УДК 616.995.122-07
https://doi.org/10.20538/1682-0363-2023-1-132-142

Foresight in the diagnosis of trematodiasis: innovations versus routine methods

Perina E.A., Khmelevskaya E.S., Fedorova O.S., Ivanov V.V.

Siberian State Medical University
2, Moscow Trakt, Tomsk, 634050, Russian Federation

ABSTRACT

Aim. To analyze modern methods for the diagnosis of trematodiasis in experimental and epidemiological studies.

Trematodiasis is a group of common parasitic diseases that are a socially sensitive health problem worldwide. According to World Health Organization, more than 250 million people are affected by trematode infections globally. The most common types of human trematode infections are diseases caused by *Schistosoma, Fasciola, Clonorchis*, and *Opisthorchis* pathogens. Diagnosis of trematodiasis is often multistage and includes identification of disease symptoms, analysis of medical history, and use of various laboratory tests. Clinical presentation of parasitic infections often varies, making a definitive diagnosis difficult. Various tools are used to diagnose trematode infections: epidemiological criteria, laboratory tests (complete blood count and blood biochemistry, serological methods), instrumental methods (abdominal X-ray and ultrasound), and parasitological techniques, which often have insufficient sensitivity and specificity. Therefore, development of modern and effective non-invasive methods for detection of trematode infections with high sensitivity and specificity, including screening in endemic regions, is relevant.

The present review analyzes the results of 90 clinical trials and experimental studies on the diagnosis of trematode infections using the PubMed search engine and the eLibrary database. The review analyzes original articles published from January 1, 2015 to December 31, 2021.

Most studies confirm that the absence of a standard diagnostic approach highlights obvious convenience of utilizing a combined approach to reliable diagnosis of trematodiasis. An adequate combination of different diagnostic tests makes it possible to diagnose the disease correctly, devise a correct treatment and follow-up strategy, and organize preventive measures.

Keywords: trematode, opisthorchiasis, clonorchiasis, duodenal probe, microscopic helminth detection, immunoassay, molecular diagnosis, molecular genetic diagnosis, endoscopic examination, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound examination (US)

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The study was supported by the RFBR grant within the research project No. 19-515-70004 "Tools to diagnose carcinogenic liver fluke infection".

For citation: Perina E.A., Khmelevskaya E.S., Fedorova O.S., Ivanov V.V. Foresight in the diagnosis of trematodiasis: innovations versus routine methods. *Bulletin of Siberian Medicine.* 2023;22(1):132–142. https://doi.org/10.20538/1682-0363-2023-1-132-142.

✉ *Perina Ekaterina A.,* catherineperina@gmail.com

Форсайт диагностики трематодозов: инновации против рутинных методов

Перина Е.А., Хмелевская Е.С., Федорова О.С., Иванов В.В.

Сибирский государственный медицинский университет (СибГМУ)
Россия, 634050, г. Томск, Московский тракт, 2

РЕЗЮМЕ

Цель данного обзора литературы – провести анализ современных методов диагностики трематодозов в экспериментальных и эпидемиологических исследованиях.

Трематодозы – распространенные паразитарные заболевания, являющиеся важной проблемой общемирового здравоохранения. По данным Всемирной организации здравоохранения, трематодозами поражено более 250 млн человек. Наиболее распространенными видами трематодозов человека являются заболевания, вызванные возбудителями *Schistosoma, Fasciola, Clonorchis* и *Opisthorchis*. Диагностика трематодозов часто бывает комбинированной и многоступенчатой – выявление симптомов заболевания, сбор эпидемиологического анамнеза и использование различных лабораторных исследований. Клиническая картина паразитарных инвазий часто варьирует, что затрудняет окончательный диагноз. Для диагностики трематодозов используют различные диагностические инструменты: эпидемиологические критерии, методы лабораторной диагностики (общий и биохимический анализ крови, серологические методы), инструментальные методы (рентгенологические и ультразвуковые исследования органов брюшной полости), паразитологические методы, нередко обладающие недостаточной чувствительностью и специфичностью. В этой связи актуальна разработка современных и эффективных неинвазивных способов детекции трематодозов, в том числе для скрининговой диагностики в эндемичных регионах.

В работе проведен анализ 90 научных публикаций результатов клинических и экспериментальных исследований в области диагностики трематодозов с использованием электронно-поисковой системы PubMed и научной электронной библиотеки Elibrary. В обзоре представлены оригинальные статьи, опубликованные с 1 января 2015 г. по 31 декабря 2021 г.

Большинство исследований подтверждает, что отсутствие стандартного диагностического подхода подчеркивает очевидное удобство применения комбинированного подхода для получения достоверного диагноза трематодоза. Адекватное сочетание различных диагностических тестов позволяет правильно диагностировать заболевание, составить правильный план лечения и последующего наблюдения, организовать меры профилактики.

Ключевые слова: трематодоз, описторхоз, клонорхоз, дуоденальное зондирование, гельминтоовоскопия, иммуноферментный анализ, молекулярно-генетическая диагностика, эндоскопическое исследование, компьютерная томография (КТ), магнитно-резонансная томография (МРТ), ультразвуковое исследование (УЗИ)

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.

Источник финансирования. Исследование выполнено при финансовой поддержке РФФИ в рамках научного проекта «Идентификация новых диагностических маркеров для разработки технологий популяционного скрининга трематодозов» № 19-515-70004.

Для цитирования: Перина Е.А., Хмелевская Е.С., Федорова О.С., Иванов В.В. Форсайт диагностики трематодозов: инновации против рутинных методов. *Бюллетень сибирской медицины.* 2023;22(1):132–142. https://doi.org/10.20538/1682-0363-2023-1-132-142.

INTRODUCTION

Trematodiasis is a group of common parasitic diseases that are a socially sensitive health problem worldwide. According to the World Health Organization (WHO), it affects more than 250 million people in many countries on five continents [1–5]. The most common types of human trematode infection are diseases caused by *Schistosoma, Fasciola, Clonorchis,* and *Opisthorchis*. People acquire trematodes while

swimming via skin and mucous membranes, by accidental ingestion of water containing parasite cysts, and by consumption of inadequately processed or raw fish.

Helminth invasion of the biliary tract is an important medical problem, especially in tropical and subtropical endemic areas [6]. Many endemic regions (China, Philippines, Cambodia, Laos) have launched national programs to achieve control of invasions [7]. Trematodiasis control worldwide is aimed at reducing the risk of infection. For this purpose, mass prophylactic anthelmintic treatment is offered in endemic areas. All this is due to difficult diagnosis of these diseases, which is often combined and multistage and includes identifying symptoms of the disease, taking a biological history, and using various laboratory tests. The clinical presentation of parasitic infections often varies, making a definitive diagnosis difficult. Various diagnostic tools are used to diagnose trematodes: epidemiological criteria, laboratory diagnostic methods (complete blood count and blood biochemistry, serological tests), instrumental methods (abdominal X-ray and ultrasound), parasitological techniques [8]. Specific diagnostic methods are detection of eggs in feces, urine, and / or duodenal contents [6, 9]. However, it is recognized that parasitological methods show low sensitivity in detecting mild infestations; consequently, there remains a need to develop more sensitive and specific diagnostic tools to monitor the prevalence of parasite invasion [9–12].

The aim of this literature review was to analyze modern methods for the diagnosis of trematodiasis in experimental and epidemiological studies.

METHODS

The present review analyzes the results of clinical trials and experimental studies on the diagnosis of trematode infections using the PubMed search engine and the eLibrary database. The review includes original articles published from January 1, 2015 to December 31, 2021. Primary search for publications on the diagnosis of trematodiasis was carried out. The keywords used for the search were “trematodiasis”, “opisthorchiasis”, “clonorchiasis”, “duodenal sounding”, “helminthovoscopy”, “enzyme-linked immunosorbent assay”, “metabolomics”, “proteomics”, “molecular genetic diagnosis”, “PCR”, “endoscopic examination”, “CT”, “MRI”, “ultrasound”, “X-ray”. Approximately 350 publications in Russian and over 1,500 publications in English were identified.

At the first stage, we selected articles the title of which mentioned methods for diagnosing trematodiasis; at the same time, we excluded reviews and articles duplicating information. At the second stage, we analyzed abstracts of the publications and excluded works in which routine methods and stool microscopy were used as the only research methods. At the third stage, we selected articles with access to the full text; as a result, a detailed analysis of 90 publications containing data on original modern research in the field of diagnosing trematodiasis was carried out.

MODERN MICROSCOPY TECHNOLOGIES

The results of the analysis indicate wide geographical coverage of the studies: most of them were performed in the endemic regions of Southeast Asia; however, some studies were carried out in Europe, USA, and Africa [12–15]. To confirm the diagnosis of most trematode invasions, microscopy of patient stool samples is used, since the method is simple and affordable; however, it only detects invasion of medium and high intensity [12, 16]. The sedimentation method has greater sensitivity and versatility at low invasion intensity [15, 17, 18]. Microscopy of stool, urine or duodenal samples requires a laboratory with a light microscope and qualified experienced personnel, which is not always available in endemic areas.

Some researchers propose a solution to the above problems with modern compact microscopes compatible with smartphones. So, in the study [19, 20], a comparison of a standard microscope and two mobile microscopes – Foldscope and CellScope – was carried out for the diagnosis of *S. haematobium*. Sensitivity was 55.9 and 69.6%, specificity reached 93.3 and 100%, respectively. Given possible technical improvement (increased sensitivity, increased fields of view), these devices can become pilot technology for the production of portable diagnostic microscopes.

At the same time, for the differential diagnosis of schistosomiasis, a rectal biopsy can be used, which makes it possible to achieve high sensitivity of a microscopic examination in comparison with standard serological tests [21].

ENZYME IMMUNOASSAYS

Enzyme immunoassay is a common and frequently used method in parasitology. The most common technique is enzyme-linked immunosorbent assay (ELISA). This method is based on detection of specific antibodies to present parasites secreted by the

body or parasite antigens themselves determined in venous blood or urine. This method has advantages over stool microscopy, since parasite antibodies are detected even in case of slight invasion. A study investigating seroprevalence and the relationship between the number of *O. viverrini* eggs in infested individuals and the specific antibody response showed that ELISA (based on total IgG and IgG4 antibodies to *O. viverrini*) has higher sensitivity in the analysis (98.4 and 89.8%, respectively) than the modified formalin-ethyl acetate technique (70.3%). The study also noted a positive correlation between the number of *O. viverrini* eggs in one gram of stool and IgG antibody levels [7].

However, with enzyme immunoassays, both false positive and false negative results are possible: the former appear against the background of a previous invasion, the latter – in severe immunodeficiency [22, 23]. An important disadvantage of ELISA is also the presence of cross-reactions due to antigenic similarities of various parasites. In this regard, an important task is to increase the sensitivity and specificity of the method.

Thus, to confirm the invasion by *S. japonicum*, the diagnostic potential of cathepsin B was studied (SjCatB). The results showed high sensitivity (86.7%) and specificity (96.7%), which indicates the promising diagnostic potential of this marker [24, 25].

The results of the literature review indicated that extravesicles [24, 26], P-selectin [27], soluble egg antigens [28–31], and serum immunoglobulins [32] were used to develop diagnostic tools for schistosomiasis. As part of the experimental work, specific proteins were studied in animals [33, 34], e.g. saposin-like proteins (SjSAP4 + Sj23-LHD (large hydrophilic domain)) provided the best diagnostic result with the sensitivity of 87.04% and specificity of 96.67% [24, 35–37]. A study of the inflammatory marker YKL-40 (chitinase-3 like-protein-1, also called human cartilage glycoprotein 39) in preschool children showed that it could be a potential biomarker of *S. haematobium* [38]. Serum carbonic anhydrase 1 (CA1) was proposed as another line of *S. mansoni* diagnosis [39].

To simplify screening, the point-of-care circulating cathodic antigen assay is utilized (POC-CCA), in particular, kits for detecting *S. mansoni* are used [23, 34, 40–44].

A work evaluating the use of three functionally active recombinant forms of the main secreted cathepsins (rFhCL1, rFhCL2, rFhCL3) and cathepsin B, rFhCB3 as antigens in indirect ELISA for serological diagnosis of *F. hepatica* infection in experimental and natural conditions showed that the level of antibodies to all three cathepsins L remained high during chronic invasion, but quickly decreased after drug treatment, which can be used to assess the effectiveness of deworming [45, 46].

Currently, the availability of omics studies makes it possible to study the parasite proteome and use these data to create new diagnostic kits. To improve the sensitivity, specificity, or field applicability of diagnostic kits, a search was performed for serum and urine biomarkers to determine *S. haematobium* invasion [22]. Another study evaluated the possibility of using milk instead of blood serum for early diagnosis of fascioliasis in dairy goats [47].

In the study on methods for diagnosing *F. hepatica* using ELISA, a group of researchers proposed to use a multiepitope construct of three protein epitopes cathepsin L1, a saposin-like protein 2 (SAP-2), and a 16.5-kDa tegument-associated protein (FhTP16.5), showing its high antigenicity and specificity [48]. At the same time, cathepsin L1 as a separate marker can act as a suitable antigen as well [49–52]. Some researchers studied fractionated parasite cells by conducting ELISA of proteins of different mass, rapidly yielding a reproducible method for obtaining antigens with acceptable sensitivity and specificity [53].

Monoclonal antibodies (MoAb) against recombinant *F. gigantica* glutathione peroxidase (rFgGPx) can be used for immunodiagnosis of both early and advanced fascioliasis in animals and humans [54, 55], and recombinant adenylate kinase 3 is proposed as a marker for the serodiagnosis of clonorchiasis [56]. Determining the cathepsin level in *O. viverrini* invasion also shows good results (sensitivity and specificity of 62.1 and 84.1%, respectively), so it can become an alternative immunodiagnostic tool for human opisthorchiasis in endemic areas [57, 58]. The use of monoclonal antibodies in *O. viverrini* invasion proved to be promising due to high diagnostic accuracy with the possibility of using urine samples instead of stool samples. Comparison of the concentrations of monoclonal antibodies in urine samples and stool samples showed a positive relationship between antibody concentrations and the number of eggs in one gram of feces, as well as high specificity [59–61].

In another study that used gold nanoparticles, a more than 3-fold rise in the sensitivity of the method for

detecting *O. viverrini* antigens was achieved compared to the classical method, increasing the sensitivity to 93.8 vs. 91.3%, respectively. The innovation allowed to reduce the number of reaction steps, which leads to a decrease in the waiting time for the results without a decrease in the quality of the analysis [62].

MOLECULAR GENETIC METHODS

Another method that has become widespread in the diagnosis of parasitological diseases is the polymerase chain reaction (PCR), based on detection of parasite antigens in various samples – blood serum, urine, stool. When comparing modern invasion detection methods, PCR surpasses standard microscopy of stool and urine samples and most often shows fairly high sensitivity and specificity [41, 46, 63–66]. When compared with standard methods of parasitological diagnosis, PCR shows a significant increase in the disease prevalence [67]. Thus, in a study, PCR revealed 13–15% more cases of invasion compared to microscopy [68]. With the improvement of methods for extracting DNA from samples, the sensitivity of the method can reach 100%. For example, when using the method in the experiment of mechanical disruption of parasite eggs by bead beating, a 100% positive result in the diagnosis of *S. haematobium* was achieved compared to 85% using the standard extraction procedure [69].

Along with PCR, recombinase polymerase amplification (RPA) is carried out, which allows to increase sensitivity from 66 to 87%, respectively, with 100% specificity of both methods. In fascioliasis, RPA helps to detect 47% of infections not detected by microscopy [70, 71]. The real-time RPA for diagnosing urogenital schistosomiasis targeting the *S. haematobium* Dra 1 sequence had clinical sensitivity and specificity of 98.4 and 100%, respectively, compared to the real-time PCR assay also targeting the Dra 1 sequence [72].

Another modification of PCR is loop-mediated isothermal amplification (LAMP) – a DNA amplification technique in one tube, which allows for molecular diagnosis to be carried out much cheaper and faster than PCR. A study on diagnosing *S. haematobium* invasion using LAMP showed similar sensitivity and specificity compared to PCR (100%). For *S. mansoni*, sensitivity was higher for LAMP amplification (100%) than for PCR (99%) [73]. The same method was used to study stool specimens from patients with suspected *C. sinensis* infection, achieving high sensitivity and specificity [74].

In another study, traces of *F. hepatica* infection were also determined in comparison with the standard PCR method [75]. This disease is characterized by difficult detection, often despite the symptoms, standard parasitological methods do not detect the presence of eggs. In this article, LAMP analysis showed a positive reaction even if there was only one helminth egg in the sample. In addition, visualization of the result is also quite simple – a color change in the solution is observed under ultraviolet light. Similar results were presented in a study comparing classical parasitological methods (direct wet preparation and concentration method), PCR, and LAMP for the diagnosis of *F. hepatica* in sheep fecal samples [18]. Also, the LAMP analysis allows to avoid cross-reactions with other species. In a study evaluating LAMP for the detection and monitoring of *S. mansoni* transmission foci in the intermediate host (snail of the genus *Biomphalaria)*, the LAMP method was shown to be three times more efficient than parasitological testing and more convenient for field use than other molecular methods [76].

Quite a lot of studies are being carried out to search for new targets for the diagnosis and differentiation of various invasions and the search for new antigens and their combinations [10, 15, 18, 24, 33, 65, 77–84]. As new markers, saposin-like protein [37], miRNAs isolated from serum extravesicles [85, 86], and cathepsin L3 are used in schistosomiasis [87], 27-kDa purified parasite antigen is used in fascioliasis [14], and intergenic spacer region of *F. hepatica* DNA [17] and schistosomule antigen are used in *S. mansoni* invasion [88].

The sensitivity of PCR-based methods depends on the number of copies of the gene, the number of parasite eggs, the quality of DNA, and PCR inhibitors in the sample. There are studies on improving PCR methods by influencing the *ITS2*, *cox1*, and *cyb* genes [82].

With the ever-improving capabilities of sequencing and bioinformatics tools for analyzing sequences and other highly repetitive genomic elements, real-time PCR as a diagnostic tool is becoming more common. A cluster analysis of the *S. japonicum* genome was carried out, on the basis of which a primer – probe set was developed. The resulting real-time PCR test was shown to reliably detect as little as 200 μg of *S. japonicum* genomic DNA, and when testing tiny stool samples containing a single helminth egg, the designed primer – probe set detected DNA in all samples [89]. Multiplex real-time PCR for the diagnosis of *S. haematobium* and *S. mansoni* was analyzed on

serum samples [13]. Sensitivity and specificity values based on multiplex real-time PCR for diagnosing *S. haematobium* and *S. mansoni* were calculated in the range of 87.9–100%.

Despite the advances in the use of molecular genetic methods in the diagnosis of trematodiasis, the study of new potential targets causes difficulties associated with insufficient sensitivity and cross-reactions. Thus, in the study of real-time PCR based on SjR2 and SjCHGSC19, it was shown that these markers can be used to diagnose *S. mekongi* infections in human blood serum, but the tests had low sensitivity and cross-reactions with samples positive for *S.mansoni* or *S. haematobium* [16].

IMAGING METHODS

Considerable attention is paid to imaging technologies in the diagnosis of helminthiases [90]. One study examined cases of appendicitis associated with schistosomiasis [91]. As a result, the features of computed tomography (CT) data were determined, which can be used as criteria for early detection of *S. japonicum* – large diameter, calcifications in the appendix wall together with the sigmoid colon and calcifications in the caecum, signs of perforation or abscess. Another study in Africa found that in patients diagnosed with schistosomiasis based on serological criteria, standard urinary tract and liver ultrasound is not informative, and it is possible to simplify clinical management of these patients [92].

MRI can be used for *O. felineus* invasion. It is shown that against the background of invasion, the MRI image has a characteristic pattern that is not typical of other diseases of the hepatobiliary tract. [93]. This method allows to determine areas with the greatest changes, which will allow to apply these methods in the future in routine diagnosis of opisthorchiasis. MRI is necessary for the diagnosis of neuroschistosomiasis in the invasion by *S. japonicum*, *S. mansoni,* and *S. haematobium* [94].

There are isolated cases in clinical practice when standard helminthological methods indicate the absence of invasion, but the endoscopic presentation allows to visualize release of liver fluke eggs into the lumen of the large intestine. One study showed that the histologic examination confirmed the diagnosis of schistosomiasis – intestinal samples contained multiple eosinophilic granulomas with *S. mansoni* eggs [95]. In individuals infested with *S. mansoni*, the effectiveness of point shear-wave elastography of the liver and spleen and correlation of its results with ultrasound parameters were shown [96].

As a result of such studies, we can talk about the auxiliary role of instrumental diagnostic methods that complement standard microscopic, serological or molecular biological methods.

OMIX TECHNOLOGIES

Thanks to the development of state-of-the-art molecular genetic methods, a significant breakthrough has been achieved in recent years in creating parasite protein libraries and studying their functions in life and adaptation to changing environmental conditions. Studies of the proteome are very important, since proteins are directly involved in implementation of genetic information and maintenance of the vital activity of the parasite, and their composition is directly determined by helminth and microorganism ecology.

The studies provided abundant data on *S. haematobium* proteins at various stages of the parasite life cycle and conducted a genomic and proteomic analysis of trematodes [97, 98]. The authors propose to use a data array to identify diagnostic markers, including the ones for assessing the intensity of invasion. As part of another study, a study of *O. viverrini* was conducted, three specific proteins were found – potential markers of *O. viverrini* [99]. A proteomic analysis of *S. mekongi* was carried out along with an analysis of their excretory / secretory protein composition [100] and proteomic screening of recombinant egg antigens to determine low-intensity *S. mansoni* invasion [30]. `

The number of such studies is growing, the array of data on proteins and helminth genes increases. As a result, personalized medicine develops, facilitating quick and individual diagnosis, identifying the degree of invasion associated with changes in the body, and developing point-of-care diagnostic methods and highly specific screening.

CONCLUSION

Improving the technologies for diagnosing trematodiasis is a significant task for public health, which is associated with spread of invasions in various regions of the world, significant financial costs for anthelmintic therapy, and monitoring of the disease in the population. Given the heterogeneity of parasitic invasions, including clinical variability, genetic diversity, the presence of different stages of pathology in the population, and the need for differential diagnosis of poly-helminth infection, there is a need to develop highly sensitive and highly specific screening

tests. The review of the literature showed that in recent years there has been pronounced research dynamics in this area. Modern microscopy technologies are being developed (including digital interpretation of data), tools for immunological analysis are being improved, classical methods of molecular genetic detection are being modified. Considerable attention of researchers is paid to the role of imaging methods in diagnosing pathological conditions associated with trematodiasis. Using omics technologies (diagnostic agents based on proteomic and metabolomic research methods) as promising diagnostic tools is discussed.

REFERENCES

1. Mas-Coma S., Valero M.A., Bargues M.D. Fascioliasis. *Adv. Exp. Med. Biol.* 2019;1154:71–103. DOI: 10.1007/978-3-030-18616-6_4.
2. Da Silva V.B.R., Campos B.R.K.L., de Oliveira J.F., Decout J.L., do Carmo Alves de Lima M. Medicinal chemistry of antischistosomal drugs: Praziquantel and oxamniquine. *Bioorg. Med. Chem.* 2017;25(13):3259–3277. DOI: 10.1016/j.bmc.2017.04.031.
3. Khalil R.G., Ibrahim A.M., Bakery H.H. A novel immunomodulatory, antifibrotic, and schistosomicidal agent to ameliorate liver damage in murine *Schistosomiasis mansoni*. *Int. Immunopharmacol*. 2022;113(PtA):109415. DOI: 10.1016/j.intimp.2022.109415.
4. Huang X., Kou J., Deng X., Li D., Zhang B, Cheng P. et al. Review of the control of clonorchiasis in Shandong Province, China from 1962 to 2015. *Int. J. Infect. Dis.* 2020;96:199–204. DOI: 10.1016/j.ijid.2020.04.052.
5. Yurlova N.I., Yadrenkina E.N., Rastyazhenko N.M., Serbina E.A., Glupov V.V. Opisthorchiasis in Western Siberia: Epidemiology and distribution in human, fish, snail, and animal populations. *Parasitol. Int*. 2017;66(4):355–364. DOI: 10.1016/j.parint.2016.11.017.
6. www.who.int [Internet]. Foodborne parasitic infections: Clonorchiasis and opisthorchiasis. URL: https://www.who.int/publications/i/item/WHO-UCN-NTD-VVE-2021.2
7. Phupiewkham W., Rodpai R., Inthavongsack S., Laymanivong S., Thanchomnang T., Sadaow L. et al. High prevalence of opisthorchiasis in rural populations from Khammouane Province, central Lao PDR: serological screening using total IgG- and IgG4-based ELISA. *Trans. R. Soc. Trop. Med. Hyg.* 2021;115(12):1403–1409. DOI: 10.1093/trstmh/trab066.
8. www.who.int [Internet]. Foodborne trematode infections; [cited 2022 Dec 23].URL: https://www.who.int/news-room/fact-sheets/detail/foodborne-trematode-infections
9. Pozdnyakova L.L., Krasnova E.I., Kuznetsova V.G., Malov I.V.Opisthorchiasis in adults: clinical guidelines. N: Non-profit partnership "National Society for Infectious Diseases, 2014:53 (in Russ.).
10. Siqueira L.M.V., Senra C., de Oliveira Á.A., Carneiro N.F.F., Gomes L.I., Rabello A. et al.. A real-time PCR assay for the diagnosis of intestinal schistosomiasis and cure assessment after the treatment of individuals with low parasite burden. *Front. Immunol.* 2021;11:620417. DOI: 10.3389/fimmu.2020.620417.
11. Bärenbold O., Raso G., Coulibaly J.T., N'Goran E.K., Utzinger J., Vounatsou P. Estimating sensitivity of the Kato-Katz technique for the diagnosis of *Schistosoma mansoni* and hookworm in relation to infection intensity. *PLoS Negl. Trop. Dis*. 2017;11(10):e0005953. DOI: 10.1371/journal.pntd.0005953.
12. Rahman M.O., Sassa M., Parvin N., Islam M.R., Yajima A., Ota E. Diagnostic test accuracy for detecting *Schistosoma japonicum* and *S. mekongi* in humans: A systematic review and meta-analysis. *PLoS Negl. Trop. Dis*. 2021;15(3):e0009244. DOI: 10.1371/journal.pntd.0009244.
13. Frickmann H., Lunardon L.M., Hahn A., Loderstädt U., Lindner A.K., Becker S.L. et al. Evaluation of a duplex real-time PCR in human serum for simultaneous detection and differentiation of *Schistosoma mansoni* and *Schistosoma haematobium* infections – cross-sectional study. *Travel. Med. Infect. Dis.* 2021;41:102035. DOI: 10.1016/j.tmaid.2021.102035.
14. Saadh M.J., Tanash S.A., Almaaytah A.M., Sa'adeh I.J., Aldalaen S.M., Al-Hamaideh K.D. Immunodiagnosis of cattle fascioliasis using a 27 kDa *Fasciola gigantica* antigen. *Vet. World.* 2021;14(8):2097–2101. DOI: 10.14202/vetworld.2021.2097-2101.
15. Gillardie M.L., Babba O., Mahinc C., Duthel M., de Bengy C., Morineaud C. et al. Molecular approach to the epidemiology of urinary schistosomiasis in France. *PLoS Negl. Trop. Dis*. 2021;15(7):e0009515. DOI:10.1371/journal.pntd.0009515.
16. Frickmann H., Loderstädt U., Nickel B., Poppert S., Odermatt P., Sayasone S. et al. Low sensitivity of real time PCRs targeting retrotransposon sequences for the detection of *Schistosoma japonicum* complex DNA in human serum. *Pathogens.* 2021;10(8):1067. DOI: 10.3390/pathogens10081067.
17. Amiri S., Shemshadi B., Fallahi S., Shirali S. Detection of *Fasciola hepatica* in lori sheep using polymerase Chain reaction and conventional diagnostic methods in Western Iran. *Arch. Razi. Inst*. 2021;76(2):223–229. DOI:10.22092/ari.2020.128417.1413.
18. Amiri S., Shemshadi B., Shirali S., Kheirandish F., Fallahi S. Accurate and rapid detection of *Fasciola hepatica* copro-DNA in sheep using loop-mediated isothermal amplification (LAMP) technique. *Vet. Med. Sci.* 2021;7(4):1316–1324. DOI:10.1002/vms3.455.
19. Coulibaly J.T., Ouattara M., D'Ambrosio M.V., Fletcher D.A., Keiser J., Utzinger J. et al. Accuracy of mobile phone and handheldl Light microscopy for the diagnosis of *Schistosomiasis* and intestinal *Protozoa* infections in Côte d'Ivoire. *PLoS Negl. Trop. Dis*. 2016;10(6):e0004768. DOI: 10.1371/journal.pntd.0004768.
20. Ephraim R.K., Duah E., Cybulski J.S., Prakash M., D'Ambrosio M.V., Fletcher D.A. et al. Diagnosis of *Schistosoma haematobium* infection with a mobile phone-mounted Foldscope and a reversed-lens CellScope in Ghana. *Am. J. Trop. Med. Hyg*. 2015;92(6):1253–1256. DOI: 10.4269/ajtmh.14-0741.
21. Mones A., Sherif M.M., Abdel Halim R.M. Superiority of rectal snip over serology in detection of schistosomiasis eradication: A pilot study. *Arab. J. Gastroenterol*. 2021;22(1):52–55. DOI: 10.1016/j.ajg.2020.11.001.

22. Pearson M.S., Tedla B.A., Mekonnen G.G., Proietti C., Becker L., Nakajima R. et al. Immunomics-guided discovery of serum and urine antibodies for diagnosing urogenital schistosomiasis: a biomarker identification study. *Lancet Microbe*. 2021;2(11):e617–e626. DOI: 10.1016/S2666-5247(21)00150-6.
23. Cai P., Mu Y., Weerakoon K.G., Olveda R.M., Ross A.G., McManus D.P. Performance of the point-of-care circulating cathodic antigen test in the diagnosis of *Schistosomiasis japonica* in a human cohort from Northern Samar, the Philippines. *Infect. Dis. Poverty*. 2021;10(1):121. DOI: 10.1186/s40249-021-00905-5.
24. Zhang Y., Zhao J., Wang X., Xu X., Pan W. Evaluation of six novel antigens as potential biomarkers for the early immunodiagnosis of schistosomiasis. *Parasit. Vectors.* 2015;8:447. DOI: 10.1186/s13071-015-1048-2.
25. Macalanda A.M.C., Angeles J.M.M., Moendeg K.J., Dang-Trinh M.A., Higuchi L., Kirinoki M. et al. *Schistosoma japonicum* cathepsin B as potential diagnostic antigen for Asian zoonotic schistosomiasis. *Parasitol Res.* 2019;118(9):2601–2608. DOI: 10.1007/s00436-019-06410-x.
26. Chen Y., Giri B.R., Li X., He X., Jing Z., Cheng G. Preliminary evaluation of the diagnostic potential of Schistosoma japonicum extracellular vesicle proteins for *Schistosomiasis japonica*. *Acta. Trop*. 2020;201:105184. DOI: 10.1016/j.actatropica.2019.105184.
27. Chimponda T.N., Mushayi C., Osakunor D.N.M., Vengesai A., Enwono E., Amanfo S. et al. Elevation of C-reactive protein, P-selectin and Resistin as potential inflammatory biomarkers of urogenital *Schistosomiasis exposure* in preschool children. *BMC Infect. Dis*. 2019;19(1):1071. DOI: 10.1186/s12879-019-4690-z.
28. Ferrer E., Villegas B., Mughini-Gras L., Hernández D., Jiménez V., Catalano E. et al. Diagnostic performance of parasitological, immunological and molecular tests for the diagnosis of *Schistosoma mansoni* infection in a community of low transmission in Venezuela. *Acta. Trop*. 2020;204:105360. DOI: 10.1016/j.actatropica.2020.105360.
29. Ji R., Shen Y., Shi B., Li H., Tang W., Xia C. et al. An ELISA based on soluble egg antigens for the serodiagnosis of animal schistosomiasis turkestanica. *PLoS One.* 2020;15(1):e0228184. DOI: 10.1371/journal.pone.0228184.
30. Silva-Moraes V., Shollenberger L.M., Castro-Borges W., Rabello A.L.T., Harn D.A., Medeiros L.C.S. et al. Serological proteomic screening and evaluation of a recombinant egg antigen for the diagnosis of low-intensity *Schistosoma mansoni* infections in endemic area in Brazil. *PLoS Negl. Trop. Dis.* 2019;13(3):e0006974. DOI: 10.1371/journal.pntd.0006974.
31. Rodpai R., Sadaow L., Boonroumkaew P., Phupiewkham W., Thanchomnang T., Limpanont Y. et al. Comparison of point-of-care test and enzyme-linked immunosorbent assay for detection of immunoglobulin G antibodies in the diagnosis of human *Schistosomiasis japonica*. *Int. J. Infect. Dis.* 2021;107:47–52. DOI: 10.1016/j.ijid.2021.04.039.
32. Song H.B., Kim J., Jin Y., Lee J.S., Jeoung H.G., Lee Y.H. et al. Comparison of ELISA and urine microscopy for diagnosis of *Schistosoma haematobium* infection. *J. Korean. Med. Sci.* 2018;33(33):e238. DOI: 10.3346/jkms.2018.33.e238.
33. Angeles J.M.M., Goto Y., Kirinoki M., Leonardo L.R., Moendeg K.J., Ybañez A.P. et al. Detection of canine *Schistosoma japonicum* infection using recombinant thioredoxin peroxidase-1 and tandem repeat proteins. *J. Vet. Med. Sci.* 2019;81(10):1413–1418. DOI: 10.1292/jvms.19-0126.
34. Clements M.N., Corstjens P.L.A.M., Binder S., Campbell C.H. Jr., de Dood C.J. et al. Latent class analysis to evaluate performance of point-of-care CCA for low-intensity *Schistosoma mansoni* infections in Burundi. *Parasit. Vectors*. 2018;11(1):111. DOI: 10.1186/s13071-018-2700-4.
36. Cai P., Weerakoon K.G, Mu Y., Olveda R.M., Ross A.G., Olveda D.U., McManus D.P. Comparison of Kato Katz, antibody-based ELISA and droplet digital PCR diagnosis of *Schistosoma japonicum*: Lessons learnt from a setting of low infection intensity. *PLoS Negl. Trop. Dis.* 2019;13(3):e0007228. DOI: 10.1371/journal.pntd.0007228.
37. Cai P., Weerakoon K.G., Mu Y., Olveda D.U., Piao X., Liu S. et al. A parallel comparison of antigen candidates for development of an optimized serological diagnosis of *Schistosoma japonicum* in the Philippines. *EBioMedicine.* 2017;24:237–246. DOI: 10.1016/j.ebiom.2017.09.011.
38. Liu S., Zhou X., Piao X., Hou N., Shen Y., Zou Y. et al. Saposin-like proteins, a multigene family of Schistosoma species, are biomarkers for the immunodiagnosis of *Schistosoma japonicum*. *J. Infect. Dis*. 2016;214(8):1225–1234. DOI: 10.1093/infdis/jiw188.
39. Chimponda T.N., Mduluza T. Inflammation during *Schistosoma haematobium* infection and anti-allergy in pre-school-aged children living in a rural endemic area in Zimbabwe. *Trop. Med. Int. Health*. 2020;25(5):618–623. DOI: 10.1111/tmi.13376.
40. Kardoush M.I., Ward B.J., Ndao M. Serum carbonic anhydrase 1 is a biomarker for diagnosis of human *Schistosoma mansoni* infection. *Am. J. Trop. Med. Hyg*. 2017;96(4):842–849. DOI: 10.4269/ajtmh.16-0021.
41. Viana A.G., Gazzinelli-Guimarães P.H., Castro V.N., Santos Y.L.O.D., Ruas A.C.L., Bezerra F.S.M. et al. Discrepancy between batches and impact on the sensitivity of point-of-care circulating cathodic antigen tests for *Schistosoma mansoni* infection. *Acta. Trop*. 2019;197:105049. DOI: 10.1016/j.actatropica.2019.105049.
42. Fuss A., Mazigo H.D., Tappe D., Kasang C., Mueller A. Comparison of sensitivity and specificity of three diagnostic tests to detect *Schistosoma mansoni* infections in school children in Mwanza region, Tanzania. *PLoS One.* 2018;13(8):e0202499. DOI: 10.1371/journal.pone.0202499.
43. Ferreira F.T., Fidelis T.A., Pereira T.A., Otoni A., Queiroz L.C., Amâncio F.F. et al. Sensitivity and specificity of the circulating cathodic antigen rapid urine test in the diagnosis of *Schistosomiasis mansoni* infection and evaluation of morbidity in a low- endemic area in Brazil. *Rev. Soc. Bras. Med. Trop*. 2017;50(3):358–364. DOI: 10.1590/0037-8682-0423-2016.
44. Armoo S., Cunningham L.J., Campbell S.J., Aboagye F.T., Boampong F.K., Hamidu B.A. et al. Detecting *Schistosoma mansoni* infections among pre-school-aged children in southern Ghana: a diagnostic comparison of urine-CCA, real-time PCR and Kato-Katz assays. *BMC Infect. Dis.* 2020;20(1):301. DOI: 10.1186/s12879-020-05034-2.

45. Bezerra D.F., Pinheiro M.C.C., Barbosa L., Viana A.G., Fujiwara R.T., Bezerra F.S.M. Diagnostic comparison of stool exam and point-of-care circulating cathodic antigen (POC-CCA) test for *Schistosomiasis mansoni* diagnosis in a high endemicity area in northeastern Brazil. *Parasitology.* 2021;148(4):420–426. DOI: 10.1017/S0031182020002164.
46. López Corrales J., Cwiklinski K., De Marco Verissimo C., Dorey A., Lalor R., Jewhurst H. et al. Diagnosis of sheep fasciolosis caused by *Fasciola hepatica* using cathepsin L enzyme-linked immunosorbent assays (ELISA). *Vet. Parasitol*. 2021;298:109517. DOI: 10.1016/j.vetpar.2021.109517.
47. Carnevale S., Malandrini J.B., Pantano M.L., Sawicki M., Kamenetzky L., Soria C.C. et al. Use of the PCR in a combined methodological approach for the study of human fascioliasis in an endemic area. *Acta. Parasitol*. 2021;66(2):455–460. DOI: 10.1007/s11686-020-00302-2.
48. Saad M.F., Attia M.M. Milk as a new diagnostic tool for rapid detection of fascioliasis in dairy goats using excretory/secretory antigen. *Acta. Parasitol*. 2021;66(2):336–345. DOI: 10.1007/s11686-020-00286-z.
49. Aghamolaei S., Kazemi B., Bandehpour M., Ranjbar M.M., Rouhani S., Javadi Mamaghani A. et al. Design and expression of polytopic construct of cathepsin-L1, SAP-2 and FhTP16.5 proteins of *Fasciola hepatica*. *J. Helminthol*. 2020;94:e134. DOI: 10.1017/S0022149X20000140.
50. Mokhtarian K., Akhlaghi L., Mohammadi M., Meamar A.R., Razmjou E., Khoshmirsafa M. et al. Evaluation of anti-cathepsin L1: a more reliable method for serodiagnosis of human fasciolosis. *Trans. R. Soc. Trop. Med. Hyg*. 2016;110(9):542–550. DOI: 10.1093/trstmh/trw063.
51. Meshgi B., Jalousian F., Fathi S., Jahani Z. Design and synthesis of a new peptide derived from Fasciola gigantica cathepsin L1 with potential application in serodiagnosis of fascioliasis. *Exp. Parasitol*. 2018;189:76–86. DOI: 10.1016/j.exppara.2018.04.013.
52. Sugiyama T., Ichikawa-Seki M., Sato H., Kounosu A., Tanaka M., Maruyama H. Enzyme-linked immunosorbent assay (ELISA) using recombinant Fasciola cathepsin L1 for the diagnosis of human fasciolosis caused by Fasciola hepatica/gigantica hybrid type. *Parasitol. Int.* 2021;82:102311. DOI: 10.1016/j.parint.2021.102311.
53. Xifeng W., Mengfan Q., Kai Z., Guowu Z., Jing L., Lixia W. et al. Development and evaluation of a colloidal gold immunochromatographic assay based on recombinant protein CatL1D for serodiagnosis of sheep fasciolosis. *J. Helminthol*. 2019;94:e98. DOI: 10.1017/S0022149X19000919.
54. Mokhtarian K., Akhlaghi L., Meamar A.R., Razmjou E., Manouchehri Naeini K., Gholami S. et al. Serodiagnosis of fasciolosis by fast protein liquid chromatography-fractionated excretory/secretory antigens. *Parasitol. Res*. 2016;115(8):2957–29665. DOI: 10.1007/s00436-016-5049-7.
55. Kueakhai P., Chaithirayanon K., Chaiwichien A., Samrit T., Osotprasit S., Suksomboon P. et al. Monoclonal antibody against *Fasciola gigantica* glutathione peroxidase and their immunodiagnosis potential for fasciolosis. *Vet. Parasitol*. 2019;276:108979. DOI: 10.1016/j.vetpar.2019.108979.
56. Aguayo V., Valdes B., Espino A.M. Assessment of Fasciola hepatica glutathione S-transferase as an antigen for serodiagnosis of human chronic fascioliasis. *Acta. Trop*. 2018;186:41–49. DOI: 10.1016/j.actatropica.2018.07.002.
57. Kwon S.B., Kim P., Woo H.S., Kim T.Y., Kim J.Y., Lee H.M. et al. Recombinant adenylate kinase 3 from liver fluke Clonorchis sinensis for histochemical analysis and serodiagnosis of clonorchiasis. *Parasitology*. 2018;145(12):1531–1539. DOI: 10.1017/S0031182018000434.
58. Teimoori S., Arimatsu Y., Laha T., Kaewkes S., Sereerak P., Tangkawattana S. et al. Immunodiagnosis of opisthorchiasis using parasite cathepsin *F. Parasitol. Res*. 2015;114(12):4571–4578. DOI: 10.1007/s00436-015-4703-9.
59. Teimoori S., Arimatsu Y., Laha T., Kaewkes S., Sereerak P., Sripa M. et al. Chicken IgY-based coproantigen capture ELISA for diagnosis of human opisthorchiasis. *Parasitol. Int.* 2017;66(4):443–447. DOI: 10.1016/j.parint.2015.10.011.
60. Worasith C., Kamamia C., Yakovleva A., Duenngai K., Wangboon C., Sithithaworn J. et al. Advances in the diagnosis of human opisthorchiasis: Development of *Opisthorchis viverrini* antigen detection in urine. *PLoS Negl. Trop. Dis.* 2015;9(10):e0004157. DOI: 10.1371/journal.pntd.0004157.
61. Worasith C., Wangboon C., Duenngai K., Kiatsopit N., Kopolrat K., Techasen A. et al. Comparing the performance of urine and copro-antigen detection in evaluating *Opisthorchis viverrini* infection in communities with different transmission levels in Northeast Thailand. *PLoS Negl. Trop. Dis.* 2019;13(2):e0007186. DOI: 10.1371/journal.pntd.0007186.
62. Kim J.G., Ahn C.S., Sripa B., Eom K.S., Kang I., Sohn W.M. et al. *Clonorchis sinensis* omega-class glutathione transferases are reliable biomarkers for serodiagnosis of clonorchiasis and opisthorchiasis. *Clin. Microbiol. Infect*. 2019;25(1):109.e1–109.e6. DOI: 10.1016/j.cmi.2018.03.042.
63. Taron W., Jamnongkan W., Techasen A., Phetcharaburanin J., Namwat N., Sithithaworn P. et al. AuNPs-LISA, an efficient detection assay for *Opisthorchis viverrini* (Ov) antigen in urine. *Talanta.* 2020;209:120592. DOI: 10.1016/j.talanta.2019.120592.
64. Guegan H., Fillaux J., Charpentier E., Robert-Gangneux F., Chauvin P., Guemas E. et al. Real-time PCR for diagnosis of imported schistosomiasis. *PLoS Negl. Trop*. *Dis.* 2019;13(9):e0007711. DOI: 10.1371/journal.pntd.0007711.
65. Wang N., Tang B., Hao Y., Bai X., Wang X., Li Y. et al. Acute shock caused by *Clonorchis sinensis* infection: a case report. BMC. *Infect Dis.* 2019;19(1):1014. DOI: 10.1186/s12879-019-4644-5.
66. Lamaningao P., Kanda S., Laimanivong S., Shimono T., Darcy A.W., Phyaluanglath A. et al. Development of a PCR assay for diagnosing trematode (Opisthorchis and Haplorchis) infections in human stools. *Am. J. Trop. Med. Hyg*. 2017;96(1):221–228. DOI: 10.4269/ajtmh.16-0165.
67. Meng X., Jian-Hai Y., Sheng-Kui C., Jian-Ping C., Xiao-Fan Z., Yu-Juan S. Comparison of efficiency of Kato-Katz technique and PCR assay for detecting *Clonorchis sinensis* infection. *Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi*. 2019;31(2):165–168. (In Chinese). DOI: 10.16250/j.32.1374.2018233.
68. Esiere R.K., Ibeneme E.O., Effanga E.O., Imalele E.E., Esiere M.K., Inyang-Etoh P.C. et al. Detecting *Schistosoma haematobium* infection by microscopy and polymerase chain

reaction (PCR) in school children in three senatorial districts of Cross River State, Nigeria. *J. Parasit. Dis.* 2022;46(1):272–279. DOI: 10.1007/s12639-021-01446-2.

69. Meurs L., Brienen E., Mbow M., Ochola E.A., Mboup S., Karanja D.M. et al. Is PCR the next reference standard for the diagnosis of *Schistosoma* in stool? A comparison with microscopy in Senegal and Kenya. *PLoS Negl. Trop. Dis.* 2015;9(7):e0003959. DOI: 10.1371/journal.pntd.0003959.
70. Pomari E., Perandin F., La Marca G., Bisoffi Z. Improved detection of DNA Schistosoma haematobium from eggs extracted by bead beating in urine. *Parasitol. Res.* 2019;118(2):683–686. DOI: 10.1007/s00436-018-6137-7.
71. Sun K., Xing W., Yu X., Fu W., Wang Y., Zou M. et al. Recombinase polymerase amplification combined with a lateral flow dipstick for rapid and visual detection of *Schistosoma japonicum*. *Parasit. Vectors*. 2016;9(1):476. DOI: 10.1186/s13071-016-1745-5.
72. Cabada M.M., Malaga J.L., Castellanos-Gonzalez A., Bagwell K.A., Naeger P.A., Rogers H.K. et al. Recombinase polymerase amplification compared to real-time polymerase chain reaction test for the detection of *Fasciola hepatica* in human stool. *Am. J. Trop. Med. Hyg.* 2017;96(2):341–346. DOI: 10.4269/ajtmh.16-0601.
73. Frimpong M., Kyei-Tuffuor L., Fondjo L.A., Ahor H.S., Adjei-Kusi P., Maiga-Ascofare O. et al. Evaluation of a real-time recombinase polymerase amplification assay for rapid detection of *Schistosoma haematobium* infection in resource-limited setting. *Acta. Trop.* 2021;216:105847. DOI: 10.1016/j.actatropica.2021.105847.
74. Lodh N., Mikita K., Bosompem K.M., Anyan W.K., Quartey J.K., Otchere J. et al. Point of care diagnosis of multiple schistosome parasites: Species-specific DNA detection in urine by loop-mediated isothermal amplification (LAMP). *Acta. Trop.* 2017;173:125–129. DOI: 10.1016/j.actatropica.2017.06.015.
75. Rahman S.M.M., Song H.B., Jin Y., Oh J.K., Lim M.K., Hong S.T. et al. Application of a loop-mediated isothermal amplification (LAMP) assay targeting cox1 gene for the detection of *Clonorchis sinensis* in human fecal samples. *PLoS Negl. Trop*. *Dis*. 2017;11(10):e0005995. DOI: 10.1371/journal.pntd.0005995.
76. Ghodsian S., Rouhani S., Fallahi S., Seyyedtabaei S.J., Taghipour N. Detection of spiked *Fasciola hepatica* eggs in stool specimens using LAMP technique. *Iran. J. Parasitol*. 2019;14(3):387–393.
77. Mesquita S.G., Neves F.G.D.S., Scholte R.G.C., Carvalho O.D.S., Fonseca C.T., Caldeira R.L. A loop-mediated isothermal amplification assay for *Schistosoma mansoni* detection in *Biomphalaria spp.* from schistosomiasis-endemic areas in Minas Gerais, Brazil. *Parasit. Vectors*. 2021;14(1):388. DOI: 10.1186/s13071-021-04888-y.
78. Cheng G., Li X., Qin F., Xu R., Zhang Y., Liu J. et al. Functional analysis of the Frzb2 gene in *Schistosoma japonicum*. *Vet. Res.* 2019;50(1):108. DOI: 10.1186/s13567-019-0716-1.
79. Pillay P., Downs J.A., Changalucha J.M., Brienen E.A.T, Ramarokoto C.E., Leutscher P.D.C. et al. Detection of S*chistosoma* DNA in genital specimens and urine: A comparison between five female African study populations originating from *S. haematobium* and/or *S. mansoni* endemic areas. *Acta. Trop.* 2020;204:105363. DOI: 10.1016/j.actatropica.2020.105363.
80. Diab R.G., Mady R.F., Tolba M.M., Ghazala R.A. Urinary circulating DNA and circulating antigen for diagnosis of schistosomiasis mansoni: a field study. *Trop. Med. Int. Health.* 2019;24(3):371–378. DOI: 10.1111/tmi.13193.
81. Schols R., Carolus H., Hammoud C., Mulero S., Mudavanhu A., Huyse T. A rapid diagnostic multiplex PCR approach for xenomonitoring of human and animal schistosomiasis in a 'One Health' context. *Trans. R. Soc. Trop. Med. Hyg.* 2019;113(11):722–729. DOI: 10.1093/trstmh/trz067.
82. Pumpa S., Phadungsil W., Grams R., Martviset P., Ruang-Areerate T., Mungthin M. et al. Improvement of a PCR-based method for the detection of *Opisthorchis viverrini* eggs in human stool samples by targeting internal transcribed spacer-2 (ITS-2), cytochrome oxidase subunit 1 (*cox1*), and cytochrome b (*cyb*). *J. Parasit. Dis.* 2021;45(2):474–478. DOI: 10.1007/s12639-020-01329-y.
83. Ullah H., Arbab S., Khan M.I.U., Li K., Muhammad N., Suleman Qadeer A. et al. Circulating cell-free mitochondrial DNA fragment: A possible marker for early detection of *Schistosoma japonicum*. *Infect. Genet. Evol.* 2021;88:104683. DOI: 10.1016/j.meegid.2020.104683.
84. Cnops L., Huyse T., Maniewski U., Soentjens P., Bottieau E., van Esbroeck M. et al. Acute schistosomiasis with a *Schistosoma mattheei* × *Schistosoma haematobium* hybrid species in a cluster of 34 travelers infected in South Africa. *Clin. Infect. Dis.* 2021;72(10):1693–1698. DOI: 10.1093/cid/ciaa312.
85. Meningher T., Lerman G., Regev-Rudzki N., Gold D., Ben-Dov I.Z., Sidi Y. et al Schistosomal microRNAsiIsolated from extracellular vesicles in sera of infected patients: a new tool for diagnosis and follow-up of human schistosomiasis. *J. Infect. Dis*. 2017;215(3):378–386. DOI: 10.1093/infdis/jiw539.
86. Mu Y., Cai P., Olveda R.M., Ross A.G., Olveda D.U., McManus D.P. Parasite-derived circulating microRNAs as biomarkers for the detection of human *Schistosoma japonicum* infection. *Parasitology.* 2020;147(8):889–896. DOI: 10.1017/S0031182019001690.
87. Huang W., Gu M., Cheng W., Zhao Q.P., Ming Z., Dong H. Characteristics and function of cathepsin L3 from *Schistosoma japonicum*. *Parasitol. Res.* 2020;119(5):1619–1628. DOI: 1 0.1007/s00436-020-06647-x.
88. Oyeyemi O.T., Corsini C.A., Gonçalves G., de Castro Borges W., Grenfell R.F.Q. Evaluation of schistosomula crude antigen (SCA) as a diagnostic tool for *Schistosoma mansoni* in low endemic human population. *Sci. Rep.* 2021;11(1):10530. DOI: 10.1038/s41598-021-89929-3.
89. Halili S., Grant J.R., Pilotte N., Gordon C.A., Williams S.A. Development of a novel real-time polymerase chain reaction assay for the sensitive detection of *Schistosoma japonicum* in human stool. 2021;15(10):e0009877. DOI: 10.1371/journal.pntd.0009877.
90. Wang H., Itoh S., Matsumoto Y., Nishie A., Kurihara T., Shimagaki T. et al. Surgically resected hepatic mass caused by fascioliasis. *Clin. J. Gastroenterol*. 2021;14(2):662–667. DOI: 10.1007/s12328-021-01339-0.
91. Valluru B., Zhou Z., Sah D., Du W., Ali M.O., Adam A.A. et al. Analysis of CT characteristics in the diagnosis of Schistoso-

ma japonicum associated appendicitis with clinical and pathological correlation: a diagnostic accuracy study. *Jpn. J. Radiol.* 2020;38(2):178–191. DOI:10.1007/s11604-019-00905-4.
92. Castillo-Fernández N., Soriano-Pérez M.J., Lozano-Serrano A.B., Sánchez-Sánchez J.C., Villarejo-Ordóñez A., Cuenca-Gómez J.A. et al. Usefulness of ultrasound in sub-saharan patients with a serological diagnosis of schistosomiasis. *Infection.* 2021;49(5):919–926. DOI:10.1007/s15010-021-01612-x.
93. Pershina A.G., Ivanov V.V., Efimova L.V., Shevelev O.B., Vtorushin S.V., Perevozchikova T.V. et al. Magnetic resonance imaging and spectroscopy for differential assessment of liver abnormalities induced by Opisthorchis felineus in an animal model. *PLoS Negl. Trop. Dis*. 2017;11(7):e0005778. DOI: 10.1371/journal.pntd.0005778.
94. Lu C.Y., Zhao S., Wei Y. Cerebral schistosomiasis: MRI features with pathological correlation. *Acta. Radiol*. 2021;62(5):646–652. DOI: 10.1177/0284185120934475.
95. Ebigbo A., Kahn M., Zellmer S., Messmann H. Advanced endoscopic imaging of colonic schistosomiasis. *Endoscopy.* 2021;53(7):E251–E252. DOI: 10.1055/a-1252-2637.
96. Pereira C.L.D., Santos J.C., Arruda R.M., Rodrigues M.L., Siqueira E.S., Lemos R.S. et al. Evaluation of *Schistosomiasis mansoni* morbidity by hepatic and splenic elastography. *Ultrasound Med. Biol*. 2021;47(5):1235–1243. DOI: 10.1016/j.ultrasmedbio.2021.01.022.
97. Sotillo J., Pearson M.S., Becker L., Mekonnen G.G., Amoah A.S., van Dam G. et al. In-depth proteomic characterization of *Schistosoma haematobium*: Towards the development of new tools for elimination. *PLoS Negl. Trop. Dis*. 2019;13(5):e0007362. DOI: 10.1371/journal.pntd.0007362.
98. Sotillo J., Pearson M.S., Loukas A. Trematode genomics and proteomics. *Adv. Exp. Med. Biol.* 2019;1154:411–436. DOI: 10.1007/978-3-030-18616-6_13.
99. Aksorn N., Roytrakul S., Kittisenachai S., Leelawat K., Chanvorachote P., Topanurak S. et al. Novel potential biomarkers for *Opisthorchis viverrini* infection and associated cholangiocarcinoma. *In Vivo.* 2018;32(4):871–878. DOI: 10.21873/invivo.11321.
100. Reamtong O., Simanon N., Thiangtrongjit T., Limpanont Y., Chusongsang P., Chusongsang Y. et al. Proteomic analysis of adult Schistosoma mekongi somatic and excretory-secretory proteins. *Acta. Trop*. 2020;202:105247. DOI: 10.1016/j.actatropica.2019.105247.

Authors information

Perina Ekaterina A. – Junior Researcher, Center for Preclinical Trials, Central Research Laboratory, Siberian State Medical University, Tomsk, catherineperina@gmail.com, https://orcid.org/0000-0002-4273-8228

Khmelevskaya Ekaterina S. – Cand. Sci. (Med.), Researcher, Center for Biological Research, Central Research Laboratory, Siberian State Medical University, Tomsk, kat.hmelevsk@gmail.com, https://orcid.org/0000-0003-1776-4149

Fedorova Olga S. – Dr. Sci. (Med.), Professor, Vice-Rector for Science and Post-Graduate Studies, Siberian State Medical University, Tomsk, olga.sergeevna.fedorova@gmail.com, https://orcid.org/0000-0002-7130-9609

Ivanov Vladimir V. – Cand. Sci. (Biology), Associate Professor, Head of the Center for Preclinical Trials, Central Research Laboratory, Siberian State Medical University, Tomsk, ivanovvv1953@gmail.com, https://orcid.org/0000-0003-3326-729X

(✉) **Perina Ekaterina A.,** catherineperina@gmail.com

Received 02.11.2022;
approved after peer review 14.11.2022;
accepted 07.12.2022