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REVIEW

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Prevalence of urinary schistosomiasis in women: a systematic review and meta-analysis of recently published literature (2016–2020)

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Abstract

Background: Urinary schistosomiasis is a serious threat in endemic territories of Africa and the Middle East. The status of female urinary schistosomiasis (FUS) in published literature between 2016 and 2020 was investigated.

Methods: A systematic search in PubMed, Scopus, Google Scholar, and Web of Science, based on the 'Preferred Reporting Items for Systematic Reviews and Meta-analyses' checklist, and a meta-analysis using random-effects model to calculate the weighted estimates and 95% confidence intervals (95% CIs) were done.

Results: Totally, 113 datasets reported data on 40,531 women from 21 African countries, showing a pooled prevalence of 17.5% (95% CI: 14.8–20.5%). Most studies (73) were performed in Nigeria, while highest prevalence was detected in Mozambique 58% (95% CI: 56.9–59.1%) (one study). By sample type and symptoms, vaginal lavage [25.0% (95% CI: 11.4–46.1%)] and hematuria 19.4% (95% CI: 12.2–29.4%) showed higher FUS frequency. Studies using direct microscopy diagnosed a 17.1% (95% CI: 14.5–20.1%) prevalence rate, higher than PCR-based studies 15.3% (95% CI: 6.1–33.2%). Except for sample type, all other variables had significant association with the overall prevalence of FUS.

Conclusions: More studies are needed to evaluate the true epidemiology of FUS throughout endemic regions.

Keywords: Epidemiology, Urinary schistosomiasis, Women, Meta-analysis

Background

Schistosomiasis, due to trematodes of the genus *Schistosoma* (blood flukes), is a snail-transmitted helminthiasis and the third most degenerative tropical disease with substantial morbidity/mortality rates, particularly in low- and middle-income countries [1]. With about 800 million at-risk individuals, schistosomiasis afflicts over 250 million people in tropical and subtropical territories and renders approximately 70 million disability-adjusted life years [1–3]. In endemic areas such as sub-Saharan Africa morbidity is higher among school-aged children (60–80%) than adults (20–40%), with a mortality rate of 280,000 people [4]. Six species out of 24 recognized schistosomes result in disease in humans, comprising *Schistosoma haematobium* (*S. haematobium*) the causative agent of urogenital schistosomiasis (UGS), *S. japonicum*, *S. mansoni*, *S. intercalatum*, *S. mekongi* and *S. guineensis* as agents of hepato-intestinal disease [5]. In a public health perspective, Africa and the Mideast (*S. mansoni* and *S. haematobium*), Southeast Asia (*S. japonicum*) and

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Latin America (*S. mansoni*) are considered as the most distinguished geographical hotspots for schistosomiasis [6]. Adult paired worms would stay alive in host's blood stream for about 3–10 years and produce numerous spiny eggs, rendering chronicity and pathologic outcomes of the infection [7–9].

The putative signs and symptoms of UGS were initially ascribed about 1900 Before the Common Era (BCE), when hematuria was a common finding in Egyptian males, referred to as "menstruation" [10]. Infected planorbid snails, *Bulinus* spp., are intermediate hosts releasing motile furcocercous cercariae in surrounding water supplies. Following skin cercarial invasion and migration thorough lungs and liver, *S. haematobium* worms would finally lodge in the genitourinary venous complex, in particular bladder veins, where they mature and copulate therein [11]. Although harsh disease outcomes primarily arise from the T-cell mediated, granulomatous immune responses against tissue-deposited spiny eggs of schistosomes. Such lesions would represent manifestations comprising hematuria, dysuria, itching, pelvic pain, as well as the life-threatening squamous cell carcinoma of the urinary bladder [12, 13]. Additionally, *S. haematobium* is responsible of egg-induced pathological lesions and associated symptoms in both men and women [14, 15].

An active UGS could be detected through observation of eggs in urine sediments and/or tissue biopsies [16]. For the aim of determining hotspots and control strategies, World Health Organization (WHO) has recommended microscopic-based poly-carbonate filter examination for urinary eggs as well as dipstick assays for urinary heme detection [17, 18]. Serodiagnostic assays identifying antibodies against worm antigens may demonstrate valuable credibility in symptomatic travelers, whereas they usually fail to differentiate active or previous infections, unless those employing circulating antigens [19, 20]. An encouraging degree of sensitivity and specificity have been gained in utilization of molecular assays such as polymerase chain reaction (PCR) for schistosome detection in human serum and urine samples [21]. This method is, also, beneficial for vaginal lavage analysis, revealing the likely traits of the genital schistosomiasis [22].

A very large number of female urinary schistosomiasis (FUS) studies were performed during the last two decades [23]. The emphasis of the present systematic review and meta-analysis was on the published literature during the last 5 years (2016–2020), in order to define the latest status of FUS and its prevalence based on examined subgroups. The novel findings of the present study may alert clinicians to the prevalence of this important helminthiasis and its associated consequences on the genitourinary system of infected female individuals.

Methods

The present systematic review and meta-analysis was accomplished on the basis of Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [24] (Additional file 1).

Information sources and systematic searching

Major English databases including Scopus, PubMed, Web of Science and Google Scholar were systematically searched for articles evaluating the prevalence of FUS worldwide and published during a 5-year time period, from January 2016 until the end of 2020. This procedure was conducted using the following keywords alone or in combination, using advanced search option in most databases and Medical Subject Heading (MeSH) option in PubMed databases: "Urinary Schistosomiasis" AND "Prevalence" OR "Epidemiology" AND "Female" OR "Women" Or "Girl", where "AND" and/or "OR" are Boolean operators. Hand-searching of the bibliographic list of related papers was an additional task to more cover those papers not found via database exploration. Briefly, title and abstract of the literature were accurately reviewed (H.M. and M.F.), relevant papers were included, and upon duplicate removal, full-texts of eligible papers were retrieved (T.N.). Any disagreements were obviated by discussion and consensus with the leading researchers (M.SH and A.A.).

Inclusion/exclusion criteria and data collection

Specific inclusion criteria were determined in order to thoroughly gather relevant peer-reviewed cross-sectional studies and conference reports limited to women population in a 5-year time period (2016–2020). Only those papers with specified sample size and number of FUS-positive women, diagnosed either by microscopic, filtration, sedimentation and/or molecular techniques were included in current systematic review. Other study types (case reports, letters, reviews), studies evaluating animals or other Schistosomal infections, investigations without sample size/prevalence rates or lacking full-texts were all excluded from the present systematic review and meta-analysis. Finally, a pre-designed Microsoft Excel Spreadsheet® was used to extract the required information (E.J. and S.B.), as follows: first author's last name, publication year, start and end years of studies, study type, country, province, city, sample type, diagnostic method, sample size, positive number of infected cases and clinical symptoms (hematuria and proteinuria).

Quality assessment

In the present systematic review, the Newcastle–Ottawa scale was employed to assess the quality of included studies. Those papers with the scores of < 3.5, 3.6–5.25, and

5.26–7 were categorized as low-, moderate-, and high-quality papers, respectively [25].

Data synthesis and meta-analysis

Meta-analytical approach was done according to previous studies (S.B. and D.A.) using a random-effects model [26–28]. For all included studies, point estimates and their respective 95% confidence intervals (CIs) of weighted prevalence were calculated. Heterogeneity among these studies or variation in study outcomes was visualized by drawing forest plots, calculated by I^2 and Cochrane's Q tests [29, 30]. The subgroup analysis was performed based on year, country, sample type, symptoms and diagnostic methods. The presence of publication bias was estimated by using Egger's regression test [31]. This kind of bias, if present, skews the results and published reports are not a representative sample of the available evidence anymore. The trim-and-fill method was, also, used to "estimate the number of missing studies that might exist in a meta-analysis and the effect that these studies might have had on its outcome" [32]. P-values less than 0.05 were considered statistically significant. All analytical functions were applied by Comprehensive Meta-analysis (CMA) version 2.2. (Biostat Inc., USA).

Results

The flow diagram of the systematic search process and inclusion of relevant papers is shown in Fig. 1. Initially, 3537 datasets were identified through comprehensive database exploration. After removing duplicates (1821) and those with irrelevant title and abstract (1571), 145 datasets were finally assessed for eligibility. Among these, 35 datasets were excluded with reasons (review papers, theses, conference papers and studies with confusing data) and 3 additional datasets were added through manual searching. Therefore, 106 articles containing 113 datasets were finally included in our meta-analysis (Table 1) [33–139].

Finally, 113 datasets evaluating 40,531 individuals were included in the present review. Among these, 11,308 individuals were shown to be affected by FUS and based on the random-effects model meta-analysis, the pooled prevalence of FUS was 17.5% (95% CI: 14.8–20.5%). The included studies demonstrated a strong heterogeneity ($I^2 = 98.12\%$, $P < 0.01$) (Additional file 2). Publication

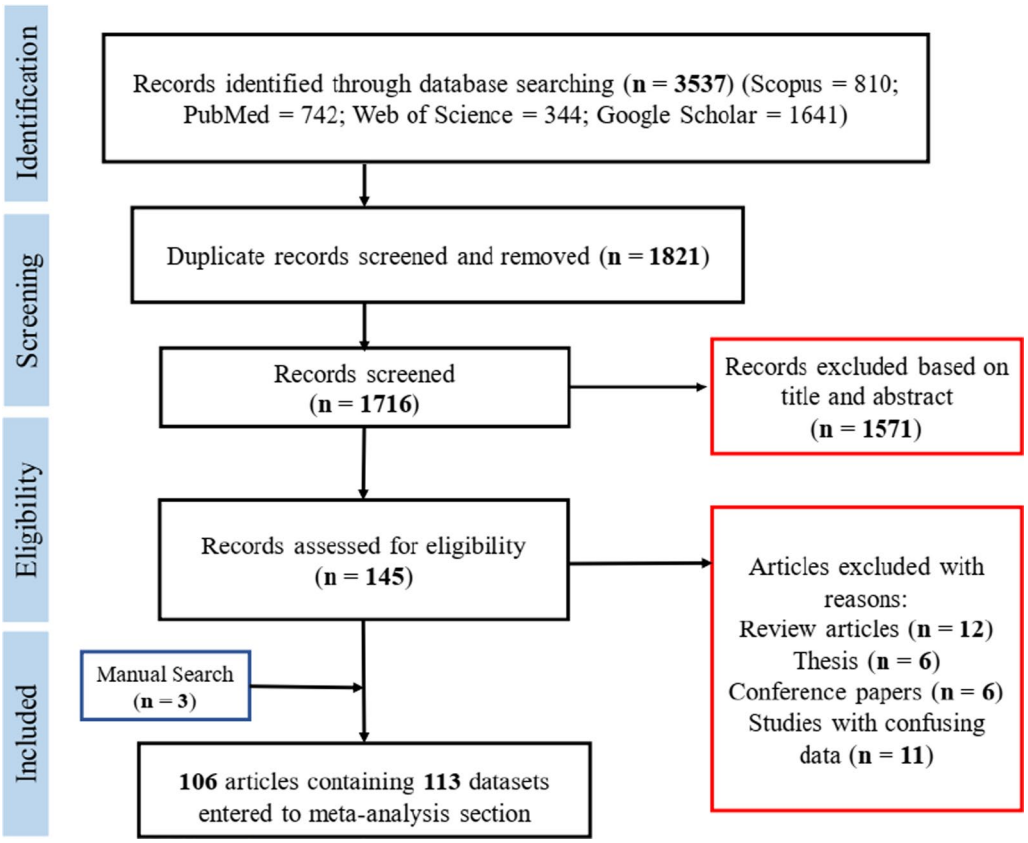

Fig. 1 PRISMA flow diagram describing included/excluded studies on FUS prevalence (2016–2020)

Table 1 Detailed characteristics of the included studies in the present systematic review and meta-analysis (2016–2020)

No.	References	Country	Province/city	Time of data collection	Sample type	Method	Sample size	Positive no	Quality assessment score
1	Awosolu, 2020 [56]	Nigeria	Osun and Kwara	2012	Urine	Filtrations and microscopic examination	258	122	5
2	Olayinka, 2020 [112]	Nigeria	Ogun	2015–2017	Urine	Microscopic examination	280	42	6
3	Awosolu, 2019 [55]	Nigeria	Ikota	2015	Urine	Microscopic examination	74	20	7
4	Otuneme, 2019 [118]	Nigeria	Ogun	2017	Urine	Microscopic examination	47	39	5
5	Muhammad, 2019 [101]	Nigeria	Sokoto	NR	Urine	Microscopic examination	107	47	5
6	Sule, 2019 [129]	Nigeria	Kano	NR	Urine	Microscopic examination	56	0	6
7	Idris, 2019 [87]	Nigeria	New-Bussa	NR	Urine	Microscopic examination	24	2	7
8	Geraji, 2019 [81]	Nigeria	Jalingo	2019	Urine	Microscopic examination	86	13	7
9	Adamu, 2019 [36]	Nigeria	Kaduna	2017	Urine	Microscopic examination	136	4	7
10	Ngwamah, 2019 [105]	Nigeria	Adamawa	NR	Urine	Microscopic examination	679	141	7
11	Aribodor, 2019 [51]	Nigeria	Enugu	2016	Urine	Microscopic examination	121	17	7
12	Sobande, 2019 [128]	Nigeria	Ogun	NR	Urine	Microscopic examination	84	40	6
13	Obisike, 2019 [110]	Nigeria	Benue	2017	Urine	Membrane filtration and (sedimentation) microscopic examination	84	20	5
14	Ahmed, 2019 [40]	Nigeria	Katsina	NR	Urine	(sedimentation) Microscopic examination	68	15	6
15	Aderibigbe, 2019 [37]	Nigeria	Kwara	NR	Urine	Microscopic examination	883	293	7
16	Noriode, 2018 [106]	Nigeria	Edo	NR	Urine	Microscopic examination	109	75	5
17	Bishop, 2016 [164]	Nigeria	Kaduna	NR	Urine	Microscopic examination	92	5	6
18	Mohammed, 2018 [95]	Nigeria	Sokoto	2016	Urine	Microscopic examination	51	18	5
19	Akinneye, 2018 [43]	Nigeria	Ondo	NR	Urine	Microscopic examination	202	22	5
20	Alabi, 2018 [46]	Nigeria	Ogun	NR	Urine	Microscopic examination	73	36	6
21	Damen, 2018 [68]	Nigeria	Plateau	NR	Urine	Microscopic examination	7	1	6
22	Yauba, 2018 [138]	Nigeria	Maiduguri	2014–2015	Urine	Microscopic examination	180	113	7
23	Abdulkareem, 2018 [34]	Nigeria	Kwara	NR	Urine	Microscopic examination	309	131	7
24	Oladeinde, 2018 [111]	Nigeria	Edo	2014	Urine	Microscopic examination	98	8	6
25	Ebong, 2018 [70]	Nigeria	Akwa Ibom	NR	Urine	Microscopic examination	199	5	7

Table 1 (continued)

No.	References	Country	Province/city	Time of data collection	Sample type	Method	Sample size	Positive no	Quality assessment score
26	Akeju Adebayo, 2018 [42]	Nigeria	Ondo	NR	Urine	Microscopic examination	1022	441	5
27	Oluwole, 2018 [114]	Nigeria	Ogun	2013	Urine	Microscopic examination	1034	43	6
28	Adewale, 2018 [38]	Nigeria	Ondo	NR	Urine	Microscopic examination	190	44	6
29	Nwachukwu, 2018 [107]	Nigeria	Imo	2014–2016	Urine	Test strip and filtration	1125	57	7
30	Nwachukwu, 2018 [108]	Nigeria	Ebonyi	2016–2017	Urine	Microscopic examination	254	8	7
31	Duwa, 2018 [69]	Nigeria	Kano	2018	Urine	Microscopic examination	105	8	5
32	Babagana, 2018 [57]	Nigeria	Borno	NR	Urine	Microscopic examination	180	31	7
33	Mohammed, 2018 [94]	Nigeria	Kebbi	2016	Urine	(Filtration) Microscopic examination	81	16	5
34	Oluwole, 2018 [114]	Nigeria	Ogun	NR	Urine and vainal lavage	Microscopic and gyneco-logic examina-tion	317	149	6
35	Kenneth, 2017 [92]	Nigeria	Edo	NR	Urine	Microscopic examination	76	6	7
36	Birma, 2017 [61]	Nigeria	Adamawa	NR	Urine	Microscopic examination	90	42	5
37	Amoo, 2017 [47]	Nigeria	Ogun	NR	Urine	Microscopic examination	160	61	6
38	Paul, 2017 [119]	Nigeria	Cross River	NR	Urine	Microscopic examination	140	24	5
39	Orpin, 2017 [116]	Nigeria	Katsina	NR	Urine	Microscopic examination	145	12	5
40	Ekanem, 2017 [71]	Nigeria	South-South	2011	Urine	Microscopic examination	177	27	6
41	Akpan, 2017 [45]	Nigeria	Cross River	NR	Urine	Microscopic examination	208	34	7
42	Elom, 2017 [73]	Nigeria	Ebonyi	NR	Urine	Microscopic examination	147	33	7
43	Akpan, 2017 [44]	Nigeria	Cross River	NR	Urine	Microscopic examination	122	1	7
44	Abubakar, 2017 [35]	Nigeria	Jigawa	2015	Urine	Microscopic examination	65	46	7
45	Dalhat, 2017 [67]	Nigeria	Sokoto	NR	Urine	Microscopic examination	140	41	7
46	Emmanuel, 2017 [75]	Nigeria	Benue	2014	Urine	Microscopic examination	207	77	6
47	Wokem, 2017 [135]	Nigeria	Abia	NR	Urine	Microscopic examination	570	215	7
48	Anorue, 2017 [49]	Nigeria	Ebonyi	2002–2003	Urine	Microscopic examination	1367	640	6
49	Orpin, 2016 [117]	Nigeria	Benue	NR	Urine	Microscopic examination	104	8	7
50	Onile, 2016 [115]	Nigeria	Eggua	2012–2013	Urine	Microscopic examination	178	45	7
51	Houmsou, 2016 [86]	Nigeria	Taraba	NR	Urine	Microscopic examination	529	231	5

Table 1 (continued)

No.	References	Country	Province/city	Time of data collection	Sample type	Method	Sample size	Positive no	Quality assessment score
52	Goodhead, 2016 [83]	Nigeria	River	NR	Urine	Microscopic examination	76	17	7
53	Usman, 2016 [133]	Nigeria	Bauchi	NR	Urine	Microscopic examination	300	58	7
54	Dahesh, 2016 [66]	Nigeria	Giza	2016	Urine	Microscopic examination	582	12	7
55	Igbeneghu, 2016 [88]	Nigeria	Osun	2016	Urine	Microscopic examination	154	60	7
56	Nafiu, 2016 [104]	Nigeria	Niger	2016	Urine	Microscopic examination	97	9	6
57	Abah, 2016 [33]	Nigeria	River	2016	Urine	Microscopic examination	184	23	5
58	Umar, 2016 [132]	Nigeria	Kano	NR	Urine	Microscopic examination	20	9	5
59	Atalabi, 2016 [52]	Nigeria	Katsina	NR	Urine	Microscopic examination	240	14	6
60	Houmsou, 2016 [86]	Nigeria	Taraba	NR	Urine	Microscopic examination	510	3	7
61	Nwibari, 2016 [165]	Nigeria	Plateau	NR	Urine	Microscopic examination	134	6	5
62	Omoruyi, 2016 [166]	Nigeria	Edo	NR	Urine	Microscopic examination	77	4	6
63	Morenikeji, 2016 [99]	Nigeria	Ogun	NR	Urine	Microscopic examination	79	60	6
64	Bashir, 2016 [60]	Nigeria	Jigawa	NR	Urine	Microscopic examination	31	2	7
65	Ganau, 2016 [79]	Nigeria	Sokoto	NR	Urine	Microscopic examination	58	24	5
66	Musa, 2016 [102]	Nigeria	Kaduna	NR	Urine	Microscopic examination	131	13	6
67	Ajakaye, 2016 [41]	Nigeria	Ondo	NR	Urine	Microscopic examination	404	50	7
68	Mong, 2016 [98]	Nigeria	Abia	NR	Urine	Microscopic examination	129	13	7
69	Atalabi, 2016 [53]	Nigeria	Katsina	2015	Urine	Microscopic examination	317	23	6
70	Oluwatoyin, 2016 [113]*	Nigeria	Ibadan	NR	Urine	Microscopic examination	507	1	7
71	Oluwatoyin, 2016 [113]	Nigeria	Ibadan	NR	Urine	Microscopic examination	507	28	6
72	Bishop, 2016 [63]	Nigeria	Kaduna	NR	Urine	Microscopic examination	251	39	5
73	Maki, 2020 [93]	Sudan	Darfur	2018	Urine	Microscopic examination	55	39	6
74	Qutoof, 2019 [122]	Sudan	Khartoum	NR	Urine	Microscopic examination	589	2	5
75	Elsiddig, 2019 [74]	Sudan	White Nile	2011	Urine	Microscopic examination	162	67	6
76	Hajissa, 2018 [85]	Sudan	Khartoum	2017–2018	Urine	Microscopic examination	95	11	6
77	Mohammed, 2018 [96]	Sudan	White Nile	NR	Urine	Microscopic examination	175	97	7
78	Talab, 2018 [167]	Sudan	White Nile	2014	Urine	(Filtration) Microscopic examination	174	97	5

Table 1 (continued)

No.	References	Country	Province/city	Time of data collection	Sample type	Method	Sample size	Positive no	Quality assessment score
79	Sulieman, 2017 [130]	Sudan	River Nile	2016	Urine	(Sedimentation) Microscopic examination	191	1	6
80	Sabah Alzain Mohamed, 2017 [124]	Sudan	El khiar	2016	Urine	Microscopic examination	76	7	5
81	Afifi, 2016 [39]	Sudan	Kassala	2013	Urine	Microscopic examination	1238	172	6
82	Elhusein, 2016 [72]	Sudan	Gezira	2016	Urine	Microscopic examination	29	0	7
83	Shukla, 2019 [126]	South Africa	KwaZulu-Natal	2011–2013	Urine and cervico-vaginal lavage	Microscopic examination	933	256	5
84	Galappaththi-Arachchige, 2018 [78]	South Africa	KwaZulu-Natal	NR	Urine	Microscopic examination	1123	292	5
85	Kabuyaya, 2017 [89]	South Africa	uMkhanyakude	2015	Urine	Microscopic examination	199	73	7
86	Galappaththi-Arachchige, 2016[168]	south Africa	KwaZulu-Natal	NR	Urine	Microscopic examination	883	270	6
87	Pillay, 2016 [169]	South Africa	KwaZulu-Natal	2010–2012	vaginal lavages and Urine	PCR	394	38	7
88		South Africa	KwaZulu-Natal	2010–2012	Urine	PCR	394	91	7
89		South Africa	KwaZulu-Natal	2010–2012	Urine	Microscopic examination	394	78	7
90	Fokuo, 2020 [76]	Ghana	Asutsuare	2014	Urine	Microscopic examination	59	8	6
91	Arhin-Wiredu, 2019 [50]	Ghana	Akyemansa	2014	Urine	Microscopic examination	161	10	6
92	Nyarko, 2018 [109]	Ghana	different municipal-ities	2016	Urine	Microscopic examination	173	7	6
93	Boye, 2016 [65]	Ghana	Apewosika and Putubiw	2013	Urine	Microscopic examination	114	16	5
94	Wilkinson, 2018 [134]	Malawi	Lilongwe	2013	Urine	Microscopic examination	96	2	6
95	Kayuni, 2017 [91]	Malawi	Mangochi	2012	Urine	Microscopic examination	226	29	6
96	Moyo, 2016 [100]	Malawi	Nkhotakota	NR	Urine	Microscopic examination	51	6	6
97	Yameny, 2018 [137]	Egypt	El-Fayoum	NR	Urine	Microscopic examination	487	33	7
98	Ghieth, 2017 [82]	Egypt	Beni Suef	NR	Urine	Microscopic examination	220	0	5
99	Kaiglova, 2020 [90]	Kenya	Kwale	2018	Urine	Microscopic examination	323	47	5
100	Mutsaka-Makuvaza, 2019 [103]	Zimbabwe	Mashonaland	2010	Urine	Microscopic examination	569	96	6
101	Woldegerima, 2019 [136]	Ethiopia	Sanja	2017–2018	Urine	Microscopic examination	189	53	7
102	Phillips, 2018 [120]	Mozambique	Cabo Delgado	2011	Urine	Microscopic examination	7538	4372	7
103	Gbalegba, 2017 [80]	Mauritania	Kaedi	2014–2015	Urine	Microscopic examination	1064	54	6

Table 1 (continued)

No.	References	Country	Province/city	Time of data collection	Sample type	Method	Sample size	Positive no	Quality assessment score
104	Simoonga, 2017 [127]	Zambia	Lusaka	NR	Urine	Microscopic examination	954	83	7
105	Balahbib, 2017 [58]	Morocco	Tata	2015	Urine	Microscopic examination	13	0	6
106	Anchang-Kimbi, 2017 [48]	Cameroon	Mount Cameroon	2014	Urine	Microscopic examination	250	117	7
107	Mombo-Ngoma, 2017 [97]	Gabon	Lambarene	2009–2013	Urine	Microscopic examination	1115	103	7
108	Greter, 2016 [84]	Chad	Chad	NR	Urine	(Filtration) Microscopic examination	96	1	7
109	Botelho, 2016 [64]	Guinea-Bissau	Guinea-Bissau	NR	Urine	Microscopic examination	43	8	6
111	Senghor, 2016 [125]	Senegal	Niakhar	2011–2014	Urine	Microscopic examination	320	149	5
111	Rasomanamihaja, 2016 [123]	Madagascar	Madagascar	2015	Urine	Microscopic examination	1043	325	5
112	Bangura, 2016 [59]	Sierra Leon	Korwama and Lewabu	2015	Urine	Microscopic examination	86	32	7
113	Zida, 2016 [139]	Burkina Faso	Bazega	2013	Urine	Microscopic examination	151	7	7

*In this dataset, *S. mansoni* was found in urine instead of *S. haematobium*

bias was checked by Egger's regression test, showed that it may have a substantial impact on total prevalence estimate (Egger's bias: 7.5, $P<0.01$) (Fig. 2). Since the heterogeneity of included studies was very high, meta-regression of subgroups such as year, country, type of sample, type of symptoms, and diagnostic method were used to overcome heterogeneity (Table 2). According to subgroup analysis of included data, the prevalence of FUS demonstrated a relatively but worrying increasing trend from 14.6% (95% CI: 11.3–18.6%) in 2016 to 28.6% (95% CI: 13.1–51.6%) in 2020, respectively. In total, studies were conducted in 21 countries, including Nigeria (73 datasets), Sudan (10 datasets), South Africa (7 datasets), Ghana (4 datasets), Malawi (3 datasets), Egypt (2 datasets), as well as Kenya, Zimbabwe, Ethiopia, Mozambique, Mauritania, Zambia, Morocco, Cameroon, Gabon, Chad, Guinea-Bissau, Senegal, Madagascar, Sierra Leone and Burkina Faso (one dataset per country). The highest prevalence rates were estimated for women in Mozambique with 58% (95% CI: 56.9–59.1%) (one study), while female individuals in Chad had the lowest prevalence rate 1.0% (95% CI: 0.1–7.0%). Year-based prevalence for the six most studied countries, showed no determined pattern for frequency of FUS, however, a relatively decreasing pattern of prevalence was recorded for Malawi (three studies) (Figs. 3, 4, 5, 6, 7, 8). Regarding sample type, urine and vaginal lavage were gathered from examined women, with vaginal lavage demonstrating a higher frequency of FUS [25.0% (95% CI: 11.4–46.1%)] than urine specimen [17.2% (95% CI: 14.5–20.3%)]. Reportedly, hematuria and proteinuria as the most prominent symptoms of FUS were estimated in some studies, showing 19.4% (95% CI: 12.2–29.4%) and 13.6% (95% CI: 6.69–24.8%) prevalence rates, correspondingly. Direct microscopy was the most frequently utilized diagnostic test, yielding a relatively higher prevalence 17.1% (95% CI: 14.5–20.1%) than PCR method 15.3% (95% CI: 6.1–33.2%); however, only two studies employed molecular method. Additional microscopy-based procedures were filtration and sedimentation, which in detail yielded a prevalence rate of 18.2% (95% CI: 5.9–43.9%) and 11.4% (95% CI: 3.6–30.9%), respectively. Altogether, subgroup analysis revealed that there were statistically significant differences between the overall prevalence of FUS and year. Of note, the quality score of the included papers is provided in Additional file 3.

Discussion

Helminth-induced diseases are ancient catastrophic phenomena in humans, some dating back to pre-biblical era, with huge but chronic and snaky damages in nature [140]. Schistosomiasis or bilharziasis is one of the most important water-borne helminthic diseases, which have always been interconnected with archaic civilizations over the

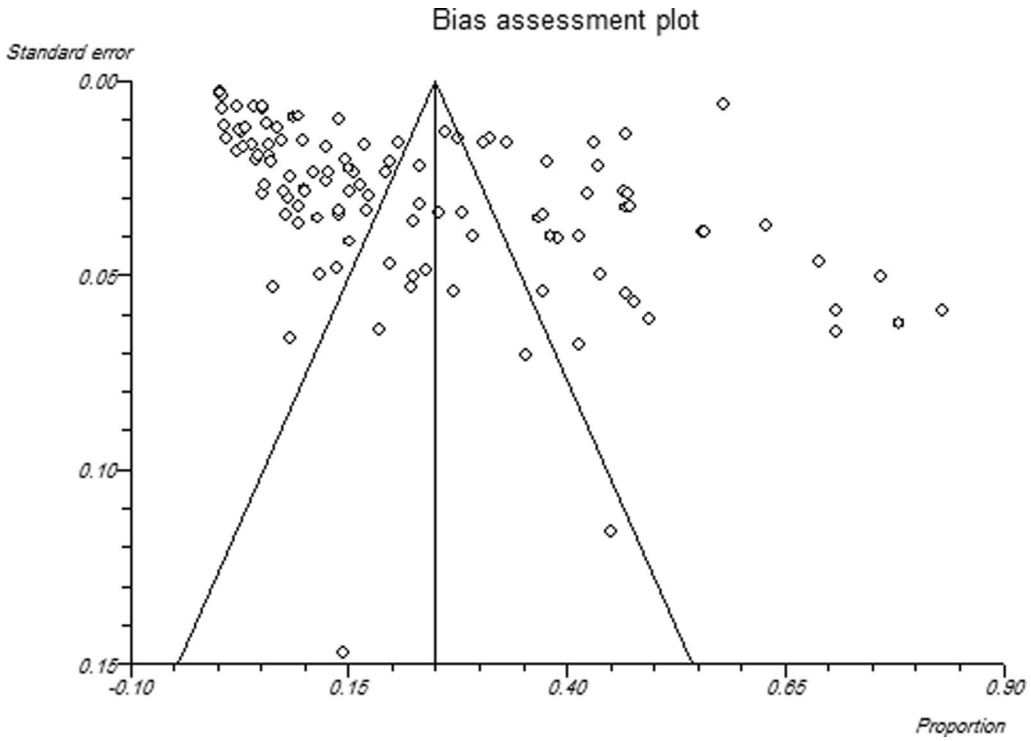

Fig. 2 A bias assessment plot from Egger for the FUS prevalence (2016–2020)

millennia, and it is still a global public health concern due to its astonishing, complex life cycle [141, 142]. Among schistosome species infecting humans, *S. haematobium* worms are the causative agents of UGS which localize within draining venous complex of the pelvic organs such as uterus, cervix and the bladder [143]. These worms are highly prolific, releasing about 3000 eggs/day, half of which are excreted through urine, while the rest are lodged within vasculature of urogenital organs. Immune-mediated pathologic processes elicited against tissue-embedded ova result in granulomatous inflammation, tissue destruction and the so-called "sandy patches" as fibrotic nodules [16]. With respect to the significance of UGS and large number of affected individuals, the present systematic review and meta-analysis was contrived in order to reveal the latest status of urinary schistosomiasis in women population based on published literature in the last 5 years and provide a premise for future clinical directions on women health.

The required information was assembled from available full-texts published between 2016 and 2020 and their overall estimates were assessed through a meticulous meta-analytical method. During last 5 years, 11,308 out of 40,531 women were suffering from urinary schistosomiasis, contributing to the global weighted prevalence of 17.5% (95% CI: 14.8–20.5%). Interestingly, all cases in the last 5 years were from African countries. This continent is probably known as the "cradle of schistosomes", since African great lakes provide a favorable milieu for the optimum evolution of both parasites and their respective intermediate hosts [144]. Schistosomiasis may have spread to Africa, particularly Egypt, in virtue of monkey importation and slave trades during fifth dynasty of pharaohs [145]. Based on our results obtained from limited number of heterogeneous investigations included in the present meta-analysis, a large number of studies (73) on FUS were done in a western African nation, Nigeria, whereas the highest prevalence rate was estimated for women in Mozambique with 58% (95% CI: 56.9–59.1%) (one study), a country in the southeast coast of Africa. Nigerian researchers have shown a substantial effort in search of urinary schistosomiasis during last 5 years by conducting 73 datasets, which could be a favorable layout for other African countries [143]. Nevertheless, the true picture of FUS prevalence throughout African territories in a 5-year time period was not accurately captured, since out of 21 countries examining female individuals, only 6 countries had sufficient studies to perform meta-analytical approach and most of the remaining had only one investigation per country. Moreover, a statistically significant gradual increase was observed in FUS prevalence based on publication year of the included literature, from

Table 2 Subgroup analysis of FUS prevalence according to year, country, type of sample, type of symptoms and diagnostic methods

Subgroup variable	Prevalence % (95% CI)	I^2 (%)	Heterogeneity (*Q*)	*P*-value	Interaction test (X^2)	*P*-value
Year						
2016	14.6 (11.3–18.6)	96.3%	1034.7	< 0.01	375.3	< 0.01
2017	17.5 (12–24.9)	97.8%	1055.2	< 0.01		
2018	19.0 (13.1–26.7)	98.8%	2179.6	< 0.01		
2019	21.7 (16.8–27.5)	93.4%	274.7	< 0.01		
2020	28.6 (13.1–51.6)	97.1%	138.2	< 0.01		
Country						
Ghana	9.1 (6.8–12.2)	73.46%	11.31	< 0.01		
Malawi	11.4 (0.8–15.4)	70.62%	6.81	< 0.01		
Nigeria	21.1 (17.6–25.0)	96.9%	2337.91	< 0.01		
South Africa	27.4 (25.6–29.2)	92.53%	80.36	< 0.01		
Sudan	55.8 (43.9–67.1)	97.59%	374.17	< 0.01	430.6	< 0.01
Egypt	1.7 (0.1–32.8)	83.57	5.90	< 0.01		
Type of sample						
Urine	17.2 (14.5–20.3)	98.11%	5949.4	< 0.01	1285.2	> 0.05
Vaginal lavage	25.0 (11.4–46.1)	98.2%	110.40	< 0.01		
Type of symptoms						
Hematuria	19.4 (12.2–29.4)	92.33%	52.19	< 0.01	82.4	< 0.01
Proteinuria	13.6 (6.69–24.8)	–	0.00	= 1.00		
Diagnostic method						
Direct microscopy	17.1 (14.5–20.1)	98.1%	6013	< 0.01	350.6	< 0.01
Filtration and microscopy	18.2 (5.9–43.9)	99.1%	563.1	< 0.01		
PCR	15.3 (6.1–33.2)	95.9%	24.64	< 0.01		
Sedimentation and microscopy	11.4 (3.6–30.9)	96.6%	59.5	< 0.01		

2016 until the end of 2020, ranging from 14.6% (95% CI: 11.3–18.6%) to 28.6% (95% CI: 13.1–51.6%), respectively. However, no such an increasing trend was observed in year-based analysis of each country; even the prevalence relatively decreased in Malawi, though only three studies were involved in this country. Such findings derived from limited number of included studies in current review may be interpreted as a spread of the endemic situation of FUS, or as a result of the increased understanding about FUS among health care professionals in each country. Nevertheless, more in-depth studies are required to further elucidate this issue.

The characteristic symptoms of UGS were prominently reported among examined women, so that a higher prevalence rate was recorded for hematuria with 19.4% (95% CI: 12.2–29.4%), in comparison to 13.6% (95% CI: 6.69–24.8%) frequency of proteinuria. As previously mentioned, disease morbidity largely results from entrapped eggs, which strongly induce a granulomatous immune response [146], characterized by Th2-type lymphocytes, alternatively activated macrophages and eosinophils [147, 148]. Thereby, the eggs are immunologically confined within the so-called "granulomas", containing proteolytic enzymes of egg origin that barricade tissue necrosis [149]. In accordance with our finding, hematuria is considered as a defining symptom in *S. haematobium* infection, mostly being accompanied by suprapubic ailment, burning micturition as well as frequent urination [150]. Poor immunoregulatory mechanisms in response to eggs provoke a lasting fibrotic reaction in the urinary tract of infected individuals [151]. The resulting obstructive uropathy elicit subsequent dreadful consequences such as the hydroureter and hydronephrosis [152]. The latter is the milestone in ascending bacterial superinfections, renal dysfunctions and the ensuing proteinuria [153]. The consequences are more horrific in affected women, since the proximity of vesical and genital venous plexuses facilitates easy migration of parasites and/or eggs, leading to harsh outcomes regarding women's reproductive health [154–156]. The subsequent lesions in genital organs, from ovaries to vagina, may be associated with pain and stress, allowing human immunodeficiency virus-1 (HIV-1) to simply access sub-epithelial target cells [157]. In a recently published meta-analysis, the chance of acquiring HIV among people suffering from schistosomiasis was 2.3-fold (95% CI: 1.2–4.3%) higher than non-infected

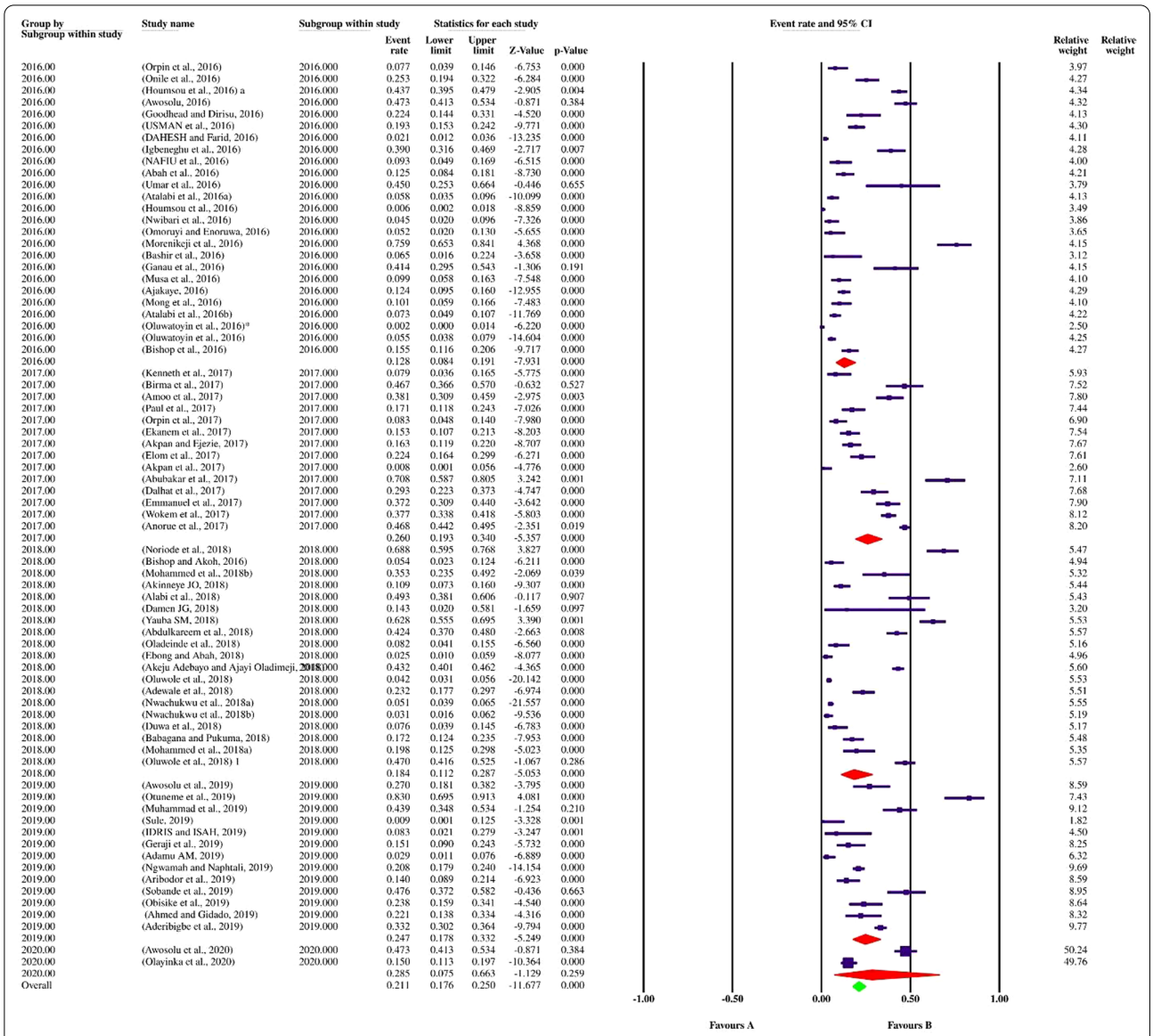

Fig. 3 Forest plot of year-based prevalence in Nigeria (2016–2020)

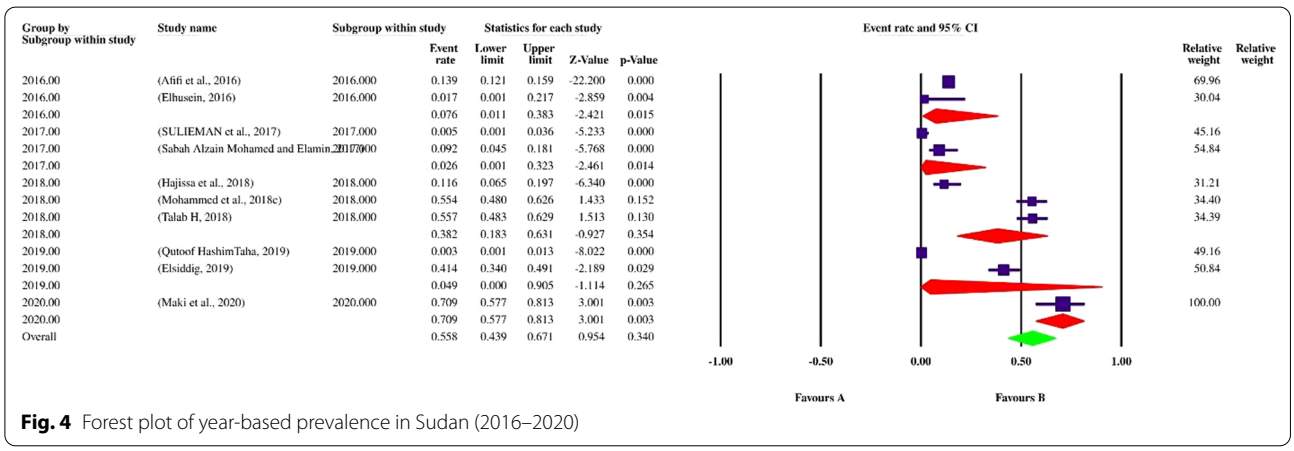

Fig. 4 Forest plot of year-based prevalence in Sudan (2016–2020)

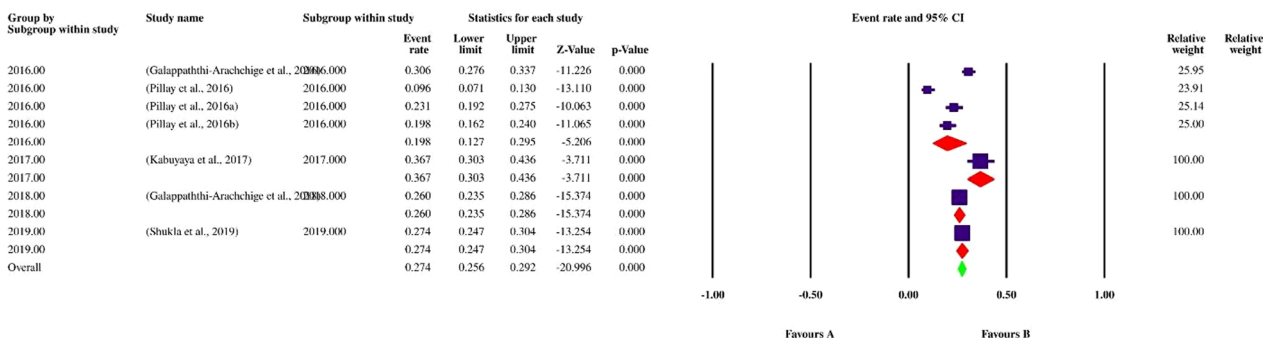

Fig. 5 Forest plot of year-based prevalence in South Africa (2016–2020)

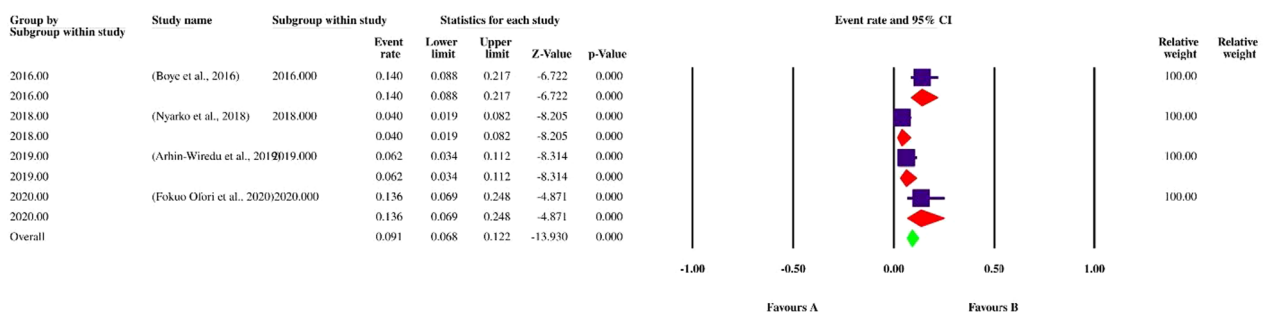

Fig. 6 Forest plot of year-based prevalence in Ghana (2016–2020)

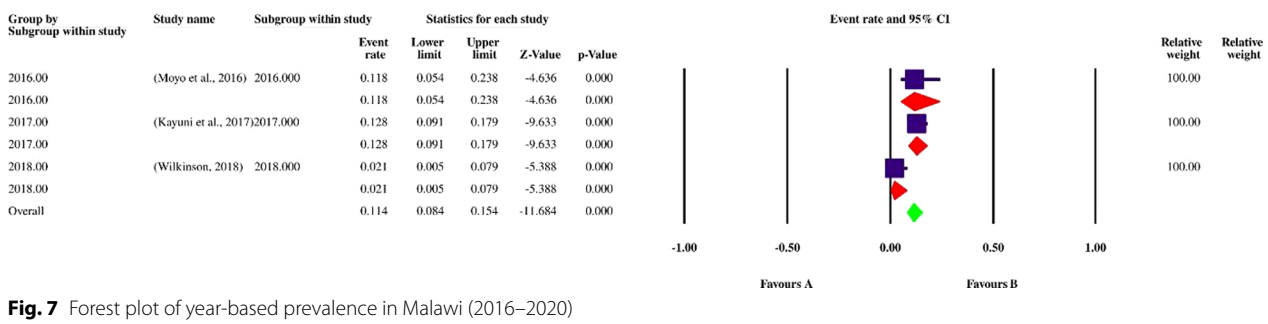

Fig. 7 Forest plot of year-based prevalence in Malawi (2016–2020)

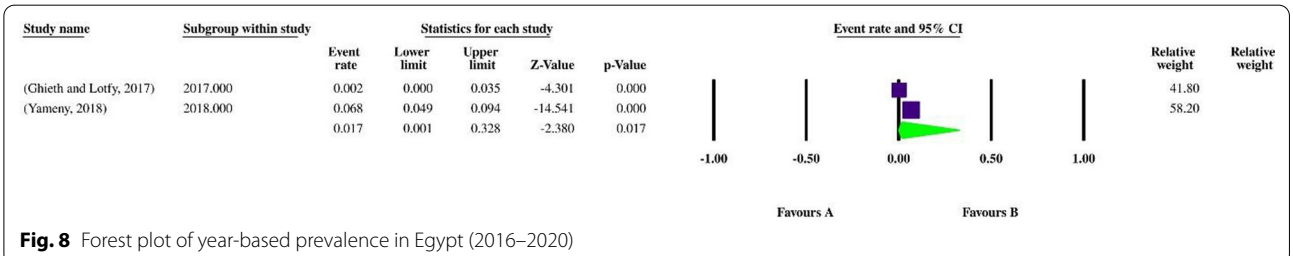

Fig. 8 Forest plot of year-based prevalence in Egypt (2016–2020)

patients [158]. Finally, the affected women might experience painful intercourse (dyspareunia), fibrotic ovaries and/or granuloma-induced tubal blockage, all of which lead to the female infertility. Hence, FUS may lead to harsh reproductive outcomes that ultimately endangers the fecundity, fertility and pregnancy of women [159].

The result of the present meta-analysis highlighted that a higher prevalence of FUS was demonstrated by vaginal lavage [25.0% (95% CI: 11.4–46.1%)] than urine specimens [17.2% (95% CI: 14.5–20.3%)]. Although there was not statistically significant difference between the total prevalence of FUS and sample type ($P > 0.05$). Moreover, the results of current review demonstrated that microscopy 17.1% (95% CI: 14.5–20.1%) contributed more to reveal the FUS prevalence than PCR method 15.3% (95% CI: 6.1–33.2%); nevertheless, only two studies utilized molecular method for diagnosis, and any deductions should accompany with caution. Notably, urine filtration (about 10 mL) that is routinely performed for egg detection was more efficient in detecting parasite eggs than sedimentation method, with 18.2% (95% CI: 5.9–43.9%) versus 11.4% (95% CI: 3.6–30.9%), respectively. Urine microscopy is the gold standard in detection of *S. haematobium* eggs in areas of endemicity [160]. However, it is not sensitive sufficiently for monitoring praziquantel therapeutic efficiency in mass drug administration (MDA) campaigns, particularly in low-transmission intensity areas, because weeks after adult worm elimination eggs are still observable in urine or some worms may have temporarily stopped shedding eggs [161]. Also, it lacks adequate sensitivity, due to the fact that eggs are only detectable in urine samples 2 months after infection onwards [162]. Therefore, it is highly recommended to carry out at least two follow-up visits and microscopic examination for more accurate diagnosis [163]. Additionally, in order to enhance the sensitivity and specificity and deter underestimation of the true disease burden, performing highly sensitive methods such as molecular techniques are inevitable [21]. As mentioned earlier, only two studies in the last 5 years used PCR method, which exhibited a remarkable prevalence rate for FUS, implicating the importance of such modalities in accurate detection of urinary schistosomiasis.

The present systematic review and meta-analysis met some limitations, including: (1) lack of adequate prevalence studies in countries other than Nigeria; (2) diagnosis of the infection mostly based on microscopic examination of urine samples; (3) inadequate number of molecular-based studies in the last 5 years, and (4) due to the nature of the systematic review and meta-analysis studies, which exclude some papers relied on a designed inclusion criteria, the provided results are only based on the information extracted from 113 datasets and any definite inference must accompany with caution. Inevitably, implementation of large-scale or nation-wide prevalence studies on FUS throughout African nations, particularly in neglected regions of the continent, using microscopy of urine specimen (gold standard method) coupled with unprecedented molecular approaches will more elucidate the true epidemiological picture of urinary schistosomiasis among women population. Consequently, such information benefits the clinicians for the prevention of the horrible sequelae of chronic FUS.

Conclusion

In conclusion, information provided in the present systematic review and meta-analysis showed that women in endemic territories in Africa are moderately at risk of acquiring FUS and its harsh consequences, including renal dysfunction, urinary bladder carcinoma as well as reproductive disorders such as dyspareunia and granuloma-induced infertility. Consequently, health assessment of FUS should be considered as a routine necessity for women in susceptible age groups such as those in active reproductive status and/or child-bearing age. Relying only on low-sensitivity microscopic results cannot rule out the presence of schistosomes in blood vessels. Hence, clinical assessment must be performed using gold standard methods, i.e., microscopic examination of urine samples, combined with highly sensitive and specific molecular approaches. Altogether, our goal on better control and prevention of urinary schistosomiasis may not be achievable, unless by a global collaboration to accurately reveal the parasite epidemiology in endemic territories.

Abbreviations

UGS: Urogenital schistosomiasis; BCE: Before common era; WHO: World Health Organization; PCR: Polymerase chain reaction; FUS: Female urinary schistosomiasis; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; MeSH: Medical subject heading; CI: Confidence interval; CMA: Comprehensive meta-analysis; HIV-1: Human immunodeficiency virus-1; MDA: Mass drug administration.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41182-022-00402-x.

Additional file 1. PRISMA checklist employed for the present systematic review.

Additional file 2. Forest plot of the FUS prevalence obtained from published literature during 2016–2020.

Additional file 3. Quality assessment analysis of the included papers using Newcastle–Ottawa scale.

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Authors' contributions
MS, SK and AA conceived the study protocol; SK, HM and SB performed the systematic search; EJ and SB extracted the required information from included papers; SB, EJ and DA performed the meta-analytical approach; NN, MF, EG and TN wrote the manuscript draft; MS and AA critically revised the manuscript. All authors have read and approved the manuscript.

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Declarations

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Competing interests
The authors declare no competing interests.

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