

Global prevalence status of avian schistosomes: A systematic review with meta-analysis

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ABSTRACT

Objectives: Human cercarial dermatitis (HCD) is a water-borne zoonotic parasitic disease. Cercariae of the avian schistosomes of several genera are frequently recognized as the causative agent of HCD. Various studies have been performed regarding prevalence of bird schistosomes in different regions of the world. So far, no study has gathered and analyzed this data systematically. The aim of this systematic review and meta-analysis study was to determine the prevalence of avian schistosomes worldwide.

Methods: Data were extracted from six available databases for studies published from 1937 to 2017. Generally, 41 studies fulfilled the inclusion criteria and were used for data extraction in this systematic review. Most of studies have been conducted on the family Anatidae.

Results: The overall prevalence of avian schistosomes was estimated to be 34.0% (95%CI, 28–41%) around the world. Furthermore, results displayed that, *Allobilharzia visceralis* and *Trichobilharzia* spp. had the highest frequency and their prevalence in the birds was 50.0% (95% CI, 3.0%–97.0%) and 32.0% (95% CI, 21.0%–0.36%), respectively. The results showed that the prevalence of avian schistosomes was 43.0% (95% CI, 29% - 56%) in the US and 38.0% (27.0% -50.0%) in Europe, which were higher than other continents, respectively.

Conclusions: The prevalence of 34% shows that the bird schistosomes are very common zoonotic worms among aquatic birds in the world. Also, this study shows the importance of avian schistosome research when facing animal and human health of the future.

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1. Introduction

The bird schistosomes are a group of blood flukes (Platyhelminthes, Digenea). They contain the largest clade of the family Schistosomatidae that includes ten genera: *Dendrobilharzia*, *Gigantobilharzia*, *Allobilharzia*, *Austrobilharzia*, *Anserobilharzia*, *Trichobilharzia*, *Bilharziella*, *Macrobilharzia*, *Ornithobilharzia* and *Jilinobilharzia*. In the two-host life cycle (fresh water snails as intermediate hosts and aquatic birds as definitive hosts), they develop as adults within venous and arterial vessels or nasal tissue of their bird host. Bird schistosomes of the genus *Trichobilharzia* are categorized as nasal and visceral groups depending on their target tissue within the final hosts (Horák et al., 2002; Brant et al., 2006). Cercariae of the bird schistosomes released from intermediate hosts are recognized as the great causative agent of human cercarial dermatitis (HCD) or Swimmer's itch which is considered an emerging disease in various parts of the World (de Gentile et al., 1996). Experiments have demonstrated that avian schistosomes can migrate and partly develop in other bodies of their non-specific mammalian hosts, causing serious health risks. Larvae of different visceral avian schistosome have been detected in the lungs of experimentally infected monkeys and rodents (Horák et al., 2002), and foot paralysis has been seen in mice infected with the neurotropic species *Trichobilharzia regenti* (Horák et al., 1999; Hrádková and Horák, 1999). Therefore, as a result of these experiments, it is thus considered conceivable that avian schistosomes may be responsible for some nervous or pulmonary symptoms in humans. HCD occurs worldwide, for example Iceland, Austria, UK, The Netherlands, Iran, Chile, China and USA (Horák et al., 2002; Farahnak and Essalat, 2003; Brant, 2007; Valdovinos and Balboa, 2008; Hörweg et al., 2006; Skírnisson et al., 2009; Žbikowska, 2003). The incidence of bird schistosomes and dermatitis caused by them depends on the presence of appropriate intermediate and final hosts. Many of the migratory bird host species used by schistosomes, particularly *Trichobilharzia*, are in the family Anatidae. Furthermore, species in the snail families Lymnaeidae, Physidae, and Planorbidae are most often used as the intermediate hosts of bird schistosomes (Brant and Loker, 2009a; Brant and Loker, 2009b; Marszewska

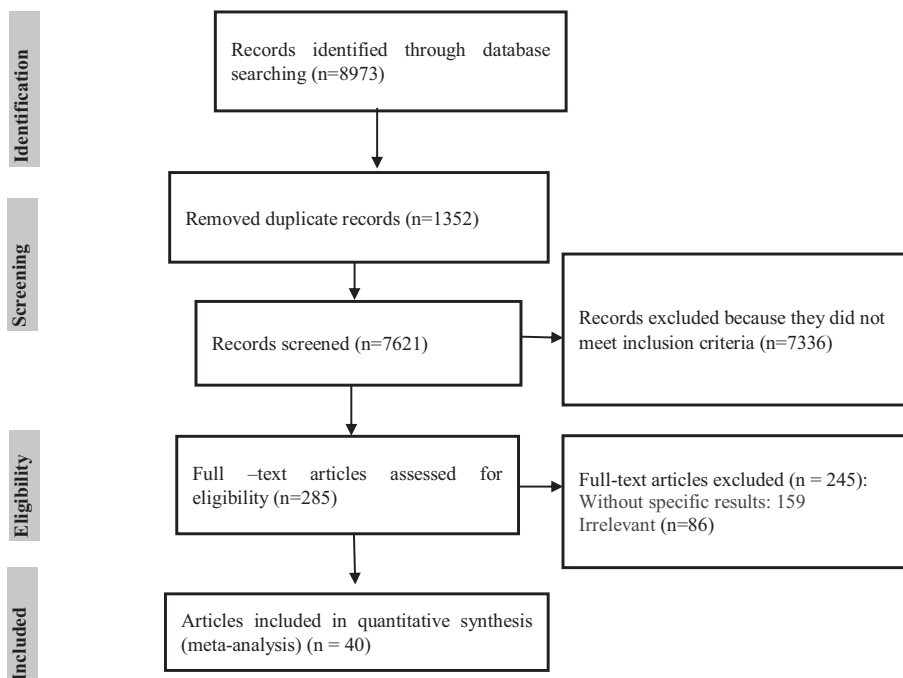


Fig. 1. PRISMA flowchart describing the study design process.

et al., 2018). While research papers document the global occurrence and burden of HCD, there are no studies that document a systematic review on the subject of the prevalence of bird schistosomes on a global scale. Therefore, it is the purpose of this study to estimate the world prevalence of avian schistosomes and thus HCD.

2. Methods

2.1. Search approach

For studies published between 1937 (based on preliminary search) and 2017, six English language databases (PubMed, Web of Science, Ebsco, Science Direct, Google Scholar and Scopus) were searched. The search terms were “Human cercarial dermatitis”, “bird schistosomes”, “avian schistosomes”, “nasal schistosomes”, “visceral schistosomes” “Pseudobilharziella”, “Trichobilharzia”, “Allobilharzia”, “Dendritobilharzia”, “Gigantobilharzia”, “Austroilharzia”, “Anserobilharzia”, “Bilharziella”, “Macrobilharzia”,

Table 1

The characteristics of selected studies for the meta-analysis.

Author	Year	Country	Continent	Methods	No. examined	No. Infected	Ref.
McLeod J. A	1937	Canada	Americas	Morphology	30	18	(McLeod, 1937)
Cheatum E. L	1941	USA	Americas	Morphology	72	41	(Cheatum, 1941)
Brackett S	1942	USA	Americas	Morphology	72	25	(Brackett, 1942)
Guth BD	1979	USA	Americas	Morphology	1244	169	(Guth et al., 1979)
Blair D	1979	Australia	Oceania	Morphology	548	310	(Blair and Ottesen, 1979)
Strohm B. C	1981	USA	Americas	Morphology	23	7	(Blankespoor and Meier, 1981)
Pence D.B	1982	USA	Americas	Morphology	5	5	(Pence and Rhodes, 1982)
Appleton C.C	1983	Western Australia	Oceania	Morphology	31	25	(Appleton, 1983)
Palmer. D	1984	Switzerland	Europe	Morphology	20	16	(Palmer and Ossent, 1984)
Appleton C·C	1986	South Africa	Africa	Morphology	1554	264	(Appleton, 1986)
Athari A	1990	Iran	Asia	Morphology	188	16	(Athari et al., 1990)
Brent R. L	1995	USA	Americas	Morphology	202	78	(Loken et al., 1995)
Barber. E	1995	USA	Americas	Morphology	96	68	(Barber and Cairra, 1995)
Kolarova. L	1997	Czech Republic	Europe	Morphology	2051	239	(Kolarova et al., 1997)
Martini F. S	1999	Spain	Europe	Morphology	8	6	(Simon-Martin and Simon-Vicente, 1999)
Rudolfova J	2002	Czech Republic	Europe	Morphology	54	13	(Rudolfova et al., 2002)
Bayssade-dufour C	2006	France	Europe	Morphological and molecular	31	11	(Bayssade-Dufour et al., 2006)
Davis NE	2006	New Zealand	Oceania	Morphology	38	27	(Davis, 2006)
Kolářová L	2006	Iceland	Europe	Morphological and molecular	27	7	(Kolářová et al., 2006)
Athari A	2006	Iran	Asia	Morphology	138	25	(Rostami-Jalilian, 2006)
Rudolfova J	2007	Czech Republic	Europe	Morphology	102	23	(Rudolfová et al., 2007)
Rudolfova J	2007	Poland	Europe	Morphology	73	21	(Rudolfová et al., 2007)
Brant SV	2007	USA	Americas	Morphological and molecular	13	12	(Brant, 2007)
Jouet D	2008	France	Europe	Morphology	115	76	(Jouet et al., 2008)
Jouet D	2009	France	Europe	Morphology	399	174	(Jouet et al., 2009)
Brant SV	2009	USA	Americas	Morphological and molecular	378	92	(Brant and Loker, 2009b)
Skírnisson K	2009	Iceland	Europe	Morphological	110	39	(Skírnisson and Kolářová, 2008)
Jouet D	2010	Iceland France	Europe	Morphological and molecular	373	150	(Jouet et al., 2010)
Mahdavi SA	2012	Iran	Asia	Morphology	110	15	(Mahdavi et al., 2013)
Maleki SH	2012	Iran	Asia	Molecular techniques	45	12	(Maleki et al., 2012)
Gohardehi SH	2013	Iran	Asia	Morphology	260	41	(Gohardehi et al., 2013)
Birmani NA	2013	Pakistan	Asia	Morphology	101	11	(Birmani et al., 2013)
Kolářová L	2013	Iceland	Europe	molecular techniques	19	14	(Kolářová, 2013)
Aldhoun JA	2014	South African	Africa	Morphology	555	45	(Aldhoun and Horne, 2015)
Jouet D	2015	Iceland	Europe	Morphological and molecular	46	3	(Joue et al., 2015)
Jouet D	2015	Iceland	Europe	Morphological and molecular	80	36	(Joue et al., 2015)
Jouet D	2015	France	Europe	Morphological and molecular	29	11	(Joue et al., 2015)
Fakhar M	2016	Iran	Asia	Morphological and molecular	508	45	(Fakhar et al., 2016)
Prüter H	2017	Germany	Europe	molecular techniques	106	35	(Prüter et al., 2017)
Hayashi k	2017	Japan	Asia	molecular techniques	13	4	(Hayashi, 2017)
Brant S. V	2017	Argentina	Americas	molecular techniques	40	1	(Brant et al., 2017)

"*Ornithobilharzia*" and "*Jilnobilharzia*" alone or combined together using "OR" and/or "AND.". The PRISMA diagram of the study plan is shown in Fig. 1.

2.2. Paper assortment

Included Studies were identified by two reviewers (EK and SD) independently and confirmed by a third reviewer (MF). Studies that met the inclusion criteria were included in this survey: (1) Full text articles available online (2) cross-sectional studies that estimated the prevalence of bird schistosomes with different diagnostic methods including morphological and molecular techniques (3) published papers in English. Duplicates, case reports, case series, experimental studies, mammalian schistosomes, published papers in other language and papers with unclear result section were excluded. In order to ensure that articles were not overlooked or not found in searches, the references of each paper were manually screened.

2.3. Quality assessment

The STROBE questionnaire was used for the determination of article quality. The questionnaire contains 22 questions with a maximum of 31 score. The score under 7.5 considered poor quality of study (Von Elm et al., 2007). For all eligible papers in this systematic review and meta-analysis, the obtained score was 18.

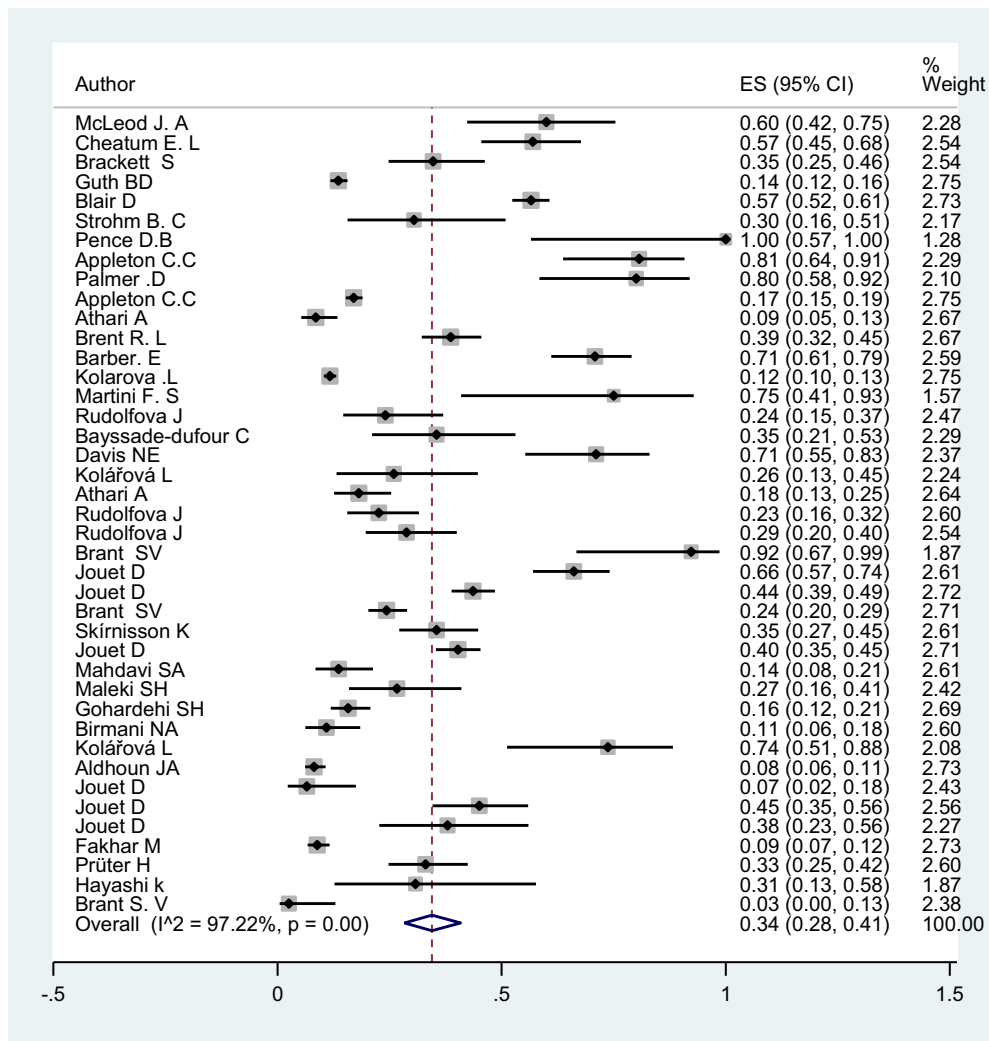


Fig. 2. Forest plot of prevalence of bird schistosomes. The middle-point in each line indicates the prevalence and the length of each line indicates the 95% confidence interval of each study. Diamonds indicate the 95% confidence interval for pooled prevalence.

2.4. Data extraction

Data were extracted from papers including author (s), publication year, type of parasite, geographical area of the study, and number of examined samples, number of positive samples, prevalence rate, and laboratory technique used for the study and entered into an Excel sheet (Table 1).

2.5. Meta-analysis

For each study, the prevalence of bird schistosomes (the number of current positive of infection cases divided to total number of sample) and standard error ($SE = \sqrt{\frac{P(1-P)}{n}}$) were calculated.

We used forest plots for estimating pooled effect sizes and the effect of each study, with 95% confidence intervals (95% CI), to provide a visual summary of the data. To evaluate heterogeneity among studies that used common approaches we used the Cochran Q-test (p -value < .1) and the I-squared index, with I^2 values between 25% and 50%, between 50% and 75% and above 75% as thresholds for low, moderate, and high heterogeneity, respectively. When heterogeneity was present we used a random effects model (DerSimonian-Laird model); otherwise a fixed effects model (Mantel-Haenszel) used to compute overall effects. Sub-group analysis was used to evaluate the association between effect size and characteristics such as continent, parasite species and method. Potential publication bias was explored using funnel plot and Egger's test which evaluated whether precision of studies is related to the magnitude of their effect size. A trim-and-fill method was performed to detect the effect of missing studies on the overall effect of meta-analysis. All statistical analyses were done with the Stata software, v. 14 (Stata Corp LP, College Station, Texas, USA).

3. Results

Our initial electronic search identified 8973 studies using our search strategy. Of those, 7336 studies were deemed ineligible after title screening. This narrowed the pool down to 285 potential studies that were then reviewed via the abstract and full text. The results of that screening excluded 245 studies because they did not meet inclusion criteria. Finally 40 articles (41 studies) were selected for inclusion in the meta-analysis (Fig. 1). From these 41 studies, the total number of birds included in meta-analysis was 9894 birds in which 2694 of them were infected. The most of the studies (17 studies) were performed in Europe.

Moreover, regarding detection method of bird schistosomes, morphological examination in 27 studies, both morphological and molecular in 9 and molecular method in 5 studies have been found (Table 1).

Based on a random effect meta-analysis ($I^2 = 97.20\%$, $P < 0.001$) the pooled prevalence of bird schistosomes among examined ducks was estimated 34.0% (95%CI: 28–41%) which it was significantly difference from $ES = 0$ ($z = 16.80$, $P < .001$) (Fig. 2).

The results of subgroup analysis showed that bird schistosomes in Americas (43%) and Europe (34%) were higher than those in other regions of the world. Prevalence of bird schistosomes by morphological examination was 36.0% (95%CI: 28.0–44.0%), molecular and morphological 32.0% (95%CI: 19.0–46.0%) and molecular was 30.0% (95%CI: 11.0–53.0%).

Allobilharzia visceralis (50%) and *Trichobilharzia* spp. (35%) had the higher prevalence than other schistosome species (Table 2).

Both Funnel plot and the results of Egger's test ($t = 2.57$, $P = .001$) showed that there is an evidence of substantial publication bias (Figure 3).

After applying fill-and-trim method, the pooled estimate of prevalence found 34.0% (95%CI: 28–41%) which there is no difference from the pooled estimate in Fig. 2.

Table 2

Subgroup meta-analysis to compare prevalence of global bird schistosomes.

	Subgroup	n	Prevalence (%) (95%CI)	I-square (%)	p
Continent	Americas	11	43.0(29.0–56.0)	96.2	<0.001
	Oceania	3	18.0(10.0–17.0)	81.3	
	Asia	8	13.0(10.0–18.0)	73.1	
	Europe	17	38.0(27.0–50.0)	87.3	
	Africa	2	14.0(13.0–16.0)	70.8	
Method	Morphological	27	36.0 (28.0–44.0)	97.6	0.79
	Morphological and molecular	9	32.0 (19.0–46.0)	95.4	
	Molecular	5	30.0 (11.0–53.0)	90.2	
	Bird schistosomes	6	31.0 (18.0–46.0)	96.50	
^a Parasite species	<i>Trichobilharzia regenti</i>	6	21.0 (6.0–37.0)	96.7	0.58
	<i>Allobilharzia visceralis</i>	4	50.0(0.30–0.97)	95.3	
	<i>Trichobilharzia sp</i>	12	32.0(0.21–0.36)	97.9	

^a For some subgroups there was only one study.

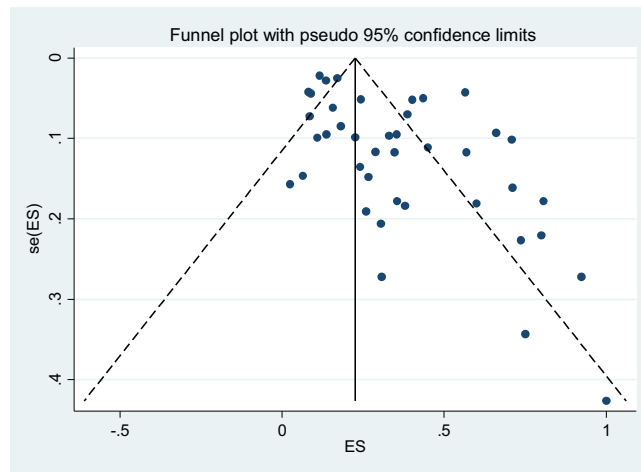


Fig. 3. Funnel plot for global prevalence of bird schistosomes.

4. Discussion

HCD is a skin condition that affects people in water bodies all over the world for both recreation and occupation. HCD can temporarily disable the inflicted person by secondary infections as a result of the constant scratching. HCD reduces the recreational use of water bodies and can lead to economic losses for those areas [57, 58]. Clearly, the avian schistosomes are responsible for the outbreaks of reported HCD around different parts of the world such as Americas, Western Europe, Asia (Kolářová, 2007; Horák et al., 2015; Marcogliese, 2001). We have conducted a comprehensive systematic review of studies that examined the prevalence of schistosomes in bird hosts worldwide. Our findings show that the total sum prevalence of avian schistosomes worldwide is 34.0% (95%CI, 28%–41%). This global rate is high, and likely higher if more countries had a history of bird examinations for parasites. Thus, it is not a local problem, but a global one with high prevalence and thus likely neglected.

Prevalence of bird schistosomes in different countries of the world is most likely related to several issues such as climate changes and land alterations, changes in the behavioral and physiological patterns and species compositions of avian hosts, changes in phenology of aquatic migratory birds to sedentary. Climate changes affect behavior of migratory birds having a key role in spread of avian schistosomes, as well, lead to variation in seasonal / temperature dependent activities in the snail and schistosomes. These changes affect the frequency of transmission of parasites and severity of infection (Skírnisson et al., 2009; Marcogliese, 2001; Cotton, 2003; Suter, 1994).

The highest and the lowest prevalence of bird schistosomes were recorded in Americas, 41% and Asia, 13%. High prevalence of birds schistosomes in Americas may attribute to the fact that high local concentration of and the close relationship between birds and snails may facilitate the transmission of parasites. The occurrence of this parasite may be influenced by the seasonal migration of their bird hosts and the susceptibility of local snail populations (Brant, 2007; Brant and Loker, 2009b). The fact that most studies have been carried out in Canada, USA, and Western Europe, may be another reason may be another reason for the high prevalence of avian schistosomes in Americas. The northern latitudes also have the highest summer concentration of wild migratory Anatidae, so it is expected that HCD will be high there.

In addition, low prevalence rate in Asia despite the large numbers and diversity of migratory anatid birds, especially in Iran may be mostly due to a low priority among researchers. Due to the wildlife conservation by the environmental organization, access to study the parasites of these birds is very difficult and unlike other countries such as USA and Canada, there is not a widespread hunting season to provide birds to examine. Likewise, the natural habitat of these migratory birds is limited, mostly located in Mazandaran Province, northern Iran.

Moreover, in Europe, France and Iceland report a high prevalence of bird schistosomes in areas with suitable natural conditions for bird schistosomes (populations of suitable snails and bird hosts). In France, there are reported cases of HCD in various fresh-water areas (de Gentile et al., 1996; Gay et al., 1999; Marszewska et al., 2016; Caumes et al., 2003) and researchers there are concerned with the distribution and diversity of bird schistosomes due to the position of this country along the migratory flyways of the bird hosts. Bird schistosomes in relationship with the increasing populations of protected water birds could clarify the increased hazard of HCD in these recreational regions (Jouet et al., 2009).

A review of studies shows that different genera of bird schistosomes play a role in the outbreaks of HCD. Kolářová et al. (2013) referred to the known causes of HCD around the world such as *Trichobilharzia*, *Gigantobilharzia* and *Austrobilharzia*. *Trichobilharzia* is the largest genus of Schistosomatidae family that covers >40 species of bird schistosomes (Horák et al., 2002). Usually, bird schistosomes were reported from geese, ducks and swans (Kolářová et al., 2013; Fain, 1955; Fain, 1956; ITO, 1960a).

Iran is located on the migration airways of water birds. Accordingly, Iran's wetlands are a temporary or permanent refuge for many migratory birds and due to specific climatic conditions and abundant food resources, Mazandaran province in northern Iran is considered a unique region for wintering of these birds. This species has been isolated from *Anas clypeata* and *Anas*

platyrrhynchos in northern Iran. In a study conducted in the Mazandaran Province, Fakhar et al. (2016) reported that isolated eggs from the nasals of *A. clypeata* and *Anas platyrhynchos* grouped in a sister clade to the European *Trichobilharzia regenti*.

Pulmonate snails such as those in the families Planorbidae, Physidae or Lymnaeidae are commonly used as intermediate hosts. It is interesting that host of avian and mammalian schistosomes causing HCD are *Indoplanorbis* and *Biomphalaria* in the Planorbidae family and *Stagnicola* in the Lymnaeidae family (Fain, 1955; Fain, 1956; ITO, 1960a; ITO, 1960b).

Regulations on the collection of bird hosts had led many to search for bird schistosomes in their feces. However, this method will detect visceral schistosomes (although if only one species is found, it cannot be ruled out that there is a second species), but not the presence of nasal schistosomes where eggs are discharged in the mucosa or hatch when the bird has its bill in the water to feed. However, birds can be surveyed throughout the year and important outcomes can be achieved by necropsy of the birds in the hunting season. It is suggested that mostly the blood system and the surrounding tissue of the preferred organs should be examined, since visceral schistosomes and their eggs are frequently found in the mesentery veins, intestinal wall, liver, kidney, heart, and lung. Nasal worms can be recovered from the nasal tissues and different parts of the CNS (Kolářová et al., 2010). It is difficult to identify cercariae to species since diverse species or genera can be morphologically similar and thus difficult to determine under the microscope (Joue et al., 2015). Future studies on the morphology of cercariae in addition to genetic work would aid in identifying these worms in the field or lab, at least to a species group. In addition to morphological information, other supporting data, for example, host species, location of the worms and their eggs, can help to determine the species (Kolářová et al., 2010). The researchers confirmed that combination of molecular methods with morphological examination of flukes facilitates taxonomical determination, life-cycle description and their geographic distribution (Rudolfova et al., 2002). Also, molecular methods may be used to identify precisely and discover phylogenetic relationships as well as make connections between adults and larvae (Brant and Loker, 2009b; Joue et al., 2015; Aldhoun et al., 2009).

Evidence shows that the emergence of HCD caused by bird schistosomes results from dispersal of schistosomes to new areas and an increased access of the snail hosts. Long term research of hosts and schistosomes in established and new endemic regions are essential to comprehend the host range and patterns of utilization of these hosts by schistosomes over time and space. Considering the infection of birds and outbreaks of HCD, it is essential for the environmental and agricultural organization and authorities of health, to collaborate in order to control this disease. Also, hygiene education should be given to those who are at *high risk* of HCD because of their occupation, *such* as rice farmers. Although these schistosomes do not establish themselves in mammals, therefore, do not cause a transmissible infection, we believe it is serious not to underestimate mammalian infections by bird schistosomes. These parasites, with their unrecognized life cycles and adaptations to different vertebrates, display an unseen region of parasitology.

In conclusion, to the best of our understanding, this is the first systematic review and meta-analysis that provides a comprehensive view of the global status of avian schistosomes in their final hosts. As a whole according to the presented data it seems that avian schistosomes are the most neglected of the neglected zoonotic parasitic worm among aquatic birds in the world. So, spreading of avian schistosomes to new areas, local abundance of the snail hosts and the use of water reservoirs for recreational and agricultural purposes, may contribute to a higher number of outbreaks of cercarial dermatitis in the world. Thus, it is suggested that the distribution and abundance of this illness should be considered in detail and appropriate trending must be performed to evaluate the outbreaks of cercarial dermatitis globally.

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Declaration of competing interest

Authors declare that have no competing interests.

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