Annals of Clinical Microbiology www.acm.or.kr

Review article

Anisakidosis in humans and animals and detection of anisakid larvae in fish and cephalopods in Korea: a literature review (1971-2022)

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Abstract

Human anisakiasis (or anisakidosis) is a disease caused by the ingestion of marine fish or cephalopods infected with anisakid nematode larvae of the genera *Anisakis, Pseudoterranova, Contracaecum*, and *Hysterothylacium*. Anisakiasis is a clinically important disease that often manifests as an acute abdominal syndrome requiring emergency medical attention and care. In Korea, at least several thousand clinical cases have been diagnosed to date; however, only a small proportion of them have been reported in the literature (1971-2022). The most common etiological agents were *Anisakis pegreffii* (reported as *Anisakis* sp., *Anisakis* type I, or erroneously *Anisakis simplex*), followed by *Pseudoterranova decipiens*, *Contracaecum* sp., and *Anisakis simplex* sensu stricto (s.s.). Most cases involved the stomach and small or large intestine, with a few involving the oral cavity (oral mucosa, pharynx, and tonsils), esophagus, omentum, and mesocolic lymph nodes. *Anisakis* allergies and host immune responses have been studied in humans and experimental animals. Marine fish and cephalopods, including sea eel (*Astroconger myriaster*), squid (*Todarodes pacificus*), yellow corvina (*Pseudosciaena manchurica*), Japanese flounder (*Paralichthys olivaceus*), codfish (*Gadus macrocephalus*), yellowtail (*Seriola quinquaradiata*), and rockfish (*Sebastes* spp.), are the most common infection sources. Surveys were performed on anisakid nematode larvae in marine fish and cephalopods caught in the western, eastern, and southern seas of Korea. The larvae recovered from fish or cephalopods caught from the western and southern seas were predominantly *A. pegreffii* larvae; however, the larvae from the eastern sea were either *A. pegreffii* larvae (in the chub mackerel, Japanese flounder, and rockfish) or *A. simplex* s.s. (in the salmon and pollock; these fish migrate through the northern North Pacific Ocean and Bering Sea and come to Korea). Health education to avoid eating raw or improperly cooked marine fish and cephalopods (particularly the viscera) is crucial for preventing human anisakidosis in Korea.

Keywords: *Anisakis pegreffii, Anisakis simplex, Pseudoterranova decipiens*, anisakidosis, Korea

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OPEN ACCESS

pISSN : 2288-0585
eISSN : 2288-6850

Ann Clin Microbiol 2024 June, 27(2): 93-130
https://doi.org/10.5145/ACM.2024.27.2.6

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Received: April 03, 2024
Revised: April 23, 2024
Accepted: April 29, 2024

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Introduction

Anisakiasis, or more broadly anisakidosis (infection with anisakid nematode larvae; Anisakidae and Raphidascarididae), is a typical example of fishborne parasitic zoonoses in localities where marine fish or cephalopods are consumed raw or improperly cooked [1]. The etiological agents include species of *Anisakis* (*A. pegreffii, A. simplex* s.s., and *A. physeteris*), *Pseudoterranova* (*P. decipiens* s.s., *P. azarasi*, and *P. cattani*), *Contracaecum* (*C. osculatum*), and *Hysterothylacium* (*H. aduncum*) [2,3]. However, 4 species, *A. pegreffii*, *A. simplex*, *P. decipiens*, and *P. azarasi*, are most frequently involved in highly endemic countries, especially Korea and Japan [3,4]. Natural definitive hosts include dolphins, porpoises, whales, seals, and rarely, large marine fish [2]. Animal or human (accidental host) infection is caused by third-stage larvae found in the viscera or muscles of various fish and cephalopod (mollusks) species [1].

The concept of this zoonotic disease (initially called 'herring worm disease' or 'codworm disease') was first introduced in 1960 by van Thiel et al. [5], who reported 11 patients complaining of acute abdominal syndrome in the Netherlands, followed by Ashby et al. [6] in England in 1964, who reported 2 such patients and reviewed 89 cases possibly due to this disease. However, the diagnosis of the causative worms at this time was erroneously *Eustoma rotundatum* [5,6]. In 1965, Asami et al. [7] and Yokogawa and Yoshimura [8] reported similar human infections in Japan and assigned the causative worms to *Anisakis*-like larvae. Since then, human anisakidosis has been reported in various locations worldwide, including Japan, Korea, the Netherlands, Spain, France, Italy, Germany, England, and the USA [1,2]. To date, at least 50,000 clinical cases have been reported in these countries [1,2]. However, this is a significant underestimation of the actual situation. For example, in Japan, an average annual incidence of 19,737 anisakidosis cases was estimated from 2018 to 2019 [4], and in Spain, an annual incidence of 7,700-8,320 anisakidosis cases was estimated [9].

The most common site of anisakidosis in humans is the stomach, followed by the intestines (small and large intestines), and rarely the oral cavity, pharynx, tonsils, and esophagus [1,2]. Extra-gastrointestinal infections may also occur in rare instances, in the peritoneum, liver, lymph nodes, omentum, mesentery, pancreas, ovaries, and lungs [2]. In gastrointestinal anisakiasis, acute abdomen, nausea, vomiting, and mucosal bleeding are the most common clinical manifestations, although some cases reveal no special clinical problems, and the larvae can be incidentally found during surgery or endoscopy [2]. Diagnosis is mainly based on the recovery of anisakid larvae from the affected lesions through gastrointestinal endoscopy or surgery. In some cases, the diagnosis is made based on sectional morphologies of the larvae in histopathological specimens [2]. Serology to detect serum antibodies, for example, enzyme-linked immunosorbent assay (ELISA), and radiography, are other diagnostic methods used to diagnose acute and/or chronic anisakidosis [2]. No anthelmintic drugs have been proven to be effective in anisakidosis patients.

In Korea, human anisakidosis is common because Koreans generally prefer to eat the raw or undercooked flesh of marine fish or cephalopods (cuttlefish, squid, and octopus). Since the first case was reported in 1971 [10], over a hundred articles have been published on clinical anisakidosis cases until 2022. The status was briefly reviewed by Sohn et al. [11] in 2015, in which 64 articles were analyzed concerning the number of cases, locality of patient occurrence, gender characteristics, source of infection (fish or cephalopods), morphological types of larvae, and predilection sites. However, since then, there has been no further review of the anisakidosis status in Korea.

Besides clinical case reports, there have been reports on the detection of anisakid larvae from marine fish and cephalopods, the occurrence of animal anisakidosis, and immunologic studies on experimental anisakidosis in animals. Thus, the present study focused on reviewing the Korean literature on human and animal anisakidosis (occurrence of clinical cases, clinicopathologic characteristics, immunity, diagnosis, and natural and experimental animal infections), as well as the status of anisakid larval infections in fish and cephalopods, larval morphology, molecular analyses, and resistance of anisakid larvae to physicochemical agents.

Literature analyzed

We searched and analyzed Korean literature on *Anisakis*, *Pseudoterranova*, anisakiasis, and anisakidosis from sources, including Google Scholar, PubMed Central, and KoreaMed. International literature to refer was also obtained from the same data sources.

Reported cases of human anisakidosis in Korea

In Korea, human anisakidosis was first reported in 1971 [10] in a patient living in Seoul complaining of a foreign body sensation and dull pain in the palatine tonsil. It was evident that these symptoms were due to infection with a larva of *Anisakis* sp. penetrating the palatine tonsil, which was extracted using forceps. The second case was reported in 1980 by Cho et al. [12] in a patient living in Seoul with an acute abdomen due to duodenal ulcer perforation. An anisakid larva section was incidentally found in the ileum of this patient.

By the end of 2022, at least 108 articles (including several abstracts) had been published on human anisakidosis cases in Korea (Tables 1-4) [3,10-116]. The total number of cases reported was 851, including 131 cases during 1971-1990, 225 cases during 1991-2000, 229 cases during 2001-2010, and 268 cases during 2011-2022, which demonstrated a chronologically increasing trend (Fig. 1). Seropositive cases were excluded if anisakid larvae were not parasitologically confirmed [117-120]. In addition, an increasing number of anisakiasis cases were reported from 2011 to 2018 in Korea based on big data analysis of Health Insurance Review Assessment claims [121]. According to this article, the annual number of anisakiasis cases registered in the Korean Health Insurance Database (2011-2018) was 333-818, including 409 cases in 2011, 333 cases in 2012, 359 cases in 2013, 409 cases in 2014, 450 cases in 2015, 491 cases in 2016, 685 cases in 2017, and 818 cases in 2018, totaling 3,954 cases during the 8 years (avg. 494 cases/year) [121]. Therefore, at least 800 cases of human anisakidosis occur annually in the Korean population. However, most of these cases were not officially reported in scientific publications (it is also uncertain whether these cases were parasitologically proven) and thus were not included in the clinical case analyses of this review.

Table 1. Case reports of anisakidosis from 1971 to 1990 in Korea

Study (yr)	No. of cases	Organ (s) involved	Larva identified	Locality of case (s)
Kim et al. (1971) [10]	1	Platine tonsil	*Anisakis* sp.	Seoul
Cho et al. (1980) [12]	1	Ileum	*Anisakis* sp.	Seoul
Lee et al. (1981) [13]	5	Stomach	*Anisakis* sp.	Busan
Chung et al. (1983) [14]	27	Stomach	*Anisakis* sp.	Busan
Paik et al. (1984) [15]	1	Ileum	*Anisakis* sp.	Seoul
Seo et al. (1984) [16]	1	Ileum	*Terranova* type A	Incheon
Jeong and Suk (1984) [17]	1	Stomach	*Anisakis* sp.	Busan
Lee et al. (1985) [18]	1	Stomach	*Terranova* type A	Incheon
Lee et al. (1986) [19]	4	Stomach	*Anisakis* sp.	Daegu
Yun and Whang (1987) [20]	1	Ileum	*Anisakis* sp.	Daegu
Kim et al. (1987) [21]	7	Stomach	*Anisakis* sp.	Daegu
Chi et al. (1988) [22]*	3	?	*Anisakis* sp.	?
Yang et al. (1988) [23]	3	Stomach	*Anisakis* sp.	Gwangju
Ko et al. (1988) [24]	3	Ileum (2), colon (1)	*Anisakis* sp.	Jinju
Han et al. (1988) [25]	6	Stomach (2), ileum (4)	*Anisakis* sp.	Pohang
Ahn et al. (1988) [26]	1	Stomach	*Anisakis* sp.	?
Jang et al. (1989) [27]	12	Stomach	*Anisakis* sp.	Pohang
Jin et al. (1989) [28]	1	Stomach	*Anisakis* sp.	Wonju
Lee HS et al. (1989) [29]	3	Stomach	*Anisakis* sp.	Chuncheon
Lee MS et al. (1989) [30]	1	Ileum	*Anisakis* sp.	Seoul
Choi et al. (1989) [31]	5	Stomach	*Anisakis* sp.	Seoul
Jung et al. (1990) [32]	1	Ileum	*Anisakis* sp.	Pohang
Park et al. (1990) [33]	1	Ileum	*Anisakis* sp.	Suwon
Im et al. (1990) [34]	39	Stomach	*Anisakis* type I (13) *Terranova* type A (1) *Contracaecum* sp. (2) Unknown (23)	Jeju
Subtotal	129	Stomach (111), intestine (14), tonsil (1), unknown (3)	*Anisakis* sp. (88), *Anisakis* type I (13), *Terranova* type A (3), *Contracaecum* sp. (2), Unknown (23)	Jeju (39), Busan (33), Pohang (19), Daegu (12), Seoul (9), Gwangju (3), Chuncheon (3), Jinju (3), Incheon (2), Wonju (1), Suwon (1), Unknown (4)

Only scientific reports (including abstracts) dealing with anisakidosis cases were included. Diagnosis based only on serological tests were excluded.
*They reported 4 anisakiasis cases but 1 of them was previously reported by Cho et al. [12].

Table 2. Case reports of anisakidosis from 1991 to 2000 in Korea

Study (yr)	No. of cases	Organ (s) involved	Larva identified	Locality of case (s)
Im and Shin (1991) [35]	3	Stomach	*Terranova* type A	Jeju (2), Seoul (1)
Kim SE et al. (1991) [36]	9	Stomach	*Anisakis* sp.	Seoul
Kim LS et al. (1991) [37]	1	Jejunum	*Anisakis* sp.	Seoul
Sohn et al. (1991) [38]	2	Stomach	*Anisakis* type I	Busan
Shin et al. (1992) [39]	1	Ileum	*Anisakis* sp.	Seoul
Lee SH et al. (1993) [40]	1	Stomach	*Anisakis* sp.	Busan
Lee HS et al. (1993) [41]	1	Stomach	*Anisakis* sp.	Daejeon
Kim et al. (1994) [42]	1	Greater omentum	?	Gwangju
Sohn and Seol (1994a) [43]	1	Stomach	*Pseudoterranova decipiens*	Busan
Sohn and Seol (1994b) [44]	1	Duodenum	*Anisakis* type I	Busan
Seol et al. (1994) [45]	20	Stomach	*Anisakis* type I	Busan
Im et al. (1995) [46]	107	Stomach	*Anisakis simplex* (82), Anisakis type II (5), *Pseudoterranova decipiens* (2), *Contracaecum* type A (1), Unknown (17)	Jeju
Shim et al. (1995) [47]	2	Ileum	*Anisakis* sp.	Daegu
Cho et al. (1996) [48]	7	Stomach	*Anisakis* sp.	Gwangmyeong
Geum et al. (1997) [49]	6	Stomach (5), duodenum (1)	*Anisakis* sp.	Daegu
Kim et al. (1997) [50]	1	Mesocolic lymphnode	*Anisakis* sp.	Seoul
Cho et al. (1998) [51]	1	Stomach	*Anisakis* sp. (?)	Seoul
Guahk et al. (1998) [52]	1	Stomach	*Anisakis* sp.	Seoul
Yoon et al. (1998) [53]	1	Stomach	?	Gwangju
Lee et al. (1998) [54]	1	Stomach	*Pseudoterranova decipiens*	Gwangmyeong
Koh et al. (1999) [55]	1	Stomach	*Pseudoterranova decipiens*	Chuncheon
Song et al. (1999) [56]	39	Stomach	*Anisakis* type I (27), *Anisakis* type II (3), *Pseudoterranova* sp. (1), Unknown (8)	Incheon
Ahn et al. (1999) [57]	1	Stomach	*Anisakis* sp.	Seoul
Park CY et al. (1999) [58]	1	Stomach	?	Seoul
Kang et al. (1999) [59]	2	Stomach	*Anisakis* sp.	Seoul
Park TG et al. (1999) [60]	1	Esophagus	*Anisakis* sp.	Pohang
Choi et al. (2000) [61]	2	Stomach	*Pseudoterranova decipiens*	Seoul
Chung et al. (2000) [62]	10	Stomach (2), small intestine (8)	*Anisakis* sp.	Gwangju
Subtotal	225	Stomach (208), intestine (14), lymph node (1), omentum (1), esophagus (1)	*Anisakis* sp. (45), *Anisakis* type I (50), *Anisakis* type II (8), *Anisakis simplex* (82), *Pseudoterranova sp.* (11), *Contracaecum* sp. (1), Unknown (28)	Jeju (109), Incheon (39), Busan (25), Seoul (21), Gwangju (12), Daegu (8), Gwangmyeong (8), Daejeon (1), Chuncheon (1), Pohang (1)

Only scientific reports dealing with anisakidosis cases (excluding serological tests) were included in this table.

Table 3. Case reports of anisakidosis from 2001 to 2010 in Korea

Study (yr)	No. of cases	Organ (s) involved	Larva identified	Locality of case (s)
Yu et al. (2001) [63]	1	Stomach	*Pseudoterranova decipiens*	Chungju
Yeum et al (2002) [64]	1	Peritoneum	*Anisakis* simplex	Jeju
Hwang et al. (2002) [65]	3	Esophagus	?	?
Choi et al. (2003) [66]	1	Stomach	*Anisakis* sp.	Busan
Lim et al. (2003) [67]	1	Stomach	*Anisakis* type I	Chuncheon
Noh et al. (2003) [68]	1	Stomach	*Anisakis simplex*	Busan
Yoon et al. (2004) [69]	1	Small intestine	*Anisakis* sp.	Sungnam
Suh et al. (2004) [70]	1	Ascending colon	*Anisakis* sp.	Seoul
Woo et al. (2004) [71]	1	Ascending colon	*Anisakis simplex*	Seoul
Kwon et al. (2004) [72]	1	Stomach	*Anisakis* sp.	Seoul
Kim et al. (2004) [73]	1	Stomach, ileum, transverse colon	*Anisakis* sp.	Sooncheon
Song et al. (2004) [74]	27	Stomach (?)	*Anisakis* sp. (21) *P. decipiens* (6)	Seoul
Suh et al. (2005) [75]	1	Stomach	*Anisakis* sp.	Seoul
Shin et al. (2006) [76]	1	Transverse colon	*Anisakis simplex*	Seoul
Park SW et al. (2006) [77]	3	Stomach	*Anisakis* sp.	Gwangju
Kim YH et al. (2006) [78]	3	Colon	*Anisakis* sp.	Seocheon
Park JY et al. (2006) [79]	1	Oral cavity, tongue	*Anisakis* type I	Gangneung
Kim JH et al. (2006) [80]	2	Stomach (1), esophagus (2)	*Anisakis* sp.	Busan
Cho et al. (2006) [81]	2	Cecum	*Anisakis* sp.	Iksan
Jang et al. (2006) [82]	1	Rectum	*Anisakis* sp.	Daejeon
Kim SH et al. (2006) [83]	1	Stomach	*Anisakis* sp.	Jeju
Kim SG et al. (2006) [84]	4	Stomach	?	Seoul
Shin et al. (2007) [85]	1	Esophagus	*Anisakis* sp.	Jeonju
Yoo et al. (2008) [86]	1	Ascending colon	*Anisakis* sp.	Seoul
Lee et al. (2008) [87]	1	Ileum	*Anisakis* sp.	Busan
Choi et al. (2008) [88]	1	Ascending colon	*Anisakis* sp.	Gwangju
Cho et al. (2009) [89]	1	Stomach, colon	*Anisakis* sp.	Gangneung
Lee et al. (2009) [90]	141	Stomach	*Anisakis* sp.	Jinju
Hong et al. (2009) [91]	1	Duodenum	*Anisakis* sp.	Seoul
Choi et al. (2009) [92]	10	?	?	?
Choi et al. (2010) [93]	11	Stomach (10), ascending colon (1)	?	Seoul
Do et al. (2010) [94]	1	Ascending colon	*Anisakis* sp.	Uijeongbu
Kang et al. (2010) [95]	1	Jejunum	*Anisakis* sp.	Iksan
Subtotal	229	Stomach (195), intestine (19), esophagus (6), oral cavity (1), peritoneum (1), unknown (10)	*Anisakis* sp. (188), *Anisakis* type I (2), *Anisakis simplex* (4), *Pseudoterranova* sp. (7), Unknown (28)	Jinju (141), Seoul (49), Busan (5), Gwangju (4), Iksan (3), Seocheon (3), Jeju (2), Gangneung (2), Sungnam (1), Daejeon (1), Chuncheon (1), Suncheon (1), Uijeongbu (1), Chungju (1), Jeonju (1), Unknown (13)

Only scientific reports dealing with anisakidosis cases (including abstracts), excluding serological tests, were included in this table.

Table 4. Case reports of anisakidosis from 2011 to 2022 in Korea

Study (yr)	No. of cases	Organ (s) involved	Larva identified	Locality of case (s)
Kim et al. (2011) [96]	4	Small intestine	*Anisakis* sp.	Seoul
Hwang et al (2012) [97]	1	Duodenum	*Anisakis* sp.	Gwangju
Cho et al. (2012) [98]	1	Stomach, colon	*Anisakis* sp.	Gangneung
Kim et al. (2012) [99]	1	Stomach	*Anisakis* sp.	Jeju
Na et al. (2013) [100]	1	Stomach	*Pseudoterranova decipiens*	Cheonan
Yoon et al. (2013) [101]	1	Ileum	*Anisakis* sp.	Gwangju
Kim T et al. (2013) [102]	59	Stomach (29), small intestine (30)	*Anisakis* sp.	Jeju
Kim SH et al. (2013) [103]	1	Stomach, colon	*Anisakis* sp.	Daejeon
Choi et al. (2014) [104]	62	Stomach	*Anisakis* sp. (52), *Pseudoterranova decipiens* (10)	Seoul
Lee et al. (2014) [105]	19	Small intestine	*Anisakis* sp.	Jeju
Kang et al. (2014) [106]	1	Stomach	*Anisakis* sp.	Iksan
Sohn et al. (2015) [11]	15	Stomach	*Anisakis* type I	Jinju
Lim et al. (2015) [107]	16	Stomach	*Anisakis pegreffii* (15)*, *Anisakis simplex* (1)	Around Seoul
Choi et al. (2017) [108]	1	Oral mucosa	*Anisakis* sp.	Cheongju
Park et al. (2018) [109]	28	Stomach	*Anisakis* sp.	Busan
Kim et al. (2018) [110]	1	Ileum	*Anisakis* sp.	Busan
Choi et al. (2019) [111]	1	Colon	*Anisakis simplex*	Incheon
Joo et al. (2019) [112]	20	Colon	*Anisakis* sp.	Seoul
Song et al. (2019) [113]	20	Stomach (19), colon (1)	*Anisakis pegreffii**	Various localities
Jeong and Ahn (2020) [114]	1	Esophagus	*Anisakis* sp.	Seoul
Joo et al. (2021) [115]	1	Stomach	*Anisakis* sp.	Busan
Cha et al. (2022) [116]	1	Palatine tonsil	*Anisakis* sp.	Daegu
Song et al. (2022) [3]	12	Stomach (11), colon (1)	*Pseudoterranova decipiens*	Various localities
Subtotal	268	Stomach (184), intestine (81), esophagus (1), oral mucosa (1), tonsil (1)	*Anisakis* sp. (193), *Anisakis* type I (15), *Anisakis simplex* (2), *Anisakis pegreffii* (35), *Pseudoterranova decipiens* (23)	Seoul (103), Jeju (79), Busan (30), Jinju (15), Gwangju (2), Incheon (1), Daegu (1), Iksan (1), Gangneung (1), Daejeon (1), Cheongju (1), Cheonan (1), Unknown (32)

Only scientific reports dealing with anisakidosis cases (including abstracts and excluding serological tests) were included in this table.
*Molecular studies were performed to identify the species anisakid nematodes involved.

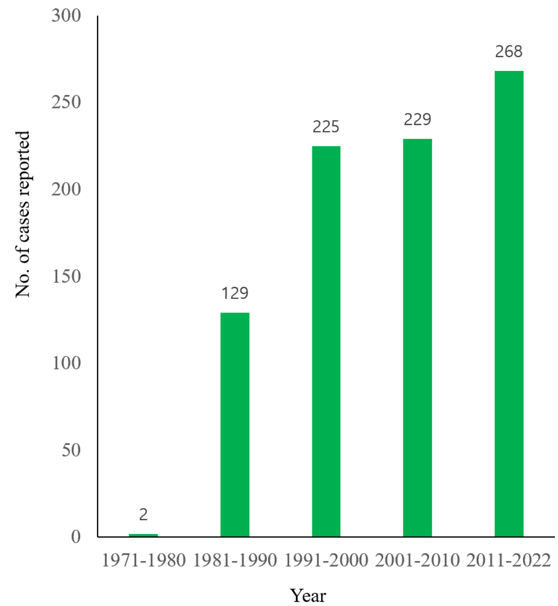

Fig. 1. Number of anisakidosis cases reported in scientific articles in Korea (1971-2022).

Geographic locality of cases

The geographic locations where anisakidosis cases were reported in Korea were variable, including Jeju (229 cases; 26.9%), Seoul (182; 21.4%), Jinju (159; 18.7%), Busan (93; 10.9%), Incheon (42; 4.9%), Gwangju (21; 2.5%), Daegu (21; 2.5%), Pohang (20; 2.4%) and other cities (Fig. 2). A strong trend was observed for cases to be more commonly diagnosed in coastal areas than in inland areas. In addition, the frequency of reports seemed to depend on the number of medical facilities available in each area.

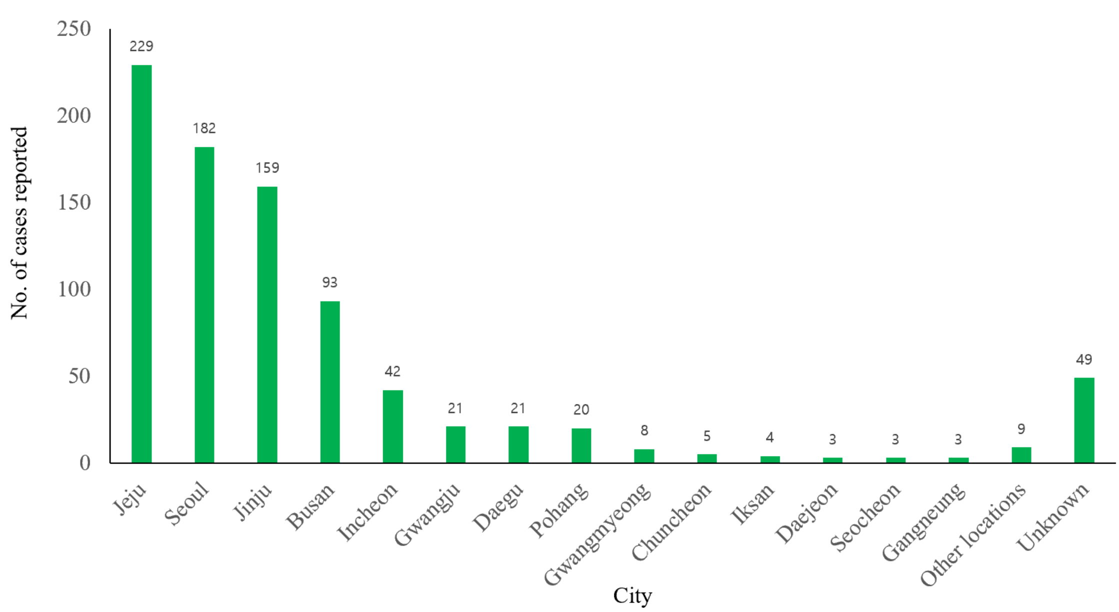

Fig. 2. Number of anisakidosis cases according to localities in Korea (1971-2022).

Source of infection

The possible sources of infection (fish or cephalopod dishes) were mentioned in most articles (Table 5). Of the 851 anisakidosis patients, approximately a quarter (25.4%) stated that they had eaten undefined or mixed fish dishes (over 2 kinds of fish). The next most common source of infection was sea eel (19.9%), followed by squid (5.2%), yellow corvina (4.2%), Japanese flounder or flatfish (3.4%), codfish (2.6%), yellowtail (1.6%), and rockfish (1.4%) (Table 5). Anchovy, seabream, skate, and shad were the next most common dishes consumed by patients with anisakidosis in Korea (Table 5). It is of special note that approximately 1/5 of the cases involved the consumption of raw or undercooked sea eels. Considering that mixed fish dishes frequently include sea eel, the number of cases associated with sea eel consumption would increase to over 1/3 of all cases. A significant concern related to this is that anisakid larvae are commonly found in the muscles of sea eel, whereas larvae are generally found in the viscera and abdominal cavity of most other types of marine fish [122-126]. Therefore, if the sea eel muscle is consumed raw, it could be possible to be infected with anisakid larvae that are frequently found alive in the muscles of this fish.

Table 5. Marine fish, cephalopods, or other marine food dishes consumed by anisakidosis patients in Korea (1971-2022)

Kinds of dish (Korean name of fish)	No. of patients (%)
Mixed fish dish* or undefined marine fish (모듬회, 생선회)	216 (25.4)
Sea eel (*Conger myriaster* or others) (붕장어)	169 (19.9)
Squid (*Todarodes pacificus* and others) (오징어류)	44 (5.2)
Yellow corvina (*Pseudosciaena manchurica*) (조기)	36 (4.2)
Flounder (*Paralichthys olivaceus* or others) (광어, 넙치, 도다리)	29 (3.4)
Codfish (*Gadus macrocephalus* or others) (대구)	22 (2.6)
Yellowtail (*Seriola quinqueradiata*) (방어)	14 (1.6)
Rockfish (*Sebastes* spp.) (우럭)	12 (1.4)
Anchovy (*Engraulis japonicus* or others) (멸치)	8 (0.9)
Seabream (*Acanthopagrus schlegeli* and others) (도미)	6 (0.7)
Skate (*Raja porosa* and others) (홍어, 간재미)	4 (0.5)
Shad (*Konosirus punctatus*) (전어)	3 (0.4)
Others (miscellaneous fish) (기타 생선류 또는 낙지)	19 (2.2)
No. of cases without mentioning the source	269 (31.6)
Total	851 (100.0)

*Cases stating that they consumed more than 2 kinds of fish or cephalopods were included in this group.

Site of infection

Among the 851 cases analyzed in this review, the most frequently involved organs were the stomach (698 cases; 82.0%) followed by the small and large intestines (88 and 40 cases, respectively, 128 cases in total; 15.0%), esophagus (8 cases; 0.9%), tonsils (2 cases; 0.2%), oral cavity/oral mucosa (2 cases; 0.2%), mesocolic lymph nodes (1 case; 0.1%), greater omentum (1 case; 0.1%), peritoneum (1 case; 0.1%), and unknown location (15 cases; 1.8%) (Fig. 3). The involvement of multiple organs, more than 2 of the stomach, ileum, and colon, has been reported in 5 cases [73,80,89,98,103].

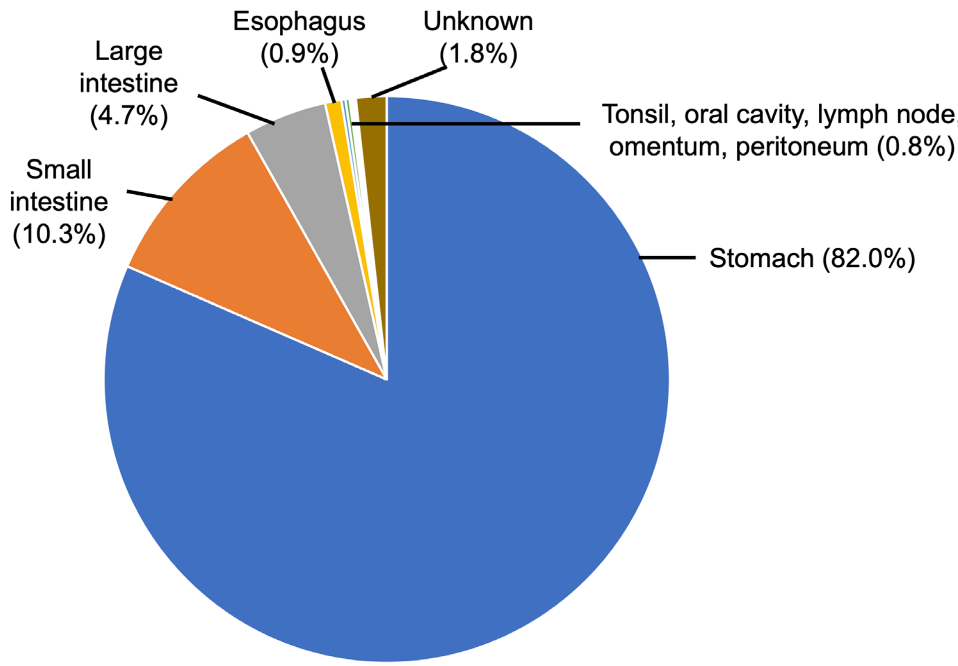

Fig. 3. Involved organs in 851 anisakidosis cases reported in Korea (1971-2022).

Species of anisakid larvae in human patients

Regarding the types (or species) of anisakid larvae detected, most of the reports simply described that the worms were anisakid larvae or *Anisakis* sp. larvae (514; 60.4%). The larvae were designated as *Anisakis* type I (*A. pegreffii* or *A. simplex* larvae) in 80 cases (9.4%), *A. simplex* larvae in 88 cases (10.3%), and *Anisakis* type II (probably *A. physeteris*) in 8 cases (0.9%). Thus, the overall number of cases reported as *Anisakis* spp. (including type I, type II, *A. pegreffii*, and *A. simplex*) was 724 (85.2%). However, molecular analyses of larvae extracted from human infections using the internal transcribed spacer (ITS) region sequences were first reported by Lim et al. [107], and 25 of 26 larvae extracted from 15 cases were confirmed to be *A. pegreffii*, and only 1 larva (1 case) was *A. simplex* s.s. Subsequently, Song et al. [113] identified 20 additional human cases of *A. pegreffii* infection through molecular analyses. Thereby, a total of 35 (4.1%) patients were confirmed to be infected with *A. pegreffii*. Based on these molecular findings, it is highly likely that the species of anisakid larvae responsible for human infections in Korea is predominantly *A. pegreffii*. Regarding *P. decipiens* s.s. (or *Terranova* type A larvae) infections, 44 cases (5.2%) were reported through morphological and/or molecular analyses. Three cases (0.4%) were caused by *Contracaecum* spp. or *Contracaecum* type A larvae [34,46]. The larvae were not identified in 79 patients (9.3%).

Different types of larvae appear to have distinct clinical features, such as affected organs or sites of infection. Of the 725 patients infected with *Anisakis* sp. larvae (including *Anisakis* sp., *Anisakis* type I, *Anisakis* type II, *A. pegreffii*, or *A. simplex* s.s.), 591 (81.5%) had infections in the stomach, 88 (12.1%) in the small intestine (duodenum, jejunum, ileum, or cecum), and 38 (5.2%) in the large intestine (ascending, transverse, descending colon or rectum). However, out of 44 cases infected with *P. decipiens* s.s. (or *Terranova* type A) larvae, 42 (95.5%) developed gastric infections, and the remaining 2 (4.5%) had 1 ileal and 1 colonic infection. These results agree with the higher potential of *P. decipiens* larvae to cause gastric infections than *Anisakis* spp. larvae. [1].

In Korea, most previous anisakidosis cases in which the extracted larvae were assigned to *Anisakis* sp. or *Anisakis* type I larvae might have been *A. pegreffii* infections; and only a small proportion might have been *A. simplex* s.s. infections. This trend is different from that in Japan, where 168 (88.9%) of 189 larvae obtained from human patients were molecularly confirmed to be *A. simplex* s.s., and only a few were *A. pegreffii* (10 larvae; 5.3%) and *P. azarasi* (11 larvae; 5.8%) [4]. However, the relative proportion of causative larval species differed according to the localities in Japan; for example, on Kyushu Island (adjacent to South Korea), 33.3% of the patients were infected with *A. pegreffii* larvae (other 66.7% were infected with *A. simplex* s.s. larvae), whereas in Hokkaido Island, Honshu, and Shikoku Islands (distant from South Korea), only 4.1%-6.7% of the patients were infected with *A. pegreffii* larvae [4]. This difference was presumed to be due to differences in larval anisakid distribution in fish caught from the Pacific Ocean, East Sea (Sea of Japan), and Yellow Sea (East China Sea) [4,107,122]. *A. simplex* s.s. larvae were more commonly detected in fish caught from Hokkaido and eastern Japan than *A. pegreffii* larvae, whereas in fish from Kyushu and Fukuoka (close to South Korea), *A. pegreffii* larvae were more frequently detected than *A. simplex* s.s. larvae [122].

Number of larvae recovered in each case

The number of anisakid larvae detected in each patient was 1 in most cases, but rarely 2-4 larvae were detected [34,56,90,99]. However, more worms were detected on rare occasions. For example, 9 specimens were detected in 2 gastric patients from Jinju [107], and 15 worms in 1 gastric patient from Seoul [107]. Of special note were 2 patients with oral cavity infections, in which over 8 and 20 larvae, respectively, were extracted using forceps; both patients had eaten raw squids [79,108]. Moreover, in an extreme case, 51 larvae were collected from the stomach of a single patient, and 3 months after the removal of these larvae by endoscopy, submucosal tumors were again found in the stomach and transverse colon which were suggested to be due to anisakid larval infections that were not removed at the time of surgery [98].

Clinical features in Korean patients

The chief complaint or major clinical feature of anisakidosis patients (n = 851) in Korea was acute abdomen (including acute epigastric pain) or acute abdominal syndrome, which was observed in 59.9% of all patients (Table 6). The next frequent clinical symptom was nausea and vomiting which was recorded in 11.6% of patients, followed by chronic gastritis or gastric pain (3.6%), intestinal obstruction, ileus, or adhesion (2.6%), diarrhea (1.9%), urticaria and/or edema (1.2%), hematemesis and/or melena (1.1%), esophageal symptoms (0.9%), and intestinal inflammation, including appendicitis (0.6%) (Table 6). Extraintestinal anisakidosis was very rare, having been reported in 7 cases, involving the oral mucosa (2 cases), tonsils (2 cases), greater omentum (1 case), mesocolic lymph nodes (1 case), and peritoneum (1 case). Notably, a considerable proportion of cases (5.3%) were asymptomatic or found incidentally during health check-ups, including endoscopy, in people who had mild gastrointestinal discomfort (Table 6). Cases with over 2 chief complaints comprised 2.4%, and symptoms and signs were not described in 7.9% of the patients.

The clinical features of Korean gastric anisakidosis cases have been reviewed several times [11,34,46,56,90]. Im et al. [34] reported that the most common clinical complaint of gastric anisakidosis among the 39 cases analyzed was sudden onset or intermittent epigastric pain (31; 79.5%), followed by nausea and vomiting (8; 20.5%). Song et al. [56] analyzed the clinical symptoms of 39 gastric anisakidosis patients and found that the most frequent symptoms were epigastric pain (34 cases; 87.2%) and epigastric discomfort (31; 79.5%), followed by nausea and vomiting (18; 46.2%), diarrhea (1; 2.6%), headache (1; 2.6%), and chest pain (1; 2.6%). Lee et al. [90] reported that the most common symptoms in 141 anisakidosis patients were acute epigastric pain (121 cases; 85.8%), followed by nausea and vomiting (40; 28.4%), mild epigastric discomfort (7; 5.0%), and hematemesis/melena (2; 1.4%). Sohn et al. [11] analyzed 15 gastric anisakidosis cases and reported that epigastric pain (14 cases; 93.3%) was the most common followed by nausea and vomiting (5; 33.3%), hematemesis (1; 6.7%), and hemoptysis (1; 6.7%).

Among intestinal anisakidosis cases (n = 128), the most common symptom was acute abdominal pain (including acute epigastric pain) (60 cases; 46.9%), followed by intestinal obstruction, adhesion, or intussusception (23; 18.0%), nausea and vomiting (19; 14.8%), diarrhea (14; 10.9%), asymptomatic or incidental finding (12; 9.4%), intestinal inflammation (5; 3.9%), and others (3; 2.3%). Esophageal anisakidosis was 8 cases [60,65,80,85,114], and the most common clinical complaint was acute epigastric pain (7 cases; 87.5%), followed by nausea and vomiting (2; 25.0%), chest pain (1; 12.5%), and epigastric fullness (1; 12.5%). In 2 oral mucosa cases [79,108], oral or substernal pain was the chief complaint, and in 2 tonsil cases, sore throat, foreign body sensation, and/or dull pain around the pharynx were the major clinical complaints.

Table 6. Clinical symptoms and signs of anisakidosis patients in Korea (1971-2022)

Chief complaints/major signs	No. of patients (%)
Acute abdomen, epigastric pain	510 (59.9)
Nausea and/or vomiting	99 (11.6)
Chronic gastritis, chronic gastric pain	31 (3.6)
Intestinal obstruction, ileus, intussusception, adhesion	22 (2.6)
Diarrhea	16 (1.9)
Urticaria, edema	12 (1.4)
Hematemesis, melena	9 (1.1)
Esophageal involvement	8 (0.9)
Submucosal tumor	5 (0.6)
Duodenitis, jejunitis, ileitis, appendicitis	5 (0.6)
Oropharyngeal/tonsil involvement	4 (0.5)
Asymptomatic/health check-up/incidentally	45 (5.3)
Multiple symptoms or miscellaneous types of symptoms*	20 (2.4)
Unknown	67 (7.9)
Total	851 (100.0)

*More than 2 kinds of symptoms or miscellaneous symptoms, including chest pain, fever, and others.

Anisakis allergy

Anisakiasis is often associated with a strong allergic response involving an elevated immunoglobulin (Ig), particularly IgE, in response to *A. simplex* or *A. pegreffii*, with clinical symptoms ranging from isolated swelling to generalized urticaria and life-threatening anaphylactic reactions several hours (or 24-36 hours) after ingestion of raw or undercooked fish [1,127-129]. Skin symptoms (especially urticaria) were the most frequent (almost 100% of patients with allergies), followed by digestive symptoms (74%) [129]. *Anisakis*-associated hypersensitivity reactions have been reported particularly in northern Spain [128] but are also known in France, Italy, Portugal, and Japan [128,130]. Genetic predisposition (HLA class II alleles) has been observed in patients with *Anisakis* allergies [128]. *A. simplex* is the dominant species implicated in human allergic responses in Spain and other countries; however, *A. pegreffii* has also been identified as a causative agent in Italy [131,132]. The allergenic potential of *P. decipiens* has been suggested by several researchers and several *P. decipiens* allergens have been shown to have proteins homologous to *A. simplex*; however, further studies are required [133].

In Korea, at least 4 articles have reported allergic reactions due to anisakidosis [83,92,99,134]. The first allergic case was a 33-year-old woman residing in Jeju who complained of repeated episodes of urticaria with severe itching, stomachache, nausea, and vomiting a few hours after eating raw fish. The skin prick test and specific IgE test were positive for *Anisakis* somatic and excretory-secretory antigens [83]. Subsequently, 10 allergic patients complaining of urticaria (100%), abdominal pain (30%), and anaphylactic reactions (30%) were reported. High serum IgE levels were detected against *A. simplex* antigens in these patients [92]. On Jeju Island, a 47-year-old male patient complained of generalized urticaria, angioedema, abdominal pain, and dyspnea, and his serum revealed a strongly positive level of *Anisakis*-specific IgE [99]. Another study on Jeju Island included 15 additional gastroallergic patients positive for *Anisakis*-specific IgE with clinical complaints of urticaria, abdominal pain, angioedema, nausea, and vomiting [134]. We believe that most of these allergic cases involved infections with *A. pegreffii*, although the specific diagnosis of the involved larvae was not confirmed in these cases.

Immunological studies on *Anisakis* allergy

Recurrent anaphylaxis due to *A. simplex* larva infection was first reported by Audicana et al. [135] in Spain. Now it has been well established that acute allergic symptoms, such as urticaria, angioedema, or anaphylaxis, accompanied by epigastric pain, nausea, and vomiting, called gastroallergic anisakiasis, are elicited by live (not dead or heat-inactivated) third-stage larvae of *A. simplex* and *A. pegreffii* [136]. This hypersensitivity reaction is often accompanied by an acute IgE-mediated generalized reaction with cutaneous (urticaria to angioedema) and/or respiratory (asthma and rhinitis) symptoms [136]. IgE bound to mast cells or basophils recognizes specific allergens, and degranulation of these cells leads to local and/or systemic allergic reactions [136]. IgE-producing parasite-derived antigens have been isolated and characterized, including Ani s 1 through Ani s 14, which are somatic antigens, excretory-secretory products (ESP), or of unknown origin [137]. Major allergens, as defined by the recognition of > 50% of sensitized individuals, were 5 kinds, including Ani s 1 (ESP; similar to thermostable serine protease inhibitors), Ani s 2 (somatic antigen; paramyosin), Ani s 7 (ESP; function unknown), Ani s 12 (origin and function unknown), and Ani s 13 (ESP; hemoglobin) [136,137]. Ani s 1 and Ani s 7 have high allergenic potential and no cross-reactivity with other allergens, whereas Ani s 2 is a pan-allergen with cross-reactivity with other foods or inhalant allergens [137].

In Korea, Cho and coworkers [138-142] performed immunological and serological studies on anisakiasis in experimental animals and humans. Kim et al. [138] found that the ESP of *A. simplex* third-stage larvae (L3) contained important allergens (12 low-molecular-weight bands ranging from 10 to 186 kDa by immunoblotting) necessary to induce *Anisakis* allergy in rats. In human anisakiasis, the binding patterns of L3-specific antibodies varied depending on the different L3-ESP preparations, and low-molecular-weight proteins appeared to be strong and specific antigens [139]. Choi et al. [140] reported high serum titers of IgG4 and IgE antibodies in 4 of 9 *Anisakis* allergy patients in Korea. Cho et al. [141] demonstrated that allergic responses induced by L3 oral infection were predominantly caused by reinfection rather than primary infection, accompanied by elevated IgE and IgM levels. The role of specific IgG, especially IgG4, has also been suggested in immune responses to intraperitoneally injected L3, as IgG4 binds to epitopes recognized by specific IgE [143]. In human anisakidosis, the importance of specific IgA has been suggested; however, its role has not been demonstrated in experimental mice and rats [139,142].

Choi et al. [143] reported that *A. pegreffii* larval extract induced airway inflammation and asthma 4 weeks after the challenge, enhancing the expression of Th2-type immune responses (IL-4, IL-5, and IL-13) in the lungs of mice. Conversely, Park et al. [144] cloned a macrophage migration inhibitory factor (MIF)-like protein from L3 of *A. simplex*. This MIF-like protein was shown to reduce Th2-related cytokines in the bronchoalveolar lavage fluid and allergen-specific IgG2a in the sera of mice, which is probably associated with host immune modulation. Treg cells were recruited to the spleen and lungs of these MIF-treated mice [144]. Park et al. [145] identified a 24 kDa protein from the ESP of *A. simplex* larvae as a possible allergen, homologous to the 22U protein of filarial nematodes and distinct from the Ani s 1 antigen, although having the same molecular weight. Park et al. [146] performed repeated intranasal applications of recombinant 22U of *A. simplex* 6 times and found that this antigen induces airway allergic inflammation accompanied by enhanced lung Th2 and Th17 responses. Kim et al. [147] isolated and characterized an α-methylacetyl CoA racemase originating from the ventriculus of *A. simplex* larvae, which may have a function in the growth and development of the larvae. Jeon et al. [148] compared the hydrolase activities (esterases, peptidases, proteases, and glycosidases) of ESP and the somatic proteins of *A. simplex* and *A. pegreffii* larvae collected from salmon in Yangyang (Namdae Stream) and mackerels in the southern sea of Korea, respectively. Cho et al. [149] studied the allergenicity of Ani s 1 (major antigen) and Ani s 9 (minor antigen) by repeated intranasal inoculation into mice and observed airway inflammation in mice with significantly elevated lung Th2 and Th17 cytokine responses. An interesting study by Cha and Ock [150] demonstrated that antigenic proteins from *A. simplex* larvae could change cytokine profiles and prevent drug-induced Crohn's disease in experimental mice.

Relationships between anisakidosis and gastrointestinal cancers

A relationship between chronic anisakid nematode infection and stomach or colon cancers has been suggested [151-154]. Some clinical cases have shown the co-localization of anisakidosis and cancer in the gastrointestinal tract [155,156]. Garcia-Perez et al. [151] provided data showing an epidemiological link between previous *Anisakis* infections and gastrointestinal cancer. In addition, products from *Anisakis* were shown to cause inflammation and DNA damage in the host [152], and the complete extract of *Anisakis* worms could induce changes in epithelial cells in vitro and *in vivo* (rats) [153]. However, in Korea, only 1 case of the co-existence of ascending colon anisakiasis and sigmoid colon cancer has been reported [86]. It is noteworthy that whereas carcinogenic stimuli should continue for a long time to undergo a neoplastic transformation of the mucosal tissues of the stomach or colon, most anisakidosis cases are detected in the acute stage, and the disease does not continue for a long time. Notably, in experimental anisakiasis in rabbits, the pathological lesions almost completely resolved in the submucosa of the stomach within 5 months after infection, and the worms were calcified, became tiny, and encircled by fibrous tissues infiltrated by inflammatory cells [157]. However, attention should be paid to patients who are repeatedly infected with anisakid nematodes because in such cases mucosal changes in the stomach and/or colon may persist for a considerably long time.

Experimental anisakiasis in laboratory animals

Studies of experimental anisakiasis in laboratory animals (regarding susceptibility, habitat, and pathology/histopathology) have been reported in at least 3 articles in Korea. Kwon and Chyu [158] observed the distribution of anisakid larvae in 2 experimental rabbits after oral inoculation with 30 L3 from day 2 to 14 post-infection (PI). On days 2-3 PI, a total of 42 larvae (live) were recovered in the stomach (33 larvae), omentum (8), and mesentery (1), and on days 7-14 PI, only 7 larvae (dead) were detected in the abscess cavity (6) and fundus submucosa (1) of the stomach wall [158]. Choi and Kim [159] infected rats and rabbits with *Anisakis* L3 and chronologically observed the distribution of the larvae within 1 day (rats) and during days 1-14 PI (rabbits); in rats, 1 larva penetrated the stomach wall within 1 hour PI, and a total of 4 larvae were found in the stomach wall by 8 hours PI, while some larvae were found in the omentum, intestinal wall, abdominal cavity, and liver within 24 hours PI. In rabbits, 22 larvae penetrated the stomach wall within 1 day, and some larvae were found in the omentum, intestinal wall, abdominal cavity, and mesentery during days 3-14 PI [159]. Hong and Lee [157] observed larval locations and gross and histopathologic findings in the stomach, small intestine, colon, and mesentery from day 13 to day 150 PI; on day 13 PI, larvae were found in the stomach (15 of 60 larvae inoculated), omentum (1), intestine (2), mesentery (5), and abdominal wall (2), and on day 90 PI, larvae were found in the stomach (12 of 60 larvae inoculated), omentum (3), intestine (2), mesentery (1), and abdominal wall (1). Only 1 larva was detected on day 150 PI in the stomach wall of a rabbit [157]. The involved tissues showed severe histopathological changes, including granuloma formation, inflammatory cell infiltrations, fibrosis, and calcification until day 90 PI, and only a few sections of tiny, calcified larvae were detected in the submucosal layer of the stomach on day 150 PI [157]. Jeon and Kim [160] performed *in vitro* (agar block plates) and *in vivo* (rats) experiments on the pathogenic potential of 2 sibling species, *A. simplex* and *A. pegreffii*, and found that *A. pegreffii* had higher penetration ability (*in vitro*) and longer survival time in rats (*in vivo*) than *A. simplex*.

Anisakid larva or adult infection in pigs, cats, and birds in Korea

Anisakis type I larva infection was found in the stomachs of 9 (2.8%) of 318 pigs in Andong, Gyeongsangbuk-do [161], and 11 (0.7%) of 1,531 pigs in Jeollanam-do [162]. One or 2 larvae [161] or 1-9 larvae [162] were observed in each case. Serological tests for swine anisakiasis were performed using indirect hemagglutination and gel diffusion tests [163]. Two studies were performed on the infection of cats with *Anisakis* sp. larvae; 1 (11.1%) of 9 autopsied cats in Seoul was found to be infected with a total of 14 *A. simplex* larvae penetrating the stomach [164], and 1 (0.2%) of 438 cats in Busan had *A. simplex* L3 infection [165]. It is worth mentioning that adult nematodes of *Contracaecum rudolphii* complex were recovered in the proventriculus of a white pelican (*Palecanus onccrotalus*) that was imported from Tanzania to Korea [166].

Anisakid larva or adult infection in a porpoise and a whale in Korea

A finless porpoise was stranded on the coast of Jeju Island with adhesive bowel disease (ABD), which is life-threatening, and nematode parasites, including *Anisakis* sp. larvae and *Crassicauda* sp., were found at autopsy. The primary cause of ABD is presumed to be a reaction related to these parasitic infections [167]. The first detection of *A. simplex* s.s. adult nematodes (n = 2) containing eggs was reported by Kim et al. [168] in the gastrointestinal tract of a common minke whale (*Balaenoptera acutorostrata* Lacépède, 1804) that died in the sea between Namhae and Bangeojin, Korea. The diagnosis was molecularly confirmed using the gene sequences of the mitochondrial cytochrome *c* oxidase 2 (*cox*2) [168].

Survey of anisakid larvae in marine fish and cephalopods in Korea

The first detection of anisakid larvae in marine fish in Korea was reported by Chun et al. [169] in 1968 (Table 7). A total of 313 fish specimens (17 species) caught from the western (Yellow Sea) and southern seas were examined, and 312 (99.7%) were found to be infected with anisakid larvae (1-334 larvae per fish) [169]. The next study was reported by Lim [170]; a total of 1,940 fish specimens (15 species) were purchased from 5 localities (caught from western and southern seas) in Korea, and the average number of anisakid larvae per fish ranged from 0.2 (damselfish; *Chromis notata*) to 156.0 (yellow corvina; *P. manchurica*). The third study was a morphological analysis of anisakid larvae collected from the yellow corvina caught in the western sea; a total of 1,026 identifiable anisakid larvae were collected from 30 fish, and *Anisakis* type I was the most common (859 larvae; 80.4%) followed by *Contracaecum* type D′ (77; 7.2%), *Contracaecum* type C′ (55; 5.1%), *Contracaecum* type D (18; 1.7%), *Contracaecum* type A (13; 1.2%), *Contracaecum* type V (3; 0.28%), and *Raphidascaris* sp. (1; 0.09%) [123].

Thereafter, at least 19 studies reported anisakid larval infections in fish and cephalopods in the vicinity of Korean seawater [171-189]. Eight studies that examined more than 7 species of fish or cephalopods are presented in Table 7 [125,169,170,171,177,178,182,183]. Among the 99 species of fish/cephalopods examined, 82 were infected with anisakid larvae (mostly *Anisakis* spp.) (Table 7). The major (positive in over 3 studies) infected fish/cephalopods were 15 species, including sea eel (*C. myriaster*), chub mackerel (*Scomber japonicus*), hairtail (*Trichiurus lepturus*), anchovy (*Engraulis japonicus*), silver pomfret (*Pampus argenteus*), yellow corvina (*P. manchurica*), yellowtail (*Seriola quinqueradiata*), jack mackerel (*Trachurus japonicus*), white croaker (*Argyrosomus argentatus*), herring (*Clupea palassii*), red seabream (*Pagrus major*), Japanese flounder (*P. olivaceus*), flathead (*Platycephalus indicus*), rockfish (*Sebastes inermis*), and Japanese common squid (*T. pacificus*) (Table 7). The reason why chub mackerels are not ranked among the 12 most common fish consumed by human patients in Korea (Table 5) seems to be that mackerels are less frequently consumed raw by the Korean people.

In addition, chum salmon (*Oncorhynchus keta*) purchased from the eastern coastal areas (Taep'o Port in Sokcho City and Namdae Stream in Yangyang, Gangwon-do) were examined in 3 studies; the infection rate was 100%, with the mean number of larvae per fish ranging from 28.9 to 108.0 [172,179,181]. Masu salmon (*Oncorhynchus masou masou*) purchased from the eastern part (Joomunjin) of Gangwon-do were also examined, and the recovered larvae were molecularly identified as *A. simplex* s.s. L3 by polymerase chain reaction-based restriction fragment length polymorphism (PCR-RFLP) analysis [180]. Sea eels (*C. myriaster*) were studied 5 more times in Korea; Chai et al. [124] examined 26 sea eels purchased from the Noryangjin Fish Market in Seoul, and among them, 15 (57.5%) were positive for anisakid larvae (90.1 larvae/fish), including *Anisakis* type I (564/1,351 larvae; 41.7%) followed by *Contracaecum* spp. (787/1,351; 58.3%). Song and Hwang [126] examined 382 sea eels purchased from Busan, of which 259 (67.8%) were infected with 1,768 anisakid larvae (*Anisakis* spp. and *Contracaecum* spp.). Cho et al. [183] examined 20 sea eels caught in Tongyeong City, Gyeongsangnam-do, and recovered 129 *Anisakis* type I larvae; these larvae were molecularly analyzed using PCR-RFLP and sequencing of the ITS region and *cox*2 genes, and 112 (86.8%) were confirmed to be *A. pegreffii*, 10 (7.8%) were *Anisakis typica*, and 7 (5.4%) were unidentified [183]. Lee et al. [186] examined sea eels (*C. myriaster*), chub mackerels (*S. japonicus*), and hairtails (*T. lepturus*) from the seawater of Korea and performed molecular analyses (PCR-RFLP) on the larvae; 136 (97.1%) of 140 larvae were *A. pegreffii*, and the remaining 4 (2.9%) were *A. typica*. Neves [188] also examined sea eels (*C. myriaster*), chub mackerels (*S. japonicus*), and yellow croakers (*Larimichthys polyactis*) caught from the western, southern, and eastern coasts of Korea to detect anisakid larvae. Bak et al. [184] caught chub mackerels from the western, southern, and eastern coasts of Korea and examined them for anisakid larvae; 231 (55.4%) of the 417 mackerels were positive, with a total number of larvae of 1,628 (7.0 larvae/fish). Molecular studies (PCR-RFLP of ITS and sequencing of *cox*2) of these larvae revealed that most of them were *A. pegreffii* (94.3%), and small proportions were *A. simplex* s.s. (0.4%), a hybrid of *A. pegreffii* and *A. simplex* (2.5%), or *Hysterothylacium* sp. (2.8%) [184].

Jeong and Song [176] examined yellow corvina (*P. manchurica*) (n = 551) purchased from seawater around Jeju Island and recovered 4,386 larvae (8.5 larvae/fish) comprising 3,428 *Anisakis* type I larvae and 958 *Contracaecum* spp. larvae. Anchovies were examined in 2 more studies [174,189] in addition to the 4 studies in Table 7 [170,171,177,182]; Song et al. [174] purchased a total of 2,180 anchovies (*E. japonica*) from the eastern and southern seas and 171 (7.8%) were found to be infected with anisakid larvae (*Anisakis* type I or II, *Anisakis* sp., and *Contracaecum* type B or type C). Chang et al. [189] purchased anchovies from the southern sea and found anisakid larvae in 39 (19.5%) of 200 specimens (51 larvae in total; 1.3/fish); molecular analyses using ITS gene sequences revealed that 28 larvae were *A. pegreffii*, 12 were *Hysterothylacium sinense*, and 11 were *H. aduncum*. The large-head hairtail (*T. japonicus*) (n = 9) purchased from Jeju Island was examined for anisakid larvae (1,259; 139.9/fish) using PCR-RFLP of ITS and *cox*2 sequencing; *A. pegreffii* larvae (1,243/1,259; 98.7%) were most commonly detected, followed by a hybrid of *A. pegreffii* and *A. simplex* s.s. (6/1,259; 0.5%), *Hysterothylacium* sp. larvae (2/1,259; 0.2%), and unknown species (8/1,259; 0.5%) [187]. Regarding a squid species (*T. pacificus*), 1 more study was available [175] in addition to 3 studies shown in Table 7 [125,177,182]; 272 squids purchased from Busan (southern sea) were examined, and *Anisakis* type I, type II, *Contracaecum* types A and D larvae were recovered.

There may be questions about the possibility of anisakid larval infection in cultured marine fish. As fish farms are usually located near coastal areas, remote from the sea where whales and other sea mammals thrive, and within the farm there seems to be no infected first intermediate host (shrimp-like crustaceans) with anisakid larvae, cultured fish can be regarded to be safe from anisakid larval infection.

Table 7. Species of marine fish examined for anisakid larvae* in Korea (1968-2012)†

Species of fish/cephalopods Locality surveyed	Korean common name	Chun et al. (1968) [169] West/ South Sea	Lim (1975) [170] West/South sea	Kim et al. (1988) [171] Fish market in Seoul	Woo and Kim (2000) [125] Jeju Island	Song et al. (2001) [177] South Sea	Choi et al. (2009) [178] East/South/West Seas	Choi et al. (2011) [182] Fish market in Busan	Cho et al. (2012) [183] East/South/West Sea
Acanthopagrus schlegeli	감성돔						○		●
Apogon lineatus	열동가리돔						○		
Arctoscopus japonicus	도루묵							●	
Argyrosomus argentatus	보구치	●	●			●			
Bodianus oxycephalus	사랑놀래기						●		
Branchiostegus japonicus	옥돔				●				
Chelidonichthys sp.	성대	●					●		
Chromis notata	자리돔		●		●			○	
Clupea palassii	청어						●	●	●
Clyptocephalus stellari	기름가자미	●							
Cololobis saira	꽁치		●	○					
Conger myriaster	붕장어	●		●	●	●	●	●	●
Cynoglossus semilaevis	박대							○	
Ditrema temminckii	망상어						●		
Doederleinia beycoides	눈볼대							●	
Doryteuthis kensaki	한치			○					
Enchelyopus gilli	동가시치	●							
Engraulis japonicus	멸치		●	●		●		●	
Epinephephelus akaara	붉바리		●						
Eptatretus burgeri	먹장어							●	
Erispex potti	풀미역치	●							
Evynnis japonica	붉돔								●
Gadus macrocephalus	대구	●						●	
Hemiamphus sajori	자치어							●	
Hemitripterus villosus	삼세기						●		
Hertklotsichthys zunasi	밴댕이						○		
Hexagrammos grammus	노래미						●		
Hexagrammos otakii	쥐노래미								●
Hippoglossoides pinetorum	용가자미								●
Ilisha elongata	준치							●	
Johnius grypotus	민태						●		
Konosirus punctatus	전어						●	○	○
Larimichthys crocea	참조기							●	
Lateolabrax japonicus	농어						○		●
Lateolabrax maculatus	점농어						○		

Table 7. Species of marine fish examined for anisakid larvae* in Korea (1968-2012)†(continued)

Species of fish/cephalopods Locality surveyed	Korean common name	Chun et al. (1968) [169] West/ South Sea	Lim (1975) [170] West/South sea	Kim et al. (1988) [171] Fish market in Seoul	Woo and Kim (2000) [125] Jeju Island	Song et al. (2001) [177] South Sea	Choi et al. (2009) [178] East/South/West Seas	Choi et al. (2011) [182] Fish market in Busan	Cho et al. (2012) [183] East/South/West Sea
Lepidotrigla microptera	달강어	●							
Limanda herzensteini	참가자미	●					○		
Liparis tanakai	꼼치	●						●	
Liparis tesselatus	물메기							●	
Loligo bleekeri	화살꼴뚜기							○	
Loligo chinensis	한치꼴뚜기				●				
Loligo edulis	창꼴뚜기			○					
Lophiomus setigerus	아귀						●	●	
Miichthys miiuy	민어							●	
Mugil cephalus	숭어						○	●	●
Muraenesox cinereus	갯장어						○		
Neoditrema ransonneti	인상어								
Nibea albiflora	수조기	●							
Niphon spinosis	다금바리		●						
Octopus minor variabilis	낙지			○					
Oncorhynchus masou masou	산천어								●
Oplegnathus fasciatus	돌돔						○	○	
Pagrus major	참돔		●				●	●	
Pampus argenteus	병어		●			●	●	●	
Pampus echinogaster	덕대						○		
Paralichthy olivaceus	넙치(광어)						●	●	●
Parapristipama trilineatum	벤자리		●						
Platycephalus indicus	양태						●	●	●
Platyrhina sinensis	목탁가오리							●	
Pleurogrammus azonus	임연수어							●	●
Pleuronectes yohohamae	문치가자미						●		
Pleuronichthys cornutus	도다리	●				●	○		○
Priachanthus macrachanthus	홍치						○		
Psenopsis anomala	샛돔						○		
Pseudolabrus japonicus	황놀래기								
Pseudosciaena crocea	부세							○	
Pseudosciaena manchurica	조기	●	●	●				●	
Raja porosa	간재미						●		
Saurida undosquamis	메퉁이						●		
Scomber japonicus	고등어	●	●	●	●	●	●	●	

Table 7. Species of marine fish examined for anisakid larvae* in Korea (1968-2012)† (continued)

Species of fish/cephalopods Locality surveyed	Korean common name	Chun et al. (1968) [169] West/ South Sea	Lim (1975) [170] West/South sea	Kim et al. (1988) [171] Fish market in Seoul	Woo and Kim (2000) [125] Jeju Island	Song et al. (2001) [177] South Sea	Choi et al. (2009) [178] East/South/West Seas	Choi et al. (2011) [182] Fish market in Busan	Cho et al. (2012) [183] East/South/West Sea
Scomberomorus niphonius	삼치			○			○	●	
Scombrops boops	게르치							●	
Scorpaenodes littoralis	쏨뱅이								●
Sebastes hubbsi	우럭볼락		●						
Sebastes inermis	볼락						●	●	●
Sebastes longispinis	흰꼬리볼락						●		
Sebastes pachycephalus	우럭						●	●	
Sebastes schlegeli	조피볼락								●
Sebastes thompsoni	불볼락								●
Sebastiscus marmoratus	쏨뱅이								
Semicossyphus reticulatus	혹돔							●	
Sepia esculenta	참갑오징어			●				●	
Seriola quinqueradiata	방어			●			●	●	●
Silago sihama	보리멸						●		
Sparus swinhonis	감정돔		●						
Sphyraena pinguis	꼬치고기						●		
Stephanolepis cirrhifer	쥐치						●	●	
Stromateoides argenteus	병어			●					
Takifugu chinensis	복어					●		●	
Takifugu niphobles	복섬						○		
Takifugu pardalis	졸복						○		
Tanakius kitaharai	갈가자미							●	
Thamnaconus modestus	말쥐치								○
Theragra chalcogramma	명태					●		●	
Todarodes pacificus	살오징어				●	●		●	
Trachurus japonicus	전갱이	●	●				●	●	
Trichiurus lepturus	갈치	●	●	●	●	●	●	●	
Xystrias gregorjewi	물가자미	●							
Zoarces gilli	등가시치						●		

● positive for anisakid larvae; ○ negative for anisakid larvae.
*Anisakid larvae recovered were mostly *Anisakis* type I (*A. pegreffii* or *A. simplex*) followed by *Contracaecum* type A, B, C, C′, D, D′ (probably *Contracaecum osculatum* for all these types), *Contracaecum* type V or others, *Terranova* type A (*P. decipiens*) or type B (*P. decipiens*), *Raphidascaris* sp., and very rarely *Anisakis* type II (*A. physeteris*).
†Only studies which examined more than 7 species of fish were included in this table.

Morphological studies of anisakid larvae in Korea

Various morphological types of anisakid larvae have been reported since the reports by Yamaguti [190], Berland [191], and Koyama et al. [192]. *Anisakis* type I (*A. pegreffii*, *A. simplex*, and *A. typica*) and type II larvae (*A. physeteris*) were named by Berland [191]; *Contracaecum* types I through V by Yamaguti [190]; and *Terranova* types A (*P. decipiens*), B (*P. decipiens*), *Contracaecum* types A through D (*C. osculatum*), and *Raphidascaris* sp. by Koyama et al. [192]. In Korea, Chai et al. [123,124] found variants of *Contracaecum* types A, C, and D larvae in sea eel and yellow corvina, which were named *Contracaecum* types A′, C′, and D′, respectively.

Studies on anisakid larvae in fish from Korea started in 1966 but were officially reported in 1968 by Chun et al. [169]. *Anisakis* type I larvae (as *Anisakis* sp.) were detected in marine fish from the western and southern seas. Since then, several articles have been published regarding the morphology of anisakid larvae found in Korea. Rim [193] described the morphology of *Anisakis* type I larvae obtained from marine fish and swine in Gwangju, South Korea. Kim et al. [171,172] detected *Anisakis* type I; *Terranova* type B; *Contracaecum* types A, B, and D; and *Raphidascaris* sp. larvae in marine fish purchased from fish markets in Seoul and Sokcho (Gangwon-do). Woo and Kim [125] detected *Anisakis* types I and II, *Terranova* types A and B, *Contracaecum* types A, B, C, and D, and *Raphidascaris* sp. larvae in marine fish purchased from Jeju Island. Sohn and Lee [194] and Sohn [195] observed the sectional morphologies of *Anisakis* type I, *Contracaecum* type A, and type D’ larvae by light and transmission electron microscopies. Chai et al. [196] studied the morphologies (light microscopic, sectional, and scanning electron microscopic) of *P. decipiens* larvae detected from the codfish (*Notothenia neglecta*) caught in the Antarctic Ocean near the South Pole.

Serological studies on human and animal anisakidosis

Hong and Lee [157] studied the changing patterns of IgG in experimental rabbit anisakiasis for 150 days PI. IgG levels started to increase from day 3 PI, peaked on day 30 PI, maintained a plateau during days 30-90 PI, and then decreased to almost control levels on day 150 PI [157]. The serological diagnosis of human anisakidosis patients in Korea was first reported by Lee et al. [197], who used ELISA on 12 parasite-confirmed anisakidosis cases and observed significantly elevated optical density values in 11 of the 12 patients (0.229-1.547 in 12 patients vs 0.103-0.353 in 5 controls). They also performed immunoblotting on sera from humans and experimental rabbits and found that the 46 kDa L3 antigen was highly sensitive and specific for *Anisakis* infection [197]. Quan et al. [198] compared different types of antigens used in ELISA for anisakiasis in rabbits and found that ESP was the most suitable antigen. Yang et al. [199] performed ELISA and immunoblotting to observe the changing patterns of serum IgM and IgG in experimental rabbits and detected at least 41 reactive bands; IgM reacted to 7 bands and IgG reacted to 8 bands. Choi et al. [200] observed the antibody responses of experimental rabbits infected with *A. simplex* L3 using ELISA and immunoblotting; serum IgG began to increase at days 7-9 PI, reached their maximum levels by days 12-15 PI, and then decreased, while serum IgM began to increase from day 5 to 7 PI, reached a peak at day 12 PI, and then decreased. Significantly elevated levels of total and L3-specific IgE were observed in 10 gastroallergic patients [92]. However, serum IgM levels have not been studied in human anisakiasis patients in Korea and require further investigation.

Rim et al. [201] performed a seroepidemiological study using ELISA for 6 major parasitic diseases in 6,074 individuals selected from several localities in Korea. The number of anisakiasis-seropositive cases was 495 (8.1%) and varied by locality; it was higher in the southern areas of Jeollanam-do (16.9%) and some parts of Gyeongsangbuk-do (10.6%) than in other localities. Kim et al. [202] detected 33 seropositive cases by ELISA against *A. simplex* L3 ESP antigen in 498 health-examined people in 3 hospitals from southern parts of Korea; the allergen of 130 kDa could be a candidate for the serodiagnosis of anisakiasis. Chung and Lee [134] reported that 14 out of 17 patients with suspected gastroallergic anisakiasis on Jeju Island were strongly positive for *Anisakis*-specific IgE.

Molecular studies and predominance of *A. pegreffii* larvae in fish, cephalopods, and humans in Korea

In Korea, molecular studies of anisakid larvae were initiated by Kim et al. [203] in 2006 who analyzed the complete mitochondrial genome of *A. simplex* L3 from sea eel (*C. myriaster*). Thereafter, at least 23 studies were performed on the molecular genetic characteristics of anisakid larvae from Korean seawater [147,178,180,181,184-189,203-215]. Yu et al. [204] analyzed the cDNA library of *A. simplex* L3 and detected 493 expressed sequence tags (ESTs), including 21 ESTs that matched previously reported *A. simplex* genes or proteins in addition to many other EST clones related to cell functions and worm growth and development.

Subsequently, the PCR-RFLP technique was applied to detect anisakid larvae in several fish species caught in Korean seawater [205-207]. Kang et al. [205] molecularly analyzed anisakid larvae from marine fish and squids caught in Korean seawater using PCR-RFLP of the ITS gene and found that they were larvae of *A. pegreffii*. Lee et al. [206] also molecularly confirmed that most larvae from Korean sea-fish were *A. pegreffii* (47 of 60 larvae), and small proportions were *A. typica* (10 larvae), *A. simplex* s.s. (1 larva), and a hybrid of *A. pegreffii* and *A. simplex* (2 larvae). Choi et al. [178] performed molecular studies (18S ribosomal DNA; 18S rDNA) on 10 *Anisakis* type I larvae recovered from marine fish in Korean seawater, and the larvae demonstrated high identity with *A. pegreffii*. Park et al. [208] molecularly analyzed 45 anisakid larvae collected from rockfish (*S. schlegeli*) from the western sea and identified 3 species, which included *A. simplex* (17 larvae), *A. pegreffii* (4 larvae), and *Hysterothylacium* sp. (24 larvae). Kim et al. [209] molecularly analyzed 26 anisakid larvae from fish in the southern sea and found that *A. pegreffii* was the most common (17 larvae) followed by *H. aduncum* (2 larvae), *Hysterothylacium fabri* (1 larva), *Raphidascaris lophii* (1 larva), and hybrid forms (5 larvae). However, Jeon et al. [180] and Setyobudi et al. [181] reported that the anisakid larvae from masou salmon (*O. masou masou*) and chum salmon (*O. keta*), respectively, from the eastern sea analyzed by PCR-RFLP of the ITS region and *cox*2 gene were *A. simplex* s.s. Subsequently, this discrepancy was well explained by Setyobudi et al. [210] that *A. pegreffii* larvae were distributed mainly in the southern (90.7% of all anisakid larvae detected) and western seas (98.9% of all larvae detected) but less in the eastern sea of Korea based on molecular analyses of larvae collected from common squids (*T. pacificus*). A similar but interesting finding was observed by Sohn et al. [211]; all 48 larvae from 3 species of fish from the Yellow Sea (western sea) were *A. pegreffii*, whereas 79 of 80 anisakid larvae from 7 species of fish from the southern sea were *A. pegreffii,* and only 1 larva was *A. simplex* s.s. In fish from the eastern sea, the species of anisakid larvae were different depending on the species of fish; the larvae detected in Japanese flounder (*P. olivaceus*) and rockfish (*S. schlegeli*) were all *A. pegreffii*, whereas those found in 2 species of salmon (*O. masou masou* and *O. keta*) were determined to be *A. simplex* s.s. [211]. Salmon fish are considered to have been infected by anisakid larvae when they migrate from the east coast of Korea through Hokkaido (Japan), the northern North Pacific Ocean, and the Bering Sea. Similar features were observed in the distribution of *A. pegreffii* and *A. simplex* s.s. larvae in chub mackerel (*S. japonicus*) caught from the eastern, southern, and western seas [184], and it seemed that *A. pegreffii* is the dominant species in Korean chub mackerels which are mainly caught from the Tsushima Current stock, whereas Japanese chub mackerels are 2 stocks and harbor 2 kinds of larvae; *A. pegreffii* in the Tsushima Current stock and *A. simplex* s.s. in the Pacific Current stock.

The predominance of *A. pegreffii* larvae was repeatedly observed in different fish species collected from the western and southern seawater of Korea (Fig. 4); sea eel (*C. myriaster*) [185,186,188], Pacific cod (*Gadus macrocephalus*) [212], chub mackerel (*S. japonicus*) [186,188], hairtail (*T. lepturus*) [186], large-head hairtail (*Trichiurus japonicus*) [187], yellow croaker (*L. polyactis*) [188], and anchovy (*E. japonica*) [189]. Nurhidayat et al. [213] examined walleye pollock (*G. chalcogrammus*) caught from the East Sea of Korea and found that 73.5% of the anisakids were *A. simplex*; only 1.4% were *A. pegreffii* (Fig. 4). Walleye pollock inhabits cold and deep-water columns and is abundant in the northern North Pacific Ocean (Pacific Current) and the Bering Sea [213]. In addition, the predominance of *A. simplex* larvae in chum salmon caught from the East Sea (Namdae Stream, Yangyang) of Korea was confirmed by Kim et al. [214], who performed comparative transcriptome analyses of the larvae. Kim et al. [215] developed a new genetic technique to discriminate the species of anisakid larvae collected from Korean seawater and the amplification-refractory mutation system (ARMS) was found to be effective in discriminating *A. pegreffii, A. simplex*, and their hybrids.

In human infections in Korea, specific molecular diagnosis of anisakid larvae has been performed in 3 studies [3,107,113]. Lim et al. [107] performed molecular analyses of 26 larvae extracted from human infections using ITS region sequences, and the larvae from 15 (25 larvae) of 16 cases were confirmed to be *A. pegreffii*, while the larva from only 1 case (1 larva) was *A. simplex* s.s. Song et al. [113] performed molecular analyses of anisakid larvae from 20 human cases (health check-up patients) and confirmed that all of them were infected with *A. pegreffii*. Molecular studies of *Pseudoterranova* sp. larvae were performed in only 1 study by Song et al. [3]; 12 larvae collected from 12 human cases in Korea were analyzed using sequences of the mitochondrial *cox*1 and *nd*1 genes, all of which were confirmed to be *P. decipiens* s.s. larvae.

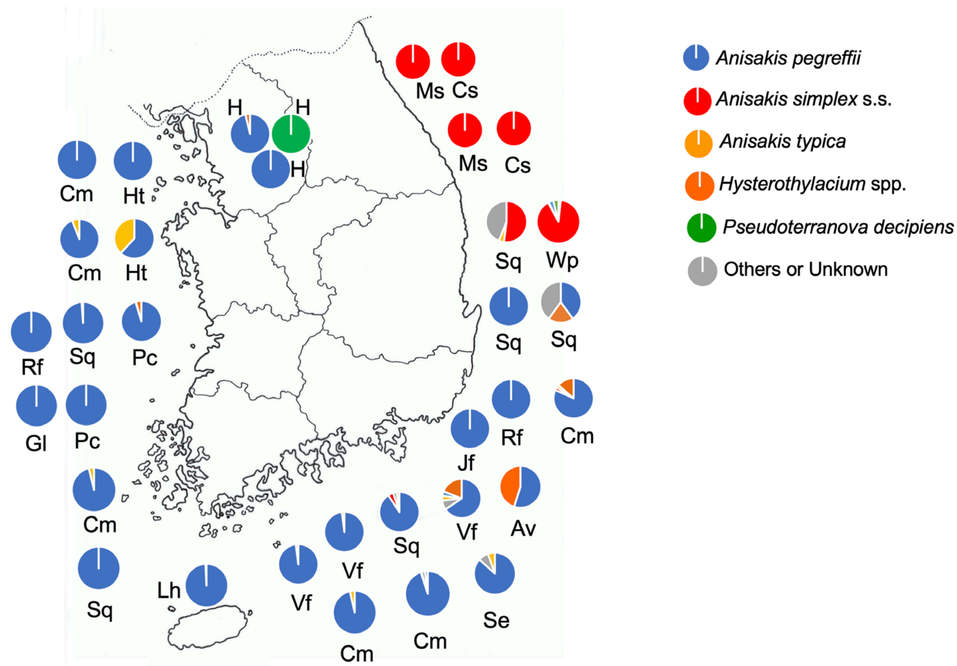

Fig. 4. Species of anisakid larvae detected in humans (nationwide, mostly from Seoul) and fish/squids from the eastern, southern, and western seas of Korea based on molecular analyses [3,107,113,178,180,181,184-189,205-213]. Av, anchovy; Cm, chub mackerel; Cs, chub salmon; Jf, Japanese flounder; Gl, greenling; H, human; Ht, hairtail; Lh, large-head hairtail; Ms, masou salmon; Pc, Pacific cod; Rf, rockfish; Se, sea eel; Sq, squid; Vf, various fish; Wp, walleye pollock.

Resistance of anisakid larvae against physicochemical stimuli, including anthelmintics

In Korea, it has been shown that anisakid larvae are highly resistant to various physicochemical stimuli, including temperature (high and low), chemical substance (salinity, acidity, alcohol, and others), irradiation, ultrasound, hydrostatic pressure, and anthelmintic drugs [170,216-224]. Lee and Chyu [216] reported that anisakid larvae survived 1, 4, 6, 3, and > 30 hours at -20°C, -15°C, -10°C, -5°C, and 0°C, respectively, and were killed when stored at 30% saline for 17 hours, 20% saline for 2 days, and 10% saline for 5 days; however, some (17%-19%) larvae lived > 10 days at 0.85% or 5% saline. In addition, anisakid larvae survived < 1 hour at 20% acetic acid, < 24 hours at 10% acetic acid, < 10 days at 5% acetic acid, < 2 days at 40% ethanol, < 3 days at 20% ethanol, and < 6 days at 10% ethanol. The larvae were highly resistant to variable concentrations of soy sauce, Japanese soy sauce, mustard, and Japanese mustard (wasabi) surviving 1 day or longer [216]. Lim [170] reported similar results. Chai et al. [217] observed high radioresistance of anisakid larvae; they demonstrated active movements even after irradiation with a surprisingly high dose of 10,000 Gy, although their infectivity to experimental rats and rabbits decreased considerably. This radioresistance was suggested to be due to the role of superoxide dismutase [218]. Jeon and Jee [219] studied the inhibitory effects of ivermectin, doramectin, and ethanol *in vitro* and found that ivermectin and ethanol had some effect on the migration and movement of anisakid larvae, whereas doramectin had no effect.

However, the inhibitory effects of ivermectin were lower *in vivo* in experimental rats [220]. Herbal extracts (*Meliae ezadarach, Dryopteris crassirhizoma,* and *Quisqualis indica* var. *villosa*) have been tested for their inhibitory effects *in vitro* against anisakid larvae [221]; however, the *in vivo* effects need to be determined. Oh et al. [222] studied the effects of freezing, salting, and combined treatment with chlorine and ultrasound on anisakid larvae inoculated in salt-fermented squid and pollock tripe; all larvae were inactivated after 48 hours at -20℃ and 24 hours at -40℃. The viability of the larvae was 81.7% and 26.7% in 5% and 10% saline solutions, respectively, after 7 days of storage, and all larvae were inactivated when submerged in 15% saline for 7 days or in 20% saline for 6 days of storage [222]. The viability of the larvae (isolated from the fish) was significantly reduced after combined treatment with low concentrations (< 2,000 ppm) of chlorine and ultrasound for 5-30 min; however, this combined treatment exerted no effects on the viability of the larvae located within the viscera of heavily infected sea eels [222]. Lee et al. [223] examined the effect of high hydrostatic pressure (HHP) on the viability of anisakid larvae in the flesh of sea eels and found that HHP at 200 MPa for 5 min could be used as a potential measure for the inactivation of anisakid larvae in fish without changes in color and sensory quality of the fish. Nam et al. [224] observed the larvicidal effects of various food condiments, including soybean sauce, Japanese mustard, vinegar, red pepper paste, saline solution, ethanol, and soju (Korean liquor); all these exhibited significant effects after several hours, but L3 is exposed to these condiments only for seconds before ingestion, so these conditions cannot be used to prevent anisakid larval infections.

Ethics statement

This was not a human population study; therefore, approval by the institutional review board and informed consent were not required.

Conflict of interest

We have no conflict of interest related to this review.

Acknowledgments

We acknowledge all Korean authors who reported the clinical cases of human and animal anisakidosis between 1971 and 2022. We also appreciate the dedicated works, including molecular studies, on the detection of anisakid larvae in marine fish and cephalopods caught near the western, southern, and eastern seas of Korea.

Funding

None.

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