











REVIEW

Health Impact of Gnathostomiasis and its Integral Approach to Parasitic Infection: A Systematic Review

Impacto en la Salud de la Gnatostomiasis y su enfoque Integral en la Infección Parasitaria: Una Revisión Sistemática

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ABSTRACT

The present study focuses on gnathostomiasis, a parasitic disease caused by the nematode gnathostoma that affects both humans and other animals, with a prevalence of 0,14 %. The aim of the study is to analyze the main research related to gnathostomiasis, its diagnosis and treatment. To achieve this objective, a systematic review of clinical cases, observational and retrospective studies of the disease was carried out, following the PRISMA methodology. The literature search, conducted between 2018 and 2022 in the Web of Science, Scopus, PubMed, Redalyc and Dialnet databases, resulted in the identification of five articles relevant and pertinent to the topic. The study findings indicate that gnathostomiasis, on the rise in Latin America and Asia, is transmitted mainly through the consumption of raw fish infected with Gnathostoma larvae. Although preventive measures and treatments, such as albendazole, are available, their efficacy is limited, and it is difficult to implement changes in dietary habits. Therefore, more research is needed to better understand the disease, develop more effective diagnostics and treatments, and raise awareness among physicians of its increasing global prevalence.

Keywords: Gnathostomiasis; Gnathostoma; Parasitic Infection; Parasitosis; Public Health.

RESUMEN

El presente estudio se centra en la gnatostomiasis, una enfermedad parasitaria causada por el nematodo gnathostoma que afecta tanto a humanos como a otros animales, con una prevalencia del 0,14 %. El objetivo del estudio fue analizar las principales investigaciones relacionadas con la gnatostomiasis, sus diagnósticos y tratamientos. Para alcanzar dicho objetivo, se realizó una revisión sistemática de casos clínicos, estudios observacionales y retrospectivos de la enfermedad, siguiendo la metodología PRISMA. La búsqueda bibliográfica, llevada a cabo entre 2018 y 2022 en las bases de datos Web of Science, Scopus, PubMed, Redalyc y Dialnet, resultó en la identificación de cinco artículos pertinentes y relevantes al tema. Las conclusiones del estudio indican que la gnatostomiasis, en aumento en América Latina y Asia, se transmite principalmente a través del consumo de pescado crudo infectado con larvas de Gnathostoma. Aunque existen medidas preventivas y tratamientos, como el albendazol, su eficacia es limitada, y resulta difícil implementar cambios en los hábitos alimentarios. Por lo tanto, es necesario llevar a cabo más investigación para entender mejor la enfermedad, desarrollar diagnósticos y tratamientos más eficaces, y concienciar a los médicos sobre su creciente prevalencia global.

Palabras clave: Gnatostomiasis; Gnathostoma; Infección Parasitaria; Parasitosis; Salud Pública.

INTRODUCTION

Gnatostomy is a parasitic zoonosis caused by nematodes of the genus *gnathostoma*, the human acquires the infection by ingesting raw or undercooked fish from fresh water that is infected with gnathostomous larvae type L3.⁽¹⁾ Because humans are an accidental host, the parasite does not complete its biological cycle and its larvae produce cutaneous, ophthalmological, neurological and visceral alterations in humans. It mainly affects the skin and from there it can migrate to deep tissues, compromising organs such as the lung, eyes, ears, gastrointestinal and genitourinary tracts, and less frequently the central nervous system.

Since ancient times, this disease has been associated with the consumption of raw fish by people living near certain rivers, such as the Yangtze Kiang. In Thailand, this disease has long been known as “Tua-chid” (painful tumor), in India, China, and Japan, it is called “Changchiang edema disease”.⁽²⁾

Gnatostomy is an emerging parasitic disease in Latin America, caused by the migration of gnathostomame larvae into the tissues of definitive and intermediate hosts.⁽³⁾ In Ecuador, cases of gnatostomy have been documented in different regions of the country, including the province of Guayas, where cases have been reported in humans and animals.⁽⁴⁾ The disease is difficult to diagnose and treat, and the lack of information on its prevalence and distribution complicates its control and prevention, in this context, the use of more effective diagnostic tools, such as PCR, can be very useful to identify pathogenic species of *gnathostoma* and improve the understanding of the epidemiology of the disease in Ecuador.⁽⁴⁾

Clinical features can be divided into immediate post-infection symptoms and cutaneous or visceral symptoms, as the case may be. Between 24 and 48 hours after ingestion of the parasite, the individual may present with malaise, fever, anorexia, nausea, vomiting, diarrhea, and abdominal pain, which may be diffuse, epigastric, or localized to the right upper quadrant.⁽⁵⁾ Treatment of gnatostomy is difficult due to the lack of an effective method for all cases and the migratory nature of the larvae. For diagnosis, daytime blood tests are performed and positive serological results for *Gnathostoma* are sought. Molecular studies are rare, but differences in DNA sequences have been identified between several *gnathostoma* species, such as *G. spinigerum* and *G. hispidum*, by commercial PCR and analysis of mitochondrial DNA rDNA and *cox-1* sequences.⁽³⁾

The aim of this article was to provide a comprehensive approach to gnatostomyiasis through a systematic review that encompasses parasitic infection and analyzes in depth the impact on human health. The study contemplated three research questions to cover the following points: regions with the highest reported cases, effectiveness of diagnostic methods and timely treatment, and the clinical spectrum, analyzing the stages of infection.

This article represents a significant contribution to both the scientific literature and medical practice by comprehensively and systematically addressing the problem of gnatostomiasis. Moreover, the article exposes the effectiveness of diagnostic and treatment methods, providing physicians and clinicians with an informed assessment of the tools available. Finally, the article delves into the clinical spectrum of gnathostomy by looking at the various stages of infection. This exploration facilitates a more complete understanding of disease progression in the human body, which could lead to early detection and more effective medical interventions.

METHOD

A systematic literature review provides a solid foundation and integrated summary of existing publications in a specific field of research. Its key objectives are to establish definitions of significant concepts, collect and analyze evidence, recognize previously employed methodologies, and detect gaps in research in the area in question.⁽⁶⁾

This study is based on the PRISMA methodology.⁽⁷⁾ The purpose is to structure in an orderly manner the evidence collected in relation to the parasitic infection gnatostomyiasis and its impact on health, analyzing geographical, clinical, and epidemiological factors; as well as the diagnosis and treatment of the disease, through the meticulous use of various methods and techniques of planning, search and presentation to ensure its reproducibility. This methodology follows an eight-step guide to conducting a systematic review of the literature, including: determining the objective of the review; creation of the protocol and training; literature search; selection for inclusion; quality assessment; data extraction; Synthesis of the studies and writing of the report.^(8,9)

Research Questions

Three research questions were established, these questions are closely aligned with the main objective, functioning as a guiding framework during the exploratory phase. The study covers three main aspects: regions with the highest reported cases, effectiveness of diagnostic methods and timely treatment, and finally the clinical spectrum, analyzing the stages of infection.

RQ1: What is the global epidemiology of gnatostomy and what are the geographic regions that have most

presented this parasitic infection?

RQ2: What is the effectiveness of different methods of diagnosing gnatostomiasis, and how do they influence the accuracy and timeliness of treatment?

RQ3: What is the clinical spectrum of gnatostomy in humans and how do the different stages of infection manifest themselves, from initial symptoms to more serious complications?

Systematization of data search and collection

We conducted a comprehensive search covering all publications between the years 2018-2023. The research was carried out in various databases, including Web of Science (WoS), Scopus, Proquest Salud, Springer, PubMed, Redalyc and Dialnet. Table 1 presents the inclusion and exclusion criteria.

Specific key terms were used to narrow the search in the scientific literature. For point of view 1 (PV1) regarding global epidemiology, the terms “Gnathostomiasis” AND [“reported cases” OR “geographical regions”] were used. In relation to point of view 2 (PV2) concerning diagnostic methods, the terms “Gnathostomiasis” AND [“diagnostic methods” OR “diagnostic procedures” OR “treatment”] were used. Finally, point of view 3 (PV3) addressed the clinical spectrum, making use of terms such as [“Gnathostomiasis” OR “parasite infection”] AND [“symptomatology” OR “clinical spectrum”]. In search engines, variations and combinations of these key terms were applied for the purpose of accessing articles related to the use of work evaluation techniques (figure 1).

N.	Inclusion	Exclusion
C1	Articles that focus specifically on the parasitic disease Gnatostomiasis.	Duplicate Documents
C2	Articles published between 2018-2023	Articles unrelated to the topic of study.
C3	Articles in English Language	Articles with low scientific impact (quartile or indexes).
C4	Articles that present original empirical data or case analyses about the symptomatology and treatment of the disease.	Articles written in areas other than health sciences.

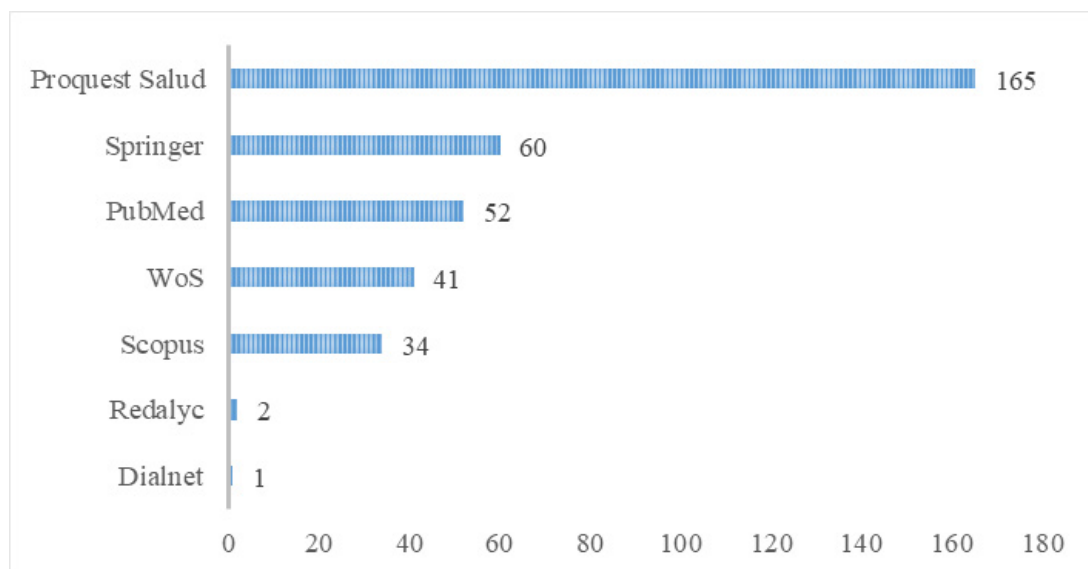


Figure 1. Number of documents per database

Selection of information

In the process of coding and selecting studies in the context of the systematic review, the following criteria were defined for identifying, screening, determining eligibility, and inclusion (figure 2).

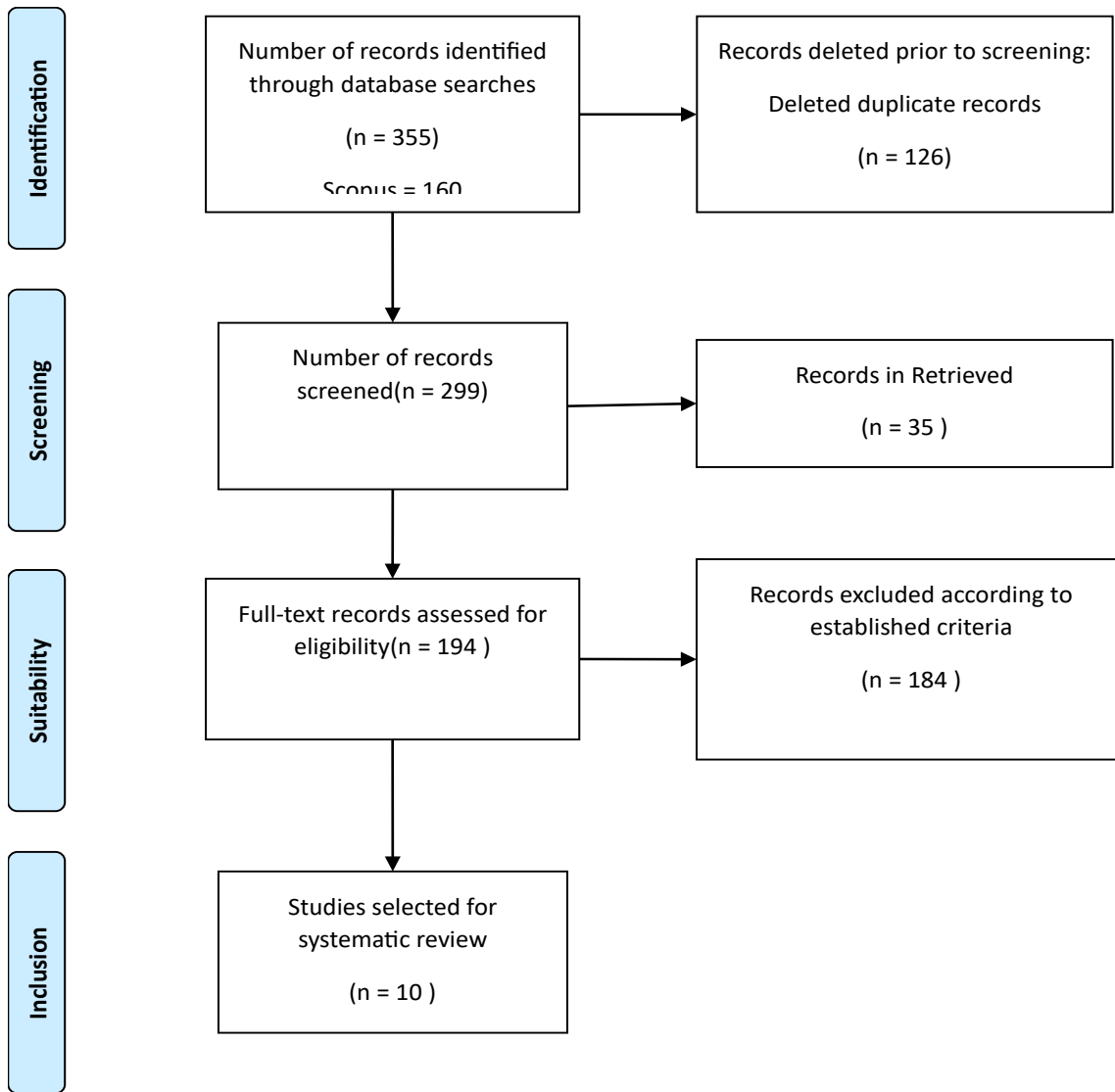


Figure 2. Four-Level Flowchart - PRISMA

Table 2. Data Extraction

N.	Title	Author(s)	Year	Region/Country	Objective/Case	Ref.
1	Human gnathostomiasis in Sri Lanka: an underreported disease?	Musumeci, Stefano; Besson, Juliette; Allgöwer, Andrea; Chappuis, François	2022	Switzerland	Case A healthy Sri Lankan man studying in Geneva experienced a sudden painful swelling in his left forearm. He was treated twice for lymphatic filariasis in Sri Lanka and briefly visited Bangladesh in 2018 with no health problems.	(10)
2	Assessment of an Immuno-Diagnostic Method for Hookworm-Related Cutaneous Larva Migrans Using Crude Extracts of <i>Ancylostoma caninum</i>	Adam, Sitthithana; Dekumyoy, Paron; Nacapunchai, Duangporn; Ketboonlue, Thawatchai and others.	2023	Thailand	The study sought to create an indirect enzyme-linked immunoassay (ELISA) to identify and diagnose LCHM by detecting IgE, IgG, and IgG1-4 in response to <i>Ancylostoma caninum</i> somatic Ag, using extracts from the adult worm.	(11)
3	Case report: eosinophilic meningitis due to gnathostoma spinigerum in an infant in southern Thailand	Thongmak, Tipaporn; Banjerdlak, Palapa; Rangitsathian, Kanokporn	2022	Thailand	We present the case of an 11-month-old boy diagnosed with eosinophilic meningitis caused by <i>Gnathostoma spinigerum</i> and review the literature related to this infection.	(12)

4	Albendazole and mebendazole as anti-parasitic and anti-cancer agents: An update	Chai, Jong; Jung, Bong; Hong, Sung.	2021	South Korea	The study reviews the use of broad-spectrum anthelmintics albendazole and mebendazole in the treatment of parasitic infections and cancers, highlighting their mechanisms of action, applications, and possible side effects.	(13)
5	Survival of immature pre-adult <i>Gnathostoma spinigerum</i> in humans after treatment with albendazole.	Kanjanapruthipong, Tapanee; Ampawong, Sumate; Thaenkham, Urusa; Tuentam, Khwanchanok; Watthanakulpanich, Dorn.	2022	Thailand	The study investigates the morphology of <i>Gnathostoma spinigerum</i> , focusing on the surface of the drug-treated immature stage, using scanning electron microscopy, to understand its structural adaptations to albendazole.	(14)
6	Evaluation of immunodiagnostic tests for human gnathostomiasis using different antigen preparations of <i>Gnathostoma spinigerum</i> larvae against IgE, IgM, IgG, IgG1-4 and IgG1 patterns of post-treated patients	leamsuwan, Issariya; Watthanakulpanich, Dorn; Chaisri, Urai; Adisakwattana, Poom; Dekumyoy, Paron.	2021	Thailand	The study had two objectives: (1) to prepare and evaluate three antigens of infectious larvae of <i>Gnathostoma spinigerum</i> to differentiate IgE, IgG, IgG1-4 and IgM in the diagnosis of gnathostomiasis; and (2) apply the selected ELISA to follow patients treated with ivermectin and albendazole.	(15)
7	Transient cerebral vasculopathy: A rare complication associated with cerebral gnathostomiasis	Saengow, Vitchayaporn; Wongfukiat, Oragarn.	2018	Thailand	This study reports for the first time transient cerebral vasculopathy, an atypical neurological manifestation of gnathostomiasis, in an 11-year-old Thai girl, who recovered spontaneously within 3 months without treatment.	(16)
8	Evaluation of rapid igg4 test for diagnosis of gnathostomiasis.	Wang, Yue; Ma, An; Liu, Xiao; Eamsobhana, Praphathip; Gan, Xiao.	2021	China, Thailand	The study developed and evaluated the dot immuno-gold filtration assay (DIGFA) as a rapid and reliable tool for the clinical diagnosis of gnathostomiasis, detecting <i>Gnathostoma</i> -specific IgG4 in human serum.	(17)
9	Molecular Identification of the Etiological Agent of Human Gnathostomiasis in an Endemic Area of Mexico	Díaz, Sylvia; Parra, Jesús; Ríos, Julián; Delgado, Francisco.	2020	Mexico	This study sought to develop a duplex-PCR amplification method of the ITS-2 region to differentiate between the parasites <i>Gnathostomabinnucleatum</i> and <i>G. turgidum</i> , and to identify <i>Gnathostoma</i> larvae in patients from Sinaloa, Mexico.	(18)
10	Case Report: The First Direct Evidence of <i>Gnathostoma spinigerum</i> Migration through Human Lung	Sivakorn, Chaisith; Promthong, Kingpeth; Dekumyoy, Paron; Viriyavejakul, Parnpen and others	2020	Thailand	This study presents the first documented case of invasion of <i>Gnathostoma</i> in the human lung, with symptoms and radiographic presentations mimicking cancer or chronic infection.	(19)

RESULTS

The present study is a topic that has been explored in medicine for several years. We reviewed 5 documents that met the selection requirements. The articles analyzed were 4 in English and 1 in Spanish. By studying the geographical distribution, the interest of the research community in gnathostomiasis as an endemic and emerging disease, and its impact on people's health, is evident. Table 1 shows the most prominent articles in relation to this topic.

Table 3. Selected studies of gnathostomiasis

N.	Description
1	<p>Author: Rosas et al. ⁽²⁰⁾ Place: Chile</p> <p>Sample: 29-year-old American woman Method/Objective: Clinical case</p> <p>Results: We discuss a singular case of imported gnathostomy, which manifested as migratory vulvar panniculitis that advanced to the abdominal wall. Initially, a bacterial infection of the skin and soft tissues was suspected due to the atypical location and presentation, but did not respond to antimicrobial treatments. Despite the fact that this parasite is unknown in our area, the history of travel to an endemic area and the consumption of risky foods, in this case, raw fish in Thailand, together with the migratory nature of the lesion and eosinophilia, led to suspicion of infection by this nematode. The diagnosis was confirmed after a positive clinical response to empirical antiparasitic treatment and a positive serological examination at an international reference center.</p>
2	<p>Author: Schimmel et al. ⁽²¹⁾ Place: Estados Unidos</p> <p>Sample: 52-year-old male Method/Objective: Case study</p> <p>Results: Gnathostomy is a disease that typically occurs 3 to 4 weeks after consuming raw fish or meat infested with larvae, manifesting itself in the form of migratory swelling of the skin and eosinophilia. Diagnosis is based on clinical presentation, but can be confirmed by skin biopsy, although larvae are rarely visible. Primary treatment is with oral albendazole or ivermectin, but symptoms may persist because of dead larvae on the skin. This report discusses the second case of autochthonous gnathostomy in the United States, indicating an increase in disease due to international travel and importation of infected species, suggesting that clinicians should be alert to the disease even in patients who have not traveled to endemic areas.</p>
3	<p>Author: Wang et al. ⁽²²⁾ Place: China</p> <p>Sample: 13 serum samples from a patient with gnathostomiasis (2011 a 2015) Method/Objective: Experimental method</p> <p>Results: A rapid, reliable, and easy-to-use immunodiagnostic test, known as the Immunogold Spot Filtration Assay (DIGFA), has been developed to facilitate the clinical diagnosis of gnathostomiasis. This useful tool identifies specific anti-gnathostoma IgG4 in human serum, using the crude extract of third-stage larvae as an antigen. The result of this test is determined by using a human anti-IgG4 monoclonal antibody linked with colloidal gold. IgG4, an antibody with unique biological properties may serve as a potent biomarker in the diagnosis of gnathostomiasis, a neglected parasitic disease. In the study, a rapid assay called DIGFA was used to detect specific IgG4 against the Gnathostoma L3 parasite, showing 100 % sensitivity and specificity in identifying the disease.</p>
4	<p>Author: Díaz-Camacho et al. ⁽²⁾ Place: México</p> <p>Sample: Clinical data and recovery of AL3A in cases of cutaneous gnathostomy Method/Objective: Clinical trials, observational and retrospective studies.</p> <p>Results: This study identified the parasite <i>Gnathostoma binucleatum</i> as the cause of human gnathostomiasis in Sinaloa, Mexico, using a duplex PCR method designed to differentiate between <i>G. binucleatum</i> and <i>G. turgidum</i>, another common species in the region. The sequences of the Transcribed Internal Spacer 2 (ITS-2) of the larvae isolated from infected patients fully coincided with those of <i>G. binucleatum</i>, validating its use as a genetic marker for the identification of species in parasitic diseases. The findings indicate that, despite the presence of <i>G. turgidum</i> in the region, only <i>G. binucleatum</i> is associated with human gnathostomiasis in the Americas. In addition, it is suggested that the infection may be linked to inadvertent ingestion of raw fish in local dishes such as seafood cocktails.</p>
5	<p>Author: Sapp et al. ⁽²³⁾ Place: Bangladesh</p> <p>Sample: 46-year-old female Method/Objective: Observational and retrospective studies.</p> <p>Results: A singular case of cutaneous gnathostomiasis caused by a subadult male worm <i>G. spinigerum</i> was identified. This case is of particular interest due to the recovery of the subadult form of the worm, which allowed for easier identification of the species. In addition, a rare manifestation of the disease was observed: the spontaneous appearance of the worm on the skin, possibly stimulated by treatment with albendazole. The mechanism behind this drug-induced migration is not yet fully understood.</p> <p>The case also raises the need to consider gnathostomiasis in the differential diagnosis in clinical practice, particularly in patients with a history of travel to endemic areas and nonspecific serological findings.</p>

DISCUSSION

Gnathostomiasis is a parasitic disease that affects both humans and animals. It is mainly transmitted through the consumption of raw or undercooked fish that contain larvae of the parasite.⁽³⁾ This disease is endemic in certain regions of the world, particularly in countries in Asia and Latin America, where the consumption of raw fish is common.⁽²⁴⁾

The symptoms of gnathostomiasis can vary depending on the migration route of the larvae in the human body. Some of the most common symptoms include epigastric pain, nausea, and vomiting that occur when the larvae pass through the gastric or duodenal wall.⁽²⁵⁾ In addition, the migration of the larvae through the abdominal organs can cause intermittent gastrointestinal symptoms for months or even years. If the larvae do invade the central nervous system or orbit, they can cause severe complications.⁽²⁾

The diagnosis of gnathostomiasis is made primarily through serological testing and the patient's history

of exposure.⁽²⁶⁾ Isolation of *Gnathostoma* worms from the lesions they cause may be rare due to the migratory properties of the larvae. Although biopsies are impractical for visceral infections, they can be useful in confirming a diagnosis in cases of skin infection.⁽²⁷⁾

As the number of travelers to endemic areas and the export of freshwater fish from these areas increases, cases of gnathostomiasis have also increased in other countries. This raises the potential risk that this zoonosis could establish itself in new areas.⁽²⁸⁾ With the aim of improving the diagnosis of gnathostomiasis, specific antigens purified from native crude extracts or generated by genetic engineering methods have been investigated.⁽²⁹⁾ However, the preparation of these specific antigens can be difficult for institutions without adequate health laboratory facilities in remote areas.⁽²¹⁾

On the other hand, a rapid immunological test, the immunogold dot filtration assay (DIGFA), has been developed to detect *Gnathostoma*-specific IgG4 in human serum using a crude L3 extract as an antigen. A duplex PCR amplification method of the ITS-2 region has also been developed to differentiate between the parasites *G. binucleatum* and *G. turgidum* and to identify *Gnathostoma* larvae obtained from biopsies of patients with gnathostomiasis.⁽²²⁾

Treatment options for gnathostomiasis mainly include oral albendazole or ivermectin. Albendazole is normally administered twice daily at a dose of 400 mg for 21 days and has been shown to have an efficacy rate of greater than 90%.⁽³⁰⁾ Ivermectin is given as a single dose of 0,2 mg/kg, which can be repeated after seven days. However, a relapse can occur, and in such cases, the same medication or a combination of both may be used. The mechanism of this outward migration remains unknown, indicating the need for further research to understand the relationship between drug treatments and the occurrence of *Gnathostoma*.⁽³¹⁾

Prevention of gnathostomiasis focuses on avoiding eating raw or undercooked meat from potential intermediate hosts, especially for travelers to endemic areas. A high degree of suspicion is required for diagnosis, particularly in patients with a history of travel to endemic regions presenting with migratory panniculitis and a lack of response to broad-spectrum antimicrobial therapy.⁽³²⁾ In addition, it is important to note that diseases such as gnathostomiasis can spread due to the popularity of cuisines that include raw fish, such as in Japanese or South American dishes.⁽³³⁾ Climatic factors can also affect the prevalence and spread of these diseases by influencing marine life populations and, consequently, the consumption of potential carrier species.⁽³⁴⁾

Educating the public and medical community about the risks of consuming raw fish and safe methods of preparation is crucial for prevention. Adherence to guidelines such as those from the U.S. Food and Drug Administration (FDA), which recommends freezing fish at certain temperatures for specific periods before consumption, can significantly reduce the risk of infection.⁽³⁵⁾ The Netherlands offers a successful example, where mandatory freezing of fish led to a drastic reduction in infection rates.⁽³⁶⁾

CONCLUSIONS

Gnathostomiasis, an emerging parasitic disease predominantly found in Latin America and Asia, is increasingly reported in non-endemic regions due to factors such as international travel and a growing preference for the consumption of raw fish delicacies. The disease is transmitted through the ingestion of cystate *Gnathostoma* larvae found in fish and other types of raw meat, leading to rapid progression of eosinophilic panniculitis, marked by subcutaneous migratory lesions.

Existing treatments, such as albendazole, show limited effectiveness, as seen in our observations of surviving *G. spinigerum* larvae after treatment, suggesting possible resistance to treatment. In addition, gaps in our understanding of the epidemiology of the disease and the lack of effective diagnostic markers further complicate its management. Therefore, public health measures such as educational campaigns, changes in eating habits, and treatment of definitive hosts with anthelmintics are essential.

In addition, future research should focus on understanding the genomics and immunobiology of *Gnathostoma* to uncover the molecular mechanisms involved in its ability to evade the host immune system. Finally, physicians around the world should be alert to the increasing prevalence of gnathostomiasis, especially in patients presenting with epidemiological and clinical conditions compatible with the disease, thus underscoring the status of the disease as an important foodborne parasitic zoonoses.

REFERENCES

1. Liu GH, Sun MM, Elsheikha HM, Fu YT, Sugiyama H, Ando K, et al. Human gnathostomiasis: a neglected food-borne zoonosis. *Parasit Vectors*. 2020 Dec 1;13(1). <https://doi.org/10.1186/s13071-020-04494-4>
2. Díaz-Camacho SP, Parra-Unda JR, Ríos-Sicairos J, Delgado-Vargas F. Molecular Identification of the Etiological Agent of Human Gnathostomiasis in an Endemic Area of Mexico. *Jpn J Infect Dis [Internet]*. 2019 [cited 2023 Jun 11];73(1):44-50. Available from: <https://pubmed.ncbi.nlm.nih.gov/31564694/>
3. Herman JS, Chiodini PL. Gnathostomiasis, another emerging imported disease. *Clin Microbiol Rev*. 2009

Jul;22(3):484-92. <https://doi.org/10.1128/cmr.00003-09>

4. Cevallos JC, Guerrero J, Romero D, Rosales MJ, Tello L. Prevalencia de gnatostomiasis humana en el Ecuador. *Rev Fac Cienc Med.* 2014;40(1):35-40.

5. Jurado LF PDLRBMME. Gnatostomiasis cutánea, primer caso confirmado en Colombia. *Biomedica.* 2015;35:462-70. <http://dx.doi.org/10.7705/biomedica.v35i4.2547>

6. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Vol. 372, *The BMJ.* BMJ Publishing Group; 2021. 372(71). <https://doi.org/10.1136/bmj.n71>

7. PRISMA Statement. PRISMA endorses [Internet]. 2021 [cited 2023 Jul 11]. Available from: <http://www.prisma-statement.org/Endorsement/PRISMAEndorsers?AspxAutoDetectCookieSupport=1>

8. Baker JD. The Purpose, Process, and Methods of Writing a Literature Review. *AORN J* [Internet]. 2016 Mar 1 [cited 2023 Jun 8];103(3):265-9. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1016/j.aorn.2016.01.016>

9. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Revista Espanola de Nutricion Humana y Dietetica.* 2016;20(2):148-60. <https://doi.org/10.1186/2046-4053-4-1>

10. Musumeci S, Besson J, Allgöwer A, Chappuis F. Human gnathostomiasis in Sri Lanka: an underreported disease? *J Travel Med.* 2022 Jan 1;29(1). <https://doi.org/10.1093/jtm/taab145>

11. Adam S, Dekumyoy P, Nacapunchai D, Ketboonlue T, Charunwatthana P, Dhitavat J, et al. Assessment of an Immuno-Diagnostic Method for Hookworm-Related Cutaneous Larva Migrans Using Crude Extracts of *Ancylostoma caninum*. *Trop Med Infect Dis.* 2023 Apr 1;8(4). <https://doi.org/10.3390/tropicalmed8040209>

12. Thongmak T, Banjerdlak P, Rangitsathian K. Case report: eosinophilic meningitis due to gnathostoma spinigerum in an infant in southern Thailand. *Southeast Asian Journal of Tropical Medicine and Public Health* [Internet]. 2022 [cited 2023 Sep 3];53(6):531-7. Available from: <https://www.proquest.com/docview/2741033825/CC07C6A48EAC4EB7PQ/2?accountid=142712>

13. Chai JY, Jung BK, Hong SJ. Albendazole and mebendazole as anti-parasitic and anti-cancer agents: An update. Vol. 59, *Korean Journal of Parasitology.* Korean Society for Parasitology and Tropical Medicine; 2021. p. 189-225. <https://doi.org/10.3347%2Fkjp.2021.59.3.189>

14. Kanjanapruthipong T, Ampawong S, Thaenkham U, Tuentam K, Watthanakulpanich D. Survival of immature pre-adult *Gnathostoma spinigerum* in humans after treatment with albendazole. *PLoS One.* 2022 Mar 1;17(3):1-12. <https://doi.org/10.1371/journal.pone.0264766>

15. Ieamsuwan I, Watthanakulpanich D, Chaisri U, Adisakwattana P, Dekumyoy P. Evaluation of immunodiagnostic tests for human gnathostomiasis using different antigen preparations of *Gnathostoma spinigerum* larvae against IgE, IgM, IgG, IgG1-4 and IgG1 patterns of post-treated patients. *Tropical Medicine and International Health.* 2021 Dec 1;26(12):1634-44. <https://doi.org/10.1111/tmi.13679>

16. Saengow VE, Wongfukiat O. Transient cerebral vasculopathy: A rare complication associated with cerebral gnathostomiasis. *Journal of Child Science.* 2018 Jan 1;8(1):27-30. <https://doi.org/10.1055/s-0038-1641601>

17. Wang Y, Ma A, Liu XL, Eamsobhana P, Gan XX. Evaluation of rapid igg4 test for diagnosis of gnathostomiasis. *Korean Journal of Parasitology.* 2021 Jun 1;59(3):257-63. <https://doi.org/10.3347%2Fkjp.2021.59.3.257>

18. Díaz-Camacho S, Parra-Unda J, Ríos-Sicairos J, Delgado-Vargas F. Molecular Identification of the Etiological Agent of Human Gnathostomiasis in an Endemic Area of Mexico. *Jpn J Infect Dis.* 2020;73:44-50. <https://doi.org/10.7883/yoken.JJID.2019.180>

19. Sivakorn C, Promthong K, Dekumyoy P, Viriyavejakul P, Ampawong S, Pakdee W, et al. Case Report: The

First Direct Evidence of *Gnathostoma spinigerum* Migration through Human Lung. *American Journal of Tropical Medicine and Hygiene*. 2020 Sep 1;103(3):1129-34. <https://doi.org/10.4269%2Fajtmh.20-0236>

20. Rosas R, Marcotti A, Weitzel T, Thompson L. Vulvitis migratoria causada por gnatostomiasis importada. *Revista Chilena de Infectología [Internet]*. 2019;36(5):670-3. <http://dx.doi.org/10.4067/S0716-10182019000500670>

21. Schimmel J, Chao L, Luk A, Grafton L, Kadi A, Boh E. An autochthonous case of gnathostomiasis in the United States. *JAAD Case Rep*. 2020 Apr 1;6(4):337-8. <https://doi.org/10.1016/j.jdc.2020.02.019>

22. Wang Y, Ma A, Liu XL, Eamsobhana P, Gan XX. Evaluation of Rapid IgG4 Test for Diagnosis of Gnathostomiasis. *Korean J Parasitol [Internet]*. 2021 [cited 2023 Jun 11];59(3):257-63. Available from: <https://www.parahostdis.org/journal/view.php?doi=10.3347/kjp.2021.59.3.257>

23. Sapp SGH, Kaminski M, Abdallah M, Bishop HS, Fox M, Ndubuisi M, et al. Percutaneous emergence of *gnathostoma spinigerum* following praziquantel treatment. *Trop Med Infect Dis*. 2019;4(4). <https://doi.org/10.3390/tropicalmed4040145>

24. Cevallos W, SVJT, GC, PJ, & VEM. High Prevalence of *Gnathostoma* spp. in Rice Fields in Ecuador: A Neglected Parasitic Disease. *Am J Trop Med Hyg*. 2019;101:387-93.

25. Diaz JH. Gnathostomiasis: An Emerging Infection of Raw Fish Consumers in *Gnathostoma* Nematode-Endemic and Nonendemic Countries. *J Travel Med*. 2015 Sep 1;22(5):318-24. <https://doi.org/10.1111/jtm.12212>

26. Cornaglia J, Jean M, Bertrand K, Aumaître H, Roy M, Nickel B. Gnathostomiasis in Brazil: an emerging disease with a challenging diagnosis. *J Travel Med*. 2016 Jul 1;24(1). <https://doi.org/10.1093/jtm/taw074>

27. Eldridge M, Cohen SH. Cutaneous Manifestations of Infection in Returning Travelers. *Curr Infect Dis Rep*. 2014 Sep 25;16(10). <https://doi.org/10.1007/s11908-014-0426-9>

28. Moore D, McCroddan J, Dekumyoy P, Chiodini P. Gnathostomiasis: An Emerging Imported Disease. *Emerg Infect Dis*. 2003;9(6):647-50. <https://doi.org/10.3201%2Fid0906.020625>

29. Nopparatana C, Setasuban P, Chaicumpa W, Tapchaisri P. Purification of *Gnathostoma Spinigerum* specific antigen and immunodiagnosis of human Gnathostomiasis. *Int J Parasitol*. 1991;21(5):677-87. [https://doi.org/10.1016/0020-7519\(91\)90079-M](https://doi.org/10.1016/0020-7519(91)90079-M)

30. Bravo F, Gontijo B. Gnathostomiasis: An emerging infectious disease relevant to all dermatologists. *An Bras Dermatol*. 2018 Mar 1;93(2):172-80. <https://doi.org/10.1590/abd1806-4841.20187498>

31. Nontasut P, Claesson BA, Dekumyoy P, Pakdee W, Chullawichit S. Double-dose ivermectin vs albendazole for the treatment of gnathostomiasis. *Southeast Asian J Trop Med Public Health [Internet]*. 2005 [cited 2023 Jun 12];36(3):650-3. Available from: <https://pubmed.ncbi.nlm.nih.gov/16124432/>

32. Theunissen C, Bottieau E, Van Gompel A, Siozopoulou V, Bradbury RS. Presumptive *Gnathostoma binucleatum*-infection in a Belgian traveler returning from South America. *Travel Med Infect Dis*. 2016 Mar 1;14(2):170-1. <https://doi.org/10.1016/j.tmaid.2016.02.003>

33. Leroy J, Cornu M, Deleplancque AS, Loridant S, Dutoit E, Sendid B. Sushi, ceviche and gnathostomiasis - A case report and review of imported infections. *Travel Med Infect Dis*. 2017 Nov 1;20:26-30. <https://doi.org/10.1016/j.tmaid.2017.10.010>

34. Rawat P, Gautam M, Jain NC, Jain R. Intraocular gnathostomiasis: A rare case report from Central India. *Indian J Ophthalmol*. 2016 Mar 1;64(3):235-7. Doi: 10.4103/0301-4738.181747

35. US Food and Drug Administration. Department of health and human services. 2022 [cited 2023 Jun 12]. Fish and fisheries products hazards and controls guidance. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-fish-and-fishery-products-hazards-and-controls>

36. Eiras JC, Pavanelli GC, Takemoto RM, Nawa Y. Fish-borne nematodiasis in South America: Neglected emerging diseases. *J Helminthol.* 2018 Nov 1;92(6):649-54. <https://doi.org/10.1017/S0022149X17001006>

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