain is generated by an algorithm, based on answers to the signaling questions. Judgment can be a 'Low' or 'High' risk of bias, or can express 'Some concerns'. The GRADE system will also be applied. The GRADE method (Grading of Recommendations, Assessment, Development, and Evaluation) aims to provide a tool for rating the quality of evidence (particularly for effectiveness) and grading the strength of recommendations. The tool will be used for summarizing the evidence for this systematic review.

Strategy of data synthesis: Data will be extracted from various studies qualitatively. The data will be presented in a tabular format which shows the characteristics of each included study for easier interpretation. The data to be extracted will contain the name of the Database, Journal, Author, Year of publication, Country where the work was done, Title, type of study design, objectives, methodology, results, keywords, introduction, discussion, conclusion, recommendations, and references. Matrix synthesis in an Excel spreadsheet will be performed, where it will analyze and all articles will be read in their entirety. Based on these data, which makes the synthesis of the collections of the literature, will lead me to extract the principal characteristics that are associated with this systematic review. Further analysis and synthesis will be made; all depends on the needs of this systematic review according to the PRISMA checklist and the GRADE system.

Subgroup analysis: The included or Available articles will be divided into two or more subgroups, and it will be tested whether the pooled effect sizes found in these subgroups differ significantly from each other. Subgroup analyses can be considered a core component of most published meta-analyses. It will examine sources of heterogeneity.

Sensitivity analysis: Sensitivity analysis aims to prove that the findings obtained from a systematic review do not depend on arbitrary decisions. It will be performed by repeating a primary analysis (meta-analysis) by excluding some studies. In the primary analysis, all eligible studies are included in a meta-analysis; for sensitivity analysis meta-analysis will be repeated by including only studies that are definitely known to be eligible according to a certain criterion (e.g., as mentioned before, studies that do not provide all the necessary information). There are many aspects that can be studied within a sensitivity analysis, including characteristics of participants, interventions, comparators, outcomes, study design aspects, and type of publication. If the aim of the sensitivity analysis is to explore the effect of RoB, then the meta-analysis exploring this aspect may include only studies with low RoB, to see whether there will be a difference between the meta-analysis that included all studies and a meta-analysis that included only studies with low RoB.

Language restriction: There will be no language restrictions on the search.

Country(ies) involved: Nigeria/Denmark.

Other relevant information: There is currently no additional information.

Keywords: Prevalence; Risk factors; Antimicrobial Resistance; Streptococcus suis; Campylobacter species; Pigs.

Dissemination plans: The research result will be disseminated worldwide by getting the result published in the related journal. The purpose of the outreach is to raise awareness, educate the community, engage, and promote. And also, I intend to keep members of the project consortium and my institution well-informed about the progress of the project.

Contributions of each author:
Author 1 - Arhyel Mshelia - Author 1 drafted the manuscript, investigation, data collection, data curation, formal analysis and synthesis, manuscript writing, and reading as well as approved the final manuscript.
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