

The WHO ultrasonography protocol for assessing morbidity due to *Schistosoma haematobium*. Acceptance and evolution over 14 years. Systematic review

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Abstract In 2000, the World Health Organization (WHO) published an ultrasound field protocol for assessing morbidity due to schistosomiasis. The present study aims to review the acceptance of the WHO protocol for *Schistosoma haematobium*. A PubMed literature research using the keywords “ultrasound OR ultrasonography (US) AND schistosomiasis,” “US AND *S. haematobium*,” “US AND urinary schistosomiasis” from 2001 through 2014 was performed. Thirty-eight eligible publications reporting on 17,861 patients from 13 endemic and 2 non-endemic countries were analysed. Of these, 33 referred to field studies on 17,317 patients. The Niamey protocol was applied to 15,367/17,317 (88.74 %) patients in 23/33 (69.70 %) of field studies (all studies: 15,649/17,861 [87.61 %] patients (25/38 [68.42 %] studies). The

acceptance of the protocol by single country in field studies varied from 0 to 100 %. It varied over time between 55.56 % (5/9) in the period from 2001 to 2004, to 87.50 % (7/8) from 2005 to 2008, to 62.50 % (5/8) from 2009 to 2011 and 75.00 % (6/8) from 2012 through 2014 (all studies: 50 % [5/10], 88.89 % [8/9], 62.50 % [5/8], 63.64 % [7/11], respectively). The Niamey protocol was applied also in 2/5 hospital studies in 282/544 (51.84 %) patients.

The usefulness of the WHO protocol for *S. haematobium* infections is confirmed by its worldwide acceptance. Some simplifications might facilitate its use also for focused ultrasound examinations performed by less skilled examiners. Organ abnormalities due to schistosomiasis detectable by ultrasonography not yet covered by the WHO protocol should be added to the additional investigations section.

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Introduction

Ultrasonography has been applied to characterize the typical morphologic features of schistosomiasis-induced organ pathology since 1978 (Abdel-Wahab et al. 1978). Ultrasonography compared positively to cystoscopy (Degremont et al.

1985; Burki et al. 1986) and was soon used for morbidity assessment in the field (Doehring et al. 1985; Hatz 2001).

In 1991, a group of experts was convened by the World Health Organization (WHO) in order to formulate a standardized ultrasonography protocol with the aim to enable the comparison of data obtained in different endemic foci (Cairo Working Group 1991; Cairo Working Group and Jenkins 1992). This protocol was reviewed and modified during a second meeting which took place in 1996 in Niamey, Niger, in order to revise and improve the WHO methodology and published in 2000 (Niamey Working Group 2000; Hatz 2001). The aim of the present study was to analyse the ultrasonographic studies performed since the publication of the Niamey protocol in terms of worldwide acceptance and the practical experiences of those examiners and study groups who applied this protocol. Furthermore, studies with potential implications for a further amendment of the protocol were evaluated.

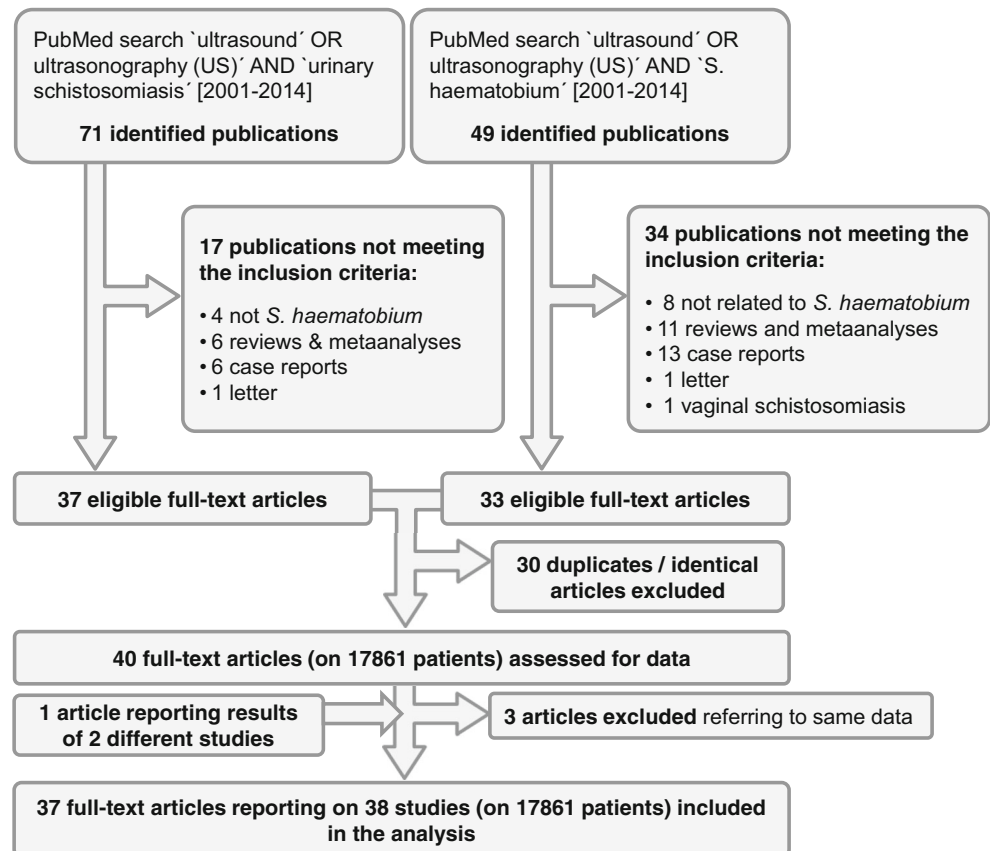
Materials and methods

The literature research process is described in detail in Fig. 1. Since the present study aims at investigating the acceptance of the protocol, contrary to a classical meta-analysis, every publication regardless of its scientific quality was considered.

Exclusion criteria were as follows: letters, reviews, meta-analysis, case reports, publications referring to *Schistosoma* species other than *S. haematobium* and localisations other than the urinary tract. Further searches were performed for studies on possible additional ultrasonographic investigations.

The main analysis criterion was whether or not the Niamey protocol was applied. Further analysis focused on the populations investigated, e.g. on pre-school-age children, school-age children or adults and on the study type (e.g. morbidity assessment prior to interventions or studies on the evolution after therapy such as regression and subsequent reappearance of lesions in populations continuously exposed to reinfection but not retreated). Moreover, it was analysed if intra- and or inter-observer agreement of ultrasound results was tested, if possible confounders such as sufficient bladder filling for bladder examination, or voiding prior to examination of the upper urinary tract were mentioned. Further searches examined in how many studies additional investigations such as residual urine or kidney pyelon fibrosis which were proposed in the WHO protocol were performed. Furthermore, searches were performed for other manifestations due to *S. haematobium* detectable by ultrasonography which in future could be proposed as to be included into the additional investigations list of the WHO protocol.

Fig. 1 Search strategy for publications on ultrasonography in *S. haematobium* infections from 2001 to 2014



Results

Forty publications on studies performed in 13 endemic and 2 non-endemic countries were eligible. Five publications referred to the same ultrasonographic results of two studies, whereas one publication reported the results of two different studies so that eventually 38 studies were analysed (Fig. 1) (Campagne et al. 2001; King et al. 2001, 2002; Keita et al. 2001, 2005; Lougue-Sorgho et al. 2002; El Baz et al. 2003; Brouwer et al. 2003; Wamachi et al. 2004; Poda et al. 2004; Garba et al. 2004; Ouma et al. 2005; Shiff et al. 2006; Koukounari et al. 2006, 2009, 2010; Nmorsi et al. 2007; Sayed et al. 2007; Nayama et al. 2007; Stothard et al. 2009; Tohon et al. 2008; Ramarakoto et al. 2008; Naples et al. 2009; Sousa-Figueiredo et al. 2009; Ekwunife et al. 2009; Lyons et al. 2009; Bonnard et al. 2011; Qazi et al. 2012; Meurs et al. 2012, 2013; Salas-Coronas et al. 2013; Elmadani et al. 2013; Gouvras et al. 2013; Zhong et al. 2013; Strahan et al. 2013; Gasmelseed et al. 2014; Njaanake et al. 2014; Ahmed et al. 2014). Out of 17,861 patients examined, 17,317 of whom were examined in the field. The Niamey protocol was applied to 15,367/17,317 (88.74 %) patients in 23/33 (69.70 %) field studies (all studies: 15,649/17,861 [87.61 %] patients (25/38 [68.42 %] studies). The acceptance of the protocol by single country in field studies varied from 0 to 100 % (Table 1). It varied over time between 55.56 % (5/9) in the period from 2001 to 2004, to 87.50 % (7/8) from 2005 to

2008, to 62.50 % (5/8) from 2009 to 2011 and 75.00 % (6/8) from 2012 through 2014 (all studies: 50 % [5/10], 88.89 % [8/9], 62.50 % [5/8], 63.64 % [7/11] respectively) (Fig. 2). The Niamey protocol was applied also in 2/5 hospital studies including 282/544 (51.84 %) patients (Nayama et al. 2007; Salas-Coronas et al. 2013). Other methods applied were either descriptive not following any published protocol or followed the former Cairo protocol (Cairo Working Group 1991; Cairo Working Group and Jenkins 1992).

The Niamey protocol was applied in all studies including pre-school-age children (8/8 [100.0 %]), in 16/23 (69.57 %) studies regarding school-age children and in 14/20 (70 %) studies on adults (7 studies comprised both children and adults. In 2 studies, no data on the age of patients were provided) (King et al. 2002, 2004; Wamachi et al. 2004; Tohon et al. 2008; Meurs et al. 2012; Meurs et al. 2013; Strahan et al. 2013; Njaanake et al. 2014). Using the Niamey protocol, 27/38 (71.05 %) studies on morbidity assessment prior to therapy were performed. Six out of 10 (60 %) studies on regression of lesions after therapy referred to the Niamey protocol (Ouma et al. 2005; Tohon et al. 2008; Ramarakoto et al. 2008; Ekwunife et al. 2009; Qazi et al. 2012; Strahan et al. 2013). Two out of 10 studies examined subsequent reappearance; however, none of the two referred to Niamey.

All four studies on inter-observer agreement referred to the Niamey protocol (King et al. 2001; Wamachi et al. 2004; Ouma et al. 2005; Bonnard et al. 2011). Since ultrasonography was not the main issue in most of these studies, inter-observer agreement results were not systematically reported on. King et al. (2001) reported that ultrasound results were confirmed by a second blinded examiner; Wamachi et al. (2004) and Ouma et al. (2005) did not specifically report on inter-observer ultrasound data, but compared ultrasonography data obtained by two blinded examiners with results of other investigations thereby suggesting that inter-observer agreement was adequate.

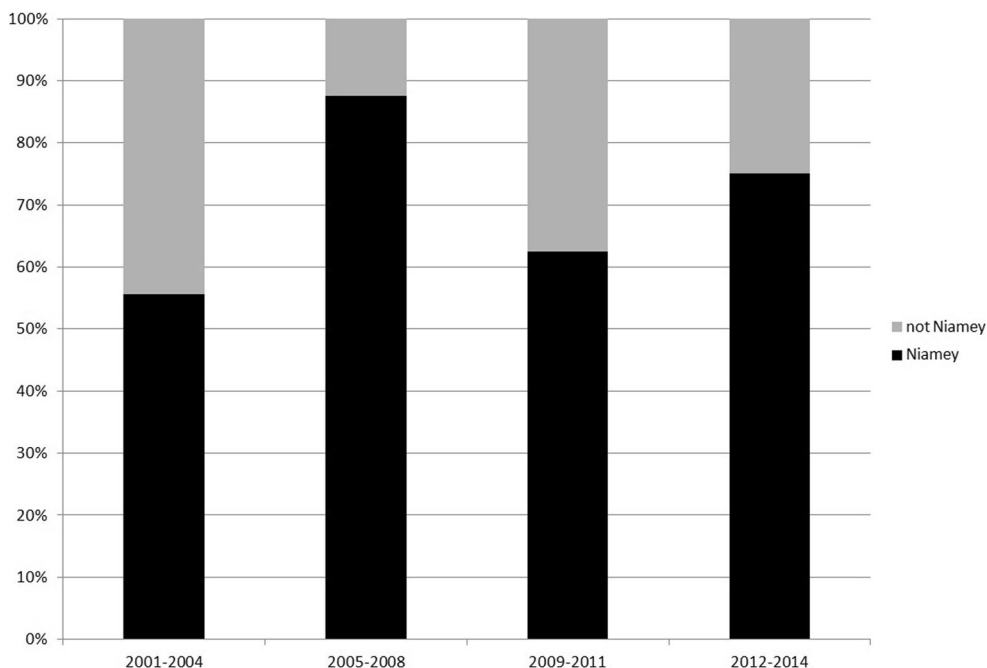
Inter-observer agreement was found excellent in a Senegalese study (Bonnard et al. 2011) where the learning curve of a learning clinician was compared to the results obtained by a teaching radiologist: The frequency of normal ultrasound images was 58 % for the teacher and 59 % for the learner. Mean score of teacher was 0.94 ± 2.01 [0–17], and mean score of learner was 1.11 ± 2.77 [0–19] without any statistical difference between them ($p = 0.08$). Of the 132 ultrasound examinations, only 12 discrepancies (9 %) were found. Among these 12 discordant ultrasound images, 8 scores had 1 point difference (67 %), 2 had 2 points difference and 2 were found to have a discrepancy of more than 2 points (8 and 10 points). Moreover, in nine of these discordant ultrasound images, it was the learner who had not seen the lesions seen by the teacher (underestimation) and in three cases it was the learner who reported lesions not seen by the teacher. By the third day of the study, after 50 examinations conducted by the learner

Table 1 Ultrasound studies on urinary tract abnormalities due to *S. haematobium* 2001–2014

| Countries | No. of studies | No. of patients | Niamey/field US | %Niamey/field st. |
|------------------------|----------------|-----------------|-----------------|-------------------|
| Mali | 4 | 6.424 | 3/4 | 75.00 |
| Kenya | 7 | 4.502 | 7/7 | 100.00 |
| Nigeria | 3 | 1.745 | 3/3 | 100.00 |
| Senegal | 3 | 881 | 3/3 | 100.00 |
| Egypt | 2 | 795 | 0/2 | 0.00 |
| Zambia | 1 | 763 | 1/1 | 100.00 |
| Ghana | 3 | 655 | 3/3 | 100.00 |
| Niger | 3 | 518 | 1*/2 | 0.00 |
| Tanzania | 4 | 500 | 1/4 | 25.00 |
| Sudan | 3 | 384 | 0/2 | 0.00 |
| Zimbabwe | 1 | 222 | 1/1 | 100.00 |
| Madagascar | 1 | 221 | 1/1 | 100.00 |
| Burkina Faso | 1 | 71 | 0/0 | n.a.* |
| <i>Imported cases:</i> | | | | |
| Spain | 1 | 178 | 1/0 | n.a.* |
| UK | 1 | 2 | 0/0 | n.a.* |
| Total | 38 | 17.861 | 23/33* | 69.70* |

*n.a.=not applicable, because these studies were hospital studies; all studies 25/38=65.79 %

Fig. 2 Acceptance of the Niamey protocol by single country in field studies



and teacher, the learner found the same result as the teacher in over 90 % of the cases. Furthermore, the sensitivity/specificity analysis showed that after day 3, the learner screened 100 % of healthy subjects, and within two more days of learning, he managed to find all the lesions seen by the teacher without making any mistake. Finally, this learning appeared to persist over time. The other three studies including inter-observer testing reported reliable inter/observer agreement, too. Possible confounders such as insufficient bladder filling during ultrasound examinations or examination of the upper urinary tract before voiding, both possibly leading to an overestimation of organ pathology were mentioned mostly in studies where the Niamey protocol was applied: in 7/12 (58.33 %) of publications mentioning adequate bladder filling (Brouwer et al. 2003; Keita et al. 2005; Shiff et al. 2006; Koukounari et al. 2006; Nmorsi et al. 2007; Ekwunife et al. 2009; Gouvras et al. 2013) and in 7/9 (77.78 %) of publications mentioning the necessity of voiding before examining the upper urinary tract (Brouwer et al. 2003; Keita et al. 2005; Koukounari et al. 2006; Nmorsi et al. 2007; Ekwunife et al. 2009; Gouvras et al. 2013; Njaanake et al. 2014).

The Niamey-Belo Horizonte protocol proposes additional optional investigations such as the determination of residual urine after voiding and the assessment of kidney pyelon fibrosis. Results on the performance of additional investigations are listed in Table 2. Of the 10 publications retrieved by PubMed search, only two were eligible (Nmorsi et al. 2007; Watanabe et al. 2011); other results comprised eight studies (five before 2000) which do not refer to ultrasonography. Watanabe et al. (2011) compared parasitological data and symptomatology using the International Prostate Symptoms

Score (I-PSS) with bladder voiding function as assessed by ultrasound and uroflowmetry. Results of this study suggested that the feeling of incomplete bladder emptying and hesitancy were better indicators for urinary schistosomiasis than the presence of residual urine. Unexpectedly, no significant residual

Table 2 Results of Searches for Additional Ultrasound (US) Investigations for exploring *S. haematobium*-related organ abnormalities

| Additional Investigations proposed in the WHO protocol | No. of hits/no. hits from 2001 to 2014 |
|--|--|
| Residual urine AND schistosomiasis | 10/5, eligible: 2 |
| US AND schistosomiasis AND kidney fibrosis | 0 |
| US AND urinary schisto AND kidney pyelon fibrosis | 0 |
| Kidney fibrosis AND schistosomiasis | 29/7, eligible: 0 |
| US AND calcifications AND schistosomiasis | 7/3, eligible: 2 |
| US AND <i>S. haematobium</i> AND calcifications | 4/1 |
| Additional Investigations not yet covered by the WHO protocol: | |
| schistosomiasis AND ureter | 168/19, eligible: 15 |
| US AND ureter AND schistosomiasis | 11/5 |
| Calculi, and urinary schistosomiasis | 84/12, eligible: 5 |
| US AND calculi AND schistosomiasis | 6/1 |
| US AND bladder cancer AND urinary schistosomiasis | 20/7 |
| US AND urogenital schistosomiasis | 156/52 |
| US AND genitourinary schistosomiasis | 88/33 |
| US AND genital schistosomiasis* | 17/8 |

*Four studies were retrieved by other searches than by PubMed

urine post voiding and no decline in urine flow rates were found in *S. haematobium*-infected boys. Contrary, volume-corrected maximum and average flow rates in *S. haematobium* infected boys were higher than in those not infected. These results suggest that cystitis associated with *S. haematobium* infection causes irritation and hypercontractility of the bladder. The second study also reported that the finding of residual urine after voiding is relatively rare (27.9 %) as compared to abnormal bladder wall thickening (55.8 %) and abnormal bladder shape (69.8 %) (Nmorsi et al. 2007).

PubMed search did not yield any study on schistosomiasis which would have reported the occurrence of kidney pyelon fibrosis. The non-occurrence of pyelon fibrosis is further confirmed by a case series and a review on kidney pathology due to schistosomiasis where kidney pyelon fibrosis was also not reported (Barsoum 2003; Shebel et al. 2012). On the other hand, five classes of glomerulonephritis have been reported to be related to not only to *S. haematobium* but more frequently to *Schistosoma mansoni*: mesangioproliferative; exudative; mesangiocapillary (membranoproliferative); focal segmental sclerosis; and amyloidosis (Barsoum 2003; Duarte et al. 2014).

Searches for ultrasonography AND schistosomiasis or *S. haematobium* AND calcifications retrieved only seven publications, of which only three were published after 2001, only two of them were eligible (Nmorsi et al. 2007; Salas-Coronas et al. 2013). These studies confirmed the notion that radiology is more sensitive than ultrasonography for detecting urinary tract calcifications (Burki et al. 1986; King 2002).

Although searches for urinary calculi possibly related to urinary schistosomiasis revealed 84 hits, only 12 of them were published since 2001, of which 5 publications were eligible (Holman et al. 2004; Hussein et al. 2006; Abdelrahim et al. 2008; Coulibaly et al. 2011; Khalaf et al. 2012). All studies were hospital based. The different frequency of occurrence of calculi of the urinary tract in schistosomiasis patients is likely to be due to the different age as calculi having been only exceptionally seen in children, who are the usual target of field surveys.

After the detailed report on ultrasonographic detection of schistosomiasis-related ureter pathology by Kardorff and Döhring (2001), 18 further studies (14 eligible) on schistosomiasis were published, mostly referring to schistosomiasis or bladder cancer-induced strictures and urological management of calculi (El-Nahas et al. 2003; Neal 2004; Ajit et al. 2005; Hussein et al. 2006; Wong-You-Cheong et al. 2006; Gilligan and Dreicer 2007; Abdelrahim et al. 2008, Badmos et al. 2009; Abou-Elela et al. 2010; Oranusi et al. 2011; Shebel et al. 2012; Bakari et al. 2012; Vancauwenberghe et al. 2013; Hasegawa et al. 2014). These studies indicate that ultrasonography has a particular potential for the detection of ureter pathology not yet explored by the Niamey protocol.

A particular challenge for ultrasonography is the early detection of schistosomiasis-related bladder cancer, with special emphasis on its detection during field surveys. Seven

ultrasound studies on this issue have been published since 2001, one of these being an interesting field study indicating that molecular bladder cancer markers are increased in early urinary schistosomiasis (Shiff et al. 2006; see also Figueiredo et al. 2014b). Two other studies were hospital observations (Lougue-Sorgho et al. 2002; Salas-Coronas et al. 2013), 1 a review (Richter 2003), 1 reported genetic abnormalities induced by schistosomiasis and 2 referred to exclusion of bladder cancer in schistosomiasis patients.

Attention has increased towards the genital manifestations of schistosomiasis where 53 works have been published since 2001.

In men, some abnormalities possibly indicating schistosomiasis have been described including hyperechogenic spots in the prostate and hydrocele (Richter et al. 2002; Ramarakoto et al. 2008; Figueiredo et al. 2014b). Searches for hydrocele AND schistosomiasis yielded seven hits (four since 2001): three publications referred to filariasis, one to schistosomiasis (Rambau et al. 2011). Another publication is not listed in PubMed (Richter et al. 2002). The search term combination ultrasound AND hydrocele AND schistosomiasis yielded no hit.

On the other hand, so far, ultrasound has not been found to be useful to detect specific abnormalities of the female upper reproductive tract (Richter et al. 1995; Ramarakoto et al. 2008). Ultrasound may, however, be helpful in diagnosing complications related to genital schistosomiasis such as sterility, vesico-vaginal fistulae and pregnancy-related problems (Richter 2000; Richter et al. 1996, 2008; Schanz et al. 2010; Figueiredo et al. 2013; Ben-Chetrit et al. 2014; Schleenvoigt et al. 2014). Searches for ultrasound AND schistosomiasis AND pregnancy yielded nine hits (two since 2001) which unfortunately were all not eligible. Search for ultrasonography AND schistosomiasis AND placenta yielded one hit only where placental schistosomiasis was excluded. The search for placenta AND schistosomiasis yielded 30 hits (15 since 2001). However, placental ultrasonographic abnormalities specifically due to schistosomiasis have not yet been looked for (for more detailed discussion, see Schleenvoigt et al. 2014).

Reports on urogenital manifestations due to *Schistosoma* spp. other than *S. haematobium* were limited to eight reports on ectopic *S. mansoni* infections and glomerulonephritis, six induced by *S. mansoni* and two reports on kidney abnormalities presumably associated with *Schistosoma intercalatum* since 2001. There was no hit for *S. guineensis*, *S. japonicum*, nor for *S. mekongi*.

Discussion

Ultrasonography is a pivotal method to assess the morbidity of the urinary tract due to schistosomiasis and its complications. At the time when the Niamey protocol was proposed, the

preceding method developed during the WHO meeting in Cairo already had proved useful and reproducible (Hatz 2001) but there is, so far, no experimental proof of the accuracy and usefulness of the protocol as modified in Niamey. Thus, the studies undertaken after the publication of the Niamey protocol constitute the practical evaluation of this modified protocol.

The protocol was accepted by most study groups in the world except some group from Egypt, the Sudan and Niger. This is surprising insofar, that the first WHO protocol had been developed in Cairo (Cairo Working Group 1991) and the second in Niger (Niamey Working Group 2000). Researchers not yet applying the protocol should be encouraged to do so, in order to provide comparable data worldwide. Moreover, although not designed for hospital use, the protocol was found useful also in the hospitals since more than half of the hospitalized patients were also examined using the Niamey protocol. The worldwide adherence to the Niamey protocol for *S. haematobium* by proportion of patients is, thus, comparable to that of the WHO protocol for *S. mansoni*-related morbidity (el Scheich et al. 2014). Acceptance of the Niamey protocol proved excellent as compared to another protocol proposed by a WHO expert group, i.e. the WHO protocol for the ultrasonographic assessment of echinococcosis (Tamarozzi et al. 2014).

Inter-observer agreement of ultrasonographic findings using the Niamey protocol was found satisfactory. Possible confounders such as insufficient bladder filling before ultrasound examination and insufficient voiding prior to examination of the upper urinary tract were addressed by the majority of study groups applying the Niamey protocol. The impact of pitfalls on overall results may be minimized further by simplifying the bladder score as well as by keeping the bladder and upper urinary tract scores separate. A simplified bladder scoring was proposed by the group of King and collaborators (King et al. 2001; Wamachi et al. 2004) partly based on a former protocol of Medhat et al. (1997) which we re-propose in a slightly modified way:

Grade 0: No abnormality of the urinary bladder wall which is less than 5 mm thick

Grade 1: Any area of bladder wall with minor thickening of the bladder wall 5–7 mm

Grade 2: Maximum bladder-wall thickening of 8–9 mm

Grade 3: Maximum bladder-wall thickening of 10 mm or more, thus including any polyp, mass or tumor

Another refinement concerning the upper urinary tract could improve its sensitivity (provided the bladder is empty after voiding), i.e. to add the note if there is a fissure of the renal pelvis between 3 and 5 and 6 to 10mm.

By these modifications, less skilled examiners might use the protocol more easily. The literature available on the

transfer of ultrasonographic skills between a radiologist and a clinician in developing countries is scanty. Recently, in analogy of the use of focused ultrasonography in emergency medicine, it has been proposed to establish training curricula for the ultrasonographic assessment of selected pathologies which can be applied by non-specialised medical personal (Heller et al. 2010). This approach has been successfully applied for the rapid assessment of trauma by clinicians, in obstetrical indications, to assess cystic echinococcosis, obstructive uropathy and to identify tuberculosis in HIV-positive patients in South Africa (Kirkpatrick 2007; Heller et al. 2010; Kimberly et al. 2010; Jang et al. 2010a, b; Del Carpio et al. 2012). The successful transfer of ultrasonographic skills from a radiologist to a clinician sufficient for assessing *S. haematobium* induced urinary tract morbidity has been confirmed in a Senegalese study (Bonnard et al. 2011). As for an on the spot orientation of sufficient bladder filling, it should be reminded that a well-filled bladder changes from an ellipsoid to a approximately cubic shape. This might, however, not occur in a schistosomal bladder with a severely thickened wall.

It must be borne in mind, that transabdominal ultrasonography with portable devices for field use is not yet sufficiently sensitive to detect early ulcerative bladder wall abnormalities, independently from which protocol is used. This explains why results obtained by dipsticks are by far more sensitive for detecting urinary schistosomiasis than ultrasonography (Lougue-Sorgho et al. 2002; van der Werf and de Vlas 2004; Keita et al. 2005; Ahmed et al. 2014). Furthermore, ultrasonography is known to be less sensitive than radiology in detecting urinary tract calcifications (Burki et al. 1986; King 2002).

Evolution of schistosomal morbidity after therapy

Six out of 10 (60 %) studies on the regression of lesions after therapy referred to the Niamey protocol (Ouma et al. 2005; Tohon et al. 2008; Ramarakoto et al. 2008; Ekwunife et al. 2009; Qazi et al. 2012; Strahan et al. 2013). Unfortunately, none of the two studies on re-appearance of lesions following therapy in re-exposed people referred to the Niamey protocol (Campagne et al. 2001; Garba et al. 2004)

However, since there is a number of studies where evolution of pathology has been assessed using the former Cairo protocol, it is likely to be applicable in this respect, too (Hatz et al. 1998; Wagatsuma et al. 1999; Richter 2000; Hatz 2001; Richter et al. 2003). By the modifications of the Niamey protocol as proposed above, the assessment of the regression and subsequent reappearance of lesions in constantly exposed individuals might be evaluated more properly. A cystoscopy study on Brazilian soldiers returning from a peacekeeping mission in Mozambique revealed that even after two rounds of adequate praziquantel therapy, 36 % of soldiers who were

no more excreting ova in the urine still had viable ova in the bladder mucosa (Silva et al. 2006), an important issue also for travel medicine, considering the potential of schistosomiasis to induce bladder cancer (Mostafa, et al. 1999; Amonkar et al. 2001). Unfortunately; this study missed the opportunity to evaluate ultrasonography in this respect. It cannot be overemphasized that a bladder mass or polyp persisting for 6 months or more in spite of antihelminthic therapy is highly suspicious for bladder cancer and that the affected patient must be referred to a adequately equipped hospital for further diagnostic investigations.

Additional investigations

The Niamey-Belo Horizonte protocol also included optional investigations such as the determination of residual urine after voiding and the assessment of kidney pyelon fibrosis. The issue of residual urine after voiding has been addressed by an intriguing study of Watanabe et al. (2011), who compared parasitological findings and symptoms using an international questionnaire developed for prostate disease with results of ultrasonography and uroflowmetry. Results of this study indicated that the feeling of incomplete bladder emptying and hesitancy were better indicators for urinary schistosomiasis than the presence of residual urine (Watanabe et al. 2011), a result which additionally to the presence of cloudy urine should be taken into account for the questionnaires designed for identifying highly endemic communities for urinary schistosomiasis (Lengeler et al. 1991; Red Urine Study Group 1995; Wagatsuma et al. 2003; Campagne et al. 2001; Chippaux et al. 2001).

As part of the morbidity due to schistosomiasis detectable by ultrasonography is not yet covered by the WHO protocol, it should be included in the additional investigations section since the detection of calculi and calcifications does not cost additional examination time and their presence should be noted. Ureter, at least at their distal end might be investigated systematically for dilatation, wall irregularities, thickenings and strictures. A glance to the prostate also in adolescents could reveal early prostate abnormalities (Ramarakoto et al. 2008; Figueiredo et al. 2014b). Depending on the cultural and investigational context, e.g. hospital or health care centre settings, ultrasound examinations of boys and men could include the scrotum to detect genital abnormalities and hydrocele. Although usually attributed to filariasis, it is known for a long time that schistosomiasis not unfrequently causes hydrocele also in the absence of filariasis coinfection (Malik and Ibrahim 1982; Richter et al. 2002).

Unfortunately, even using transvaginal probes, specific lesions of the female reproductive tract are difficult to diagnose ultrasonographically. However, complications of genital schistosomiasis, such as ectopic pregnancy possibly associated with intraabdominal bleeding are readily diagnosed

ultrasonographically (Richter 2000). The same applies to pregnant women with schistosomiasis, where so far, studies on placenta ultrasound have not been published, although it is known that schistosomiasis also involves the placenta and that the placenta is an organ which is relatively easy to scan (Kimberly et al. 2010; Ben-Chetrit et al. 2014; Schleenvoigt et al. 2014). The best documented case series on the pregnancy outcome was published by Ben-Chetrit et al. (2014) on 10 pregnant women: the course and outcome of pregnancy in 4 patients who were diagnosed and treated with praziquantel was uneventful whereas 13 babies born to 6 asymptomatic women not diagnosed during pregnancy were significantly smaller as compared with those of the infants of the women who were treated during their pregnancy (median 2.8 vs 3.5 kg). One baby was born preterm. One infected woman had three miscarriages.

As another possible limitation of ultrasonography, one could put forward that urogenital tuberculosis may sometimes mimic schistosomiasis. Ultrasonographic differential diagnostic criteria for schistosomiasis are that upper urinary tract obstruction is due to bladder and ureter pathology and thus non-specific whereas in tuberculosis hypoechogenic lesions initiate in the kidney parenchyma also affecting the papillae. In doubtful cases, parasitological and bacteriological means are required for differential diagnosis (Das et al. 1992; Tikkakoski et al. 1993; Benchekroun et al. 1997; Hsieh et al. 2006; Singh et al. 2011).

Finally, especially in a Public Health and control context aiming at assessing the morbidity due to *S. haematobium*, it must be borne in mind that ultrasound just reveals the tip of the iceberg of *S. haematobium* induced morbidity, since micro- and macrohaematuria, symptomatology and extraurinary localizations may occur also in the absence of ultrasound-detectable lesions (van der Werf and de Vlas 2004). Furthermore, genital and ectopic localizations may occur in the absence of urinary egg excretion (Poggensee et al. 1998; Ramarakoto et al. 2008; Figueiredo et al. 2014a) and indirect not appreciated morbidity, i.e. anemia due to microhaematuria is also not captured by ultrasonography (Tohon et al. 2008).

Conclusions

In general, the WHO-Niamey-Belo protocol was well accepted since its publication. However, in some regions, the protocol is still not applied regularly. Researchers of some highly endemic regions such as Egypt, the Sudan and Niger should be encouraged to use the protocol so that their data can be compared on an international scale. The scoring of bladder wall and upper urinary tract might be slightly modified to simplify its application. The Niamey protocol proved applicable for focused ultrasound assessment by less specialized

personnel. A similar protocol is also needed for assessing the morbidity due to *S. japonicum* and *Schistosoma mekongi* which should be developed shortly.

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