Validating a questionnaire to identify women in first trimester of pregnancy during preventive chemotherapy interventions against soil-transmitted helminths in North-western Tanzania

Humphrey Deogratias Mazigo (humphreymazigo@gmail.com)
atholic University of Health and Allied Sciences https://orcid.org/0000-0001-5219-6234

Antonio Montresor
World Health Organization

Research article

Keywords: Preventive chemotherapy, Women of reproductive age, soil transmitted helminth, pregnancy status.

Posted Date: August 4th, 2019

DOI: https://doi.org/10.21203/rs.2.11605/v1

Abstract

Background Women of reproductive age carry a large burden of disease from soil-transmitted helminths infections. Preventive chemotherapy with anthelminthic is an effective treatment to control soil-transmitted helminths morbidity. However, as a precautionary measure, the treatment of pregnant women is recommended only after the first trimester. This has resulted in many women of reproductive age be denied treatment because of doubt on their pregnancy status. The standard assessments of the pregnancy status (i.e. urine pregnancy rapid test or blood test) are too expensive to be used in mass drug administration campaigns. Thus, use of a simple alternative approach is recommended. The present study was conducted to evaluate the performances of a questionnaire in assessing the pregnancy status of women of reproductive age during preventive chemotherapy interventions. Methodology A questionnaire (20 questions) followed by rapid pregnancy test (RPT) were administered to a group of women of reproductive age in two districts in North-western Tanzania. Results A total of 1,217 women of reproductive age participated in the study. Overall, 10.8% of the women reported to be pregnant at the specific question in the questionnaire. The rapid pregnancy test identified 15.1% (184/1217) of the women to be pregnant. In total, 86.4% (114/1,217) of the women who reported to be pregnant during the interview were confirmed to be pregnant using the RPT. The question on pregnancy demonstrated an overall sensitivity of 62% and specificity 98.3%. Conclusion The questionnaire can be used to identify pregnant women in first trimester during preventive chemotherapy campaigns. The question on last date of start of menstrual period yield the highest sensitivity and appeared to be the key one to be used in combination with other questions. However, validation of these results in other countries with different cultures are needed to fully evaluate performance of this method.

Background

Infections with soil-transmitted helminths (STH) affect an approximately 1.5 billion people, particularly those living in rural areas of developing world characterized by poor sanitation and hygiene [1]. Approximately, one quarter of the world's population is infected with at least one species of soil-transmitted helminths, which include *Ascaris lumbricoides* (800 million people), *Trichuris trichiura* (600 million people) and hookworm (600 million people) [2]. It is estimated that, 700 million women live in areas characterized with high transmission of STH [3] and needs deworming. In 2008, it was estimated that 37.7 million of women of reproductive age (WRA) were infected with hookworm alone [4]. Nutritional and iron status impairment, micronutrients deficiencies (iron deficiency anaemia), low birth weight and maternal and neonatal death are some of the outcomes of STH infection during pregnancy [5]. Montresor and colleagues estimated that more 600,000 disability-adjusted life years (DALYs) are lost annually by WRA due to STH infections [6].

Recognizing the impact of STH infections on the health of WRA and during pregnancy, in 1994 [7], 2002 [8], and most recently in 2017, the World Health Organization recommends the regular treatment of WRA with albendazole or mebendazole, as precautionary measure the treatment of pregnant women is recommended only after the first trimester [7]. Because of the lack of a low-cost method to assess

pregnancy this approach has resulted in excluding WRA from treatment [9]. To ensure that the entire WRA group is not excluded from deworming programs, the main challenge is to identify women in their first trimester of pregnancy so that they can be excluded from treatment and offered deworming at a later time in their pregnancy.

Rapid pregnancy tests (RPT), which uses urine samples, is a gold standard approach to accurately identify women in their first trimester of pregnancy; however, these tests are too expensive to be used in large quantities as needed for deworming programs. The use of simple and less expensive tools such as questionnaire to identify individuals with a targeted condition has been proposed in the past: the red urine questionnaire has been widely used to detect children with haematuria a symptoms that, in tropical areas, is strictly related to *S. haematobium* infection [10]. Thus, is not surprising to see the red urine questionnaire have high capacity of detecting cases of schistosomiasis [11]. In pregnant women, one previous study examined the performance of a questionnaire in identifying pregnant status of women during preventive chemotherapy (PC) implementation [12]. However, the methodology used in this study was not standardized. Therefore, this study focused on validating the use of a questionnaire to identify pregnant women. Specifically, the study was comparing the sensitivity and specificity of the questionnaire to identify pregnant women with a urine-based rapid pregnant test (RPT) (gold standard) in north-western Tanzania.

Methods

Study area: The study was conducted in two districts in Mwanza Region. At Ilemela District, the study was conducted at Igalagala and Kabangaja villages located on the shorelines of Lake Victoria. In Buchosa District, the study was conducted at Kome Island. The selection of the study areas was based on the accessibility and the past history of preventive chemotherapy (PC) against STH and schistosomiasis through school-based and community-based approaches [13, 14].

Study population and inclusion criteria: The study included women living in the selected sub-villages of Kome Island, Igalagala and Kabangaja of Buchosa and Ilemela districts. Women aged 18- 49 years of age, residing in the study villages, willing to participate and that gave written informed consent were recruited into the study.

*Sample size and sampling procedures:*To calculate the sample size, we used the sample size estimator (http://epitools.ausvet.com.au/content.php?page=2Proportions). The size of the sample was determined to detect a significant difference in the two proportions of pregnant WRA (identified by respectively by questionnaire and by RPT) with 95% confidence at a power of 80%. We anticipated a proportion of true pregnancy of 10.8% in women (in accordance to crude birth rates in Tanzania that is 5.4%) [15]. A minimum sample of 474 study participants were to be recruited, due to the availability of diagnostic tests (RPT) and the willingness of WRA to participate the study, a larger sample of 1,217 women meeting all the inclusion criteria were recruited.

Questionnaire: The study adapted a questionnaire developed by WHO/NTD (supplementary file). The questionnaire composed of 21 questions that collect demographic information of women, parity, menstrual period, personal impression on being pregnant, lactation signs and symptoms relating to pregnancy. The English version of the questionnaire is attached as a supplementary document (optional). The questionnaire was translated to Kiswahili national language spoken and understood by 98% of the Tanzanian population. Before the start of the study, the questionnaire was pre-tested in a village different from the ones where the study was later conducted to check for clarity of the questions and to identify any possible ambiguity. All data were collected by trained nurses and experienced social scientists.

Pregnancy Rapid Test: After the questionnaire interview, participants were requested to submit a urine sample that was tested for pregnancy with a RPT (Core Tests® Care Technology Co. LTD, Beijing, China, LOT number: 20171204). The Core Tests® is a qualitative immune-chromatography test which detects Human Chorionic Gonadotropin hormone (hCG) in urine of pregnant women. The results of the test were interpreted according to manufacturer instruction based on color changes in the reagent strip. All test results were recorded in a form with participant identification number that allowed to link the RPT results with the results of the questionnaire.

*Data management and statistical analysis:*All collected data were entered into an Excel sheet. Data analysis was done using Stata version 15 (Stata Corp, College station, Texas, USA).

We judge the sensitivity of the questionnaire to be the main indicator of efficiency: a questionnaire able to identify a large majority (> 80%) of the pregnant women could be an extremely useful tool to exclude pregnant women during PC campaign; on the other side the mis-identification of a number of non-pregnant as pregnant due to poor specificity (example 50% specificity) and their exclusion from the intervention was considered acceptable in the context of PC campaign.

Results

Characteristics of the study participants

A total of 1,217 women from Igalagala, Kabanganja and Kome Island, participated in this study. The mean age of the study participants was 30.25 ± 8.68 years (age range: 18-49 years). Majority of the women reported to be married (62.12%) and 88.2% of the women had children (Table 1). The median number of children was 3 children (Interquartile range: 2-5 children) and 75.9% of the women had between 1-5 children. Table 1 shows the demographic characteristics of the study participants.

Reported pregnancy status and related symptoms

At the time of interview, 132 women (10.8%) self-reported to believe to be pregnant. The mean gestation age/period for those reported to be pregnant was 21.51± 10.18 weeks (range 1-36 weeks), with 37.9% of them reported to be in third trimester of pregnancy. Details on response regarding other symptoms

normally related to pregnancy (soreness of the breast, darkened areolas, increased fatigue, nausea, vomiting) are presented in Table 2.

Prevalence of pregnancy based on rapid urine pregnancy test

Overall, a total of 1,217 women submitted urine samples for detection of pregnancy status using a rapid pregnancy test. Of these, almost 96% of them indicated their willingness to receive the result of the test. Based on RPT, 184 (15.1%) resulted pregnant.

Sensitivity and specificity of the questionnaire

Of the 184 women that resulted pregnant at RPT, 114 had responded “yes” to Question 13 (Do you think you might be pregnant?) corresponding to a sensitivity of this question for pregnancy of 62% (95% CI:54.5-69.0). Of the 132 women who responded “yes” to Question 13, a total of 114 were confirmed to be pregnant using the RPT, corresponding to a specificity 86.4%. On the other hand, 6.4% (70/1085) of the women who reported not be pregnant at questionnaire were confirmed to be pregnant by RPT. Only 13.6% (18/132) of the women who reported to be pregnant during the interview were actually not pregnant (Table 3).

Table 4 shows the results of the rapid pregnancy test in relation to the reported symptoms related to pregnancy. None of the signs normally linked with pregnancy (soreness of the breast, darkened areolas, increased fatigue, nausea, vomiting), alone or combined with others, was a good predictor of an actual pregnancy status (see Table 4 for details).

Sensitivity and specificity of reported pregnancy in different sub-groups of participants

The sensitivity of the reported pregnancy (Questionnaire 13) in the questionnaires was also assessed in different sub-groups (Table 5):

*Single women:*Of the 130 single women responded to the questionnaire, 4 declared to be pregnant and 6 resulted pregnant at RPT. The sensitivity of the question 13 is not reduced in this group.

*Women with children:*Of the 174 women with children responded to the questionnaire 116 declared to feel pregnant ad 158 resulted pregnant at RPT. The sensitivity of the question 13 is not increased in this group nor if the evaluation of sensitivity of question 13 is restricted to women with more than 2, more than 4 or more than 6 children.

*Women age:*The age of the respondent seems not to be linked to the sensitivity of question 13. Table 5 shows the performances of question 13 (sensitivity, specificity, Positive Predictive Value and Negative Predictive Value) in different sub-groups.

Discussion

In this study, we tested the performances of a questionnaire designed to identify pregnant women for its possible use during PC campaigns. This low-cost tool could be useful in reducing exclusion of WRA from PC campaigns that is frequently resulting from the perceived risk of treatment of pregnant women in the first trimester [16].

The proposed questionnaire is composed by 20 questions; some of them (questions 1-7) are included with purpose of exactly identify each woman during the study. Other questions (questions 8-12) were included to explore if the answer to the questionnaire were influenced by some other condition, out hypothesis was that, for example, unmarried women would have been more reticent in responding “yes” to a direct question investigating pregnancy status than married ones or that a woman with multiple children could better recognize the early signs of pregnancy. The key question was in our opinion question 13 “Do you think you might be pregnant?” and in particular its sensitivity of correctly identify pregnancies, in case of the positive reply. We considered a poor specificity (≈50%) to be acceptable as would have resulted in exclusion of WRA from treatment but not exposed them to any (also only perceived) risk. Other questions (questions 16-20) were included to explore if the presence of symptoms frequently associated with pregnancy could be used to identify pregnant women.

Conclusion

We consider the performances of the questionnaire in Tanzania not completely satisfactory: if the questionnaire would have been used in a PC intervention targeting a male and female population of 100 000 individuals (with a crude birth rates of 6%) where 3000 pregnant women are expected to be present, only 1860 of the pregnant would have been correctly identified and excluded from treatment. Also, the signs normally linked with pregnancy (soreness of the breast, darkened areolas, increased fatigue, nausea, vomiting) resulted not to be a good predictor of an actual pregnancy status. Test of the questionnaire in different culture could be done to assess its sensitivity in different settings.

List Of Abbreviations

WRA – Women of Reproductive Age

STH – Soil-transmitted Helminths

RPT – Rapid Pregnancy Test

PC – Preventive Chemotherapy

WHO – World Health Organization

NTD – Neglected Tropical Diseases

Declarations

Ethics approval and consent to participate: Ethical approval was obtained from the joint Ethical and Review Committee of Bugando Medical Centre and Catholic University of Health and Allied Sciences (CREC/281/2018). The study received further ethical approval from the National Institute for Medical Research, National Ethical Committee (MR/53/100/541). The study received further government authority clearance from the district and village administrative authorities. Before the commencement of the study, visits were made to the villages and village leaders were met. The intention of the study was explained to the leaders first, who in turn convened meetings with community members to explain the objective of the study. Kiswahili translated informed consent forms were used to obtain consent from study participants. The objective of the study and study procedures were fully described to the study participants before asking for their informed consent. For illiterate participants, a thumb print was used to sign the consent forms. To maintain confidentiality, all the data of the study participants were kept in a closed cabinet and whenever the data were accessed no participants name was disclosed, only identification number of the participants were used to identify participants. Participation in this interview were voluntary. Participation in the study was voluntary and free. All study participants were offered to obtain the result of the pregnancy test.

Consent for publication

Not applicable

Availability of data and materials

The datasets collected and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

This work was supported by Children Without Worms (CWW), Task Force for Global Health, Georgia, United States of American. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the supporting offices.

Authors' contributions

HDM and AM designed the study, participated in data collection, analyzed and drafted the first version of the manuscript. All authors read and approved the final manuscript, contributed to the critical review and made substantial contribution to it.

Acknowledgements

We thank ALL women who participated in the study from all the study villages. We are grateful to the Catholic University of Health Sciences for logistical and financial management support.

References

1. Hotez PJ, Molyneux DH, Fenwick A, Kumaresan J, Sachs SE, Sachs JD, et al. Control of neglected tropical diseases. N Engl J Med. 2007;357(10):1018-27. Epub 2007/09/07. doi: 357/10/1018 [pii]

10.1056/NEJMra064142. PubMed PMID: 17804846.

2. Hotez PJ. One world health: neglected tropical diseases in a flat world. PLoS Negl Trop Dis. 2009;3(4):e405. Epub 2009/04/29. doi: 10.1371/journal.pntd.0000405. PubMed PMID: 19399165; PubMed Central PMCID: PMC2668801.

3. Mupfasoni D, Mikhailov A, Mbabazi P, King J, Gyorkos TW, Montresor A. Estimation of the number of women of reproductive age in trend of preventive chemotherapy for soil-transmitted (STH) infections. Plos Negl Trop Dis (in press). 2017.

4. Brooker S, Hotez PJ, Bundy DA. Hookworm-related anaemia among pregnant women: a systematic review. PLoS Negl Trop Dis. 2008;2(9):e291. doi: 10.1371/journal.pntd.0000291. PubMed PMID: 18820740; PubMed Central PMCID: PMCPMC2553481.

5. Bundy DA, Chan MS, Savioli L. Hookworm infection in pregnancy. Trans R Soc Trop Med Hyg. 1995;89(5):521-2. PubMed PMID: 8560530.

6. Montresor A, Trouleau W, Mupfasoni D, Bangert M, Joseph SA, Mikhailov A, et al. Preventive chemotherapy to control soil-transmitted helminthiasis averted more than 500 000 DALYs in 2015. Trans R Soc Trop Med Hyg. 2017;111(10):457-63. Epub 2018/01/19. doi: 10.1093/trstmh/trx082. PubMed PMID: 29346640; PubMed Central PMCID: PMCPMC5808863.

7. WHO. Report of the WHO informal consultation on hookworm infection and anaemia in girls and women. , 5–7 December 1994. WHO/CTD/SIP/961. 1995.

8. WHO. Report of the WHO informal consultation on the use of praziquantel during pregnancy/lactation and albendazole/mebendazole in children under 24 months. WHO2002Report of the WHO informal consultation on the use of praziquantel during pregnancy/lactation and albendazole/mebendazole in children under 24 months. World Health Organization, Geneva, WHO/CDS/CPE/PVC/20024 World Health Organization, Geneva, WHO/CDS/CPE/PVC/20024. 2002.

9. Gyorkos TW, Montresor A, Belizario V, Biggs BA, Bradley M, Brooker SJ, et al. The right to deworming: The case for girls and women of reproductive age. PLoS Negl Trop Dis. 2018;12(11):e0006740. Epub 2018/11/22. doi: 10.1371/journal.pntd.0006740. PubMed PMID: 30462641; PubMed Central PMCID: PMCPMC6248892 following competing interests: 1. MB is the Director of Scientific Support for

albendazole donations for GlaxoSmithKline. 2. CV is the Director, GPH; Global Program Leader STH at Johnson & Johnson. 3. RI is the Director of Children Without Worms, which was jointly founded by Johnson & Johnson and The Task Force for Global Health.

10. Lengeler C, Mshinda H, Morona D, deSavigny D. Urinary schistosomiasis: testing with urine filtration and reagent sticks for haematuria provides a comparable prevalence estimate. Acta Trop. 1993;53(1):39-50. Epub 1993/03/01. PubMed PMID: 8096108.

11. Red Urine Study Group. . Identification of high risk communities for schistosomiasis in Africa: a multi-country study, Social and Economic Research Project Reports Series 15. World Health Organization 1995, Geneva. 1995;(83).

12. Chippaux JP, Gardon-Wendel N, Ernould JC, Gardon J. [Comparison between various methods of pregnancy screening during a large-scale ivermectin treatment in Cameroon]. Bull Soc Pathol Exot. 1995;88(3):129-33. PubMed PMID: 8555769.

13. Kaatano GM, Siza JE, Mwanga JR, Min DY, Yong TS, Chai JY, et al. Integrated Schistosomiasis and Soil-Transmitted Helminthiasis Control over Five Years on Kome Island, Tanzania. Korean J Parasitol. 2015;53(5):535-43. Epub 2015/11/06. doi: 10.3347/kjp.2015.53.5.535

kjp-53-5-535 [pii]. PubMed PMID: 26537032; PubMed Central PMCID: PMC4635827.

14. Clements AC, Lwambo NJ, Blair L, Nyandindi U, Kaatano G, Kinung'hi S, et al. Bayesian spatial analysis and disease mapping: tools to enhance planning and implementation of a schistosomiasis control programme in Tanzania. Trop Med Intern Health. 2006;11(4):490-503. Epub 2006/03/24. doi: TMI1594 [pii]

10.1111/j.1365-3156.2006.01594.x. PubMed PMID: 16553932; PubMed Central PMCID: PMC2202922.

15. TDHS-MIS. Tanzania Demographic and Health Survey and Malaria Indicator Survey (TDHS-MIS), 2015-2016. Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGC, [Mainland Tanzania], Ministry of Health (MoH) [Zanzibar], National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), ICF International 2016. Dar es Salaam, Tanzania, and Rockville, Maryland, USA. 2016.

16. Gyorkos TW, Montresor A, Belizario V, Biggs BA, Bradley M, Brooker SJ, et al. The right to deworming: The case for girls and women of reproductive age. PLoS Negl Trop Dis. 2018;12(11):e0006740.

Tables

Due to technical limitations, Tables 1-5 are only available as downloads in the supplemental file section.

Table 1: Characteristics of the study participants

Table 2: Reported pregnant status and related symptoms

Table 3: Comparison of the responses to question 13 of the questionnaire and the results of the Rapid Pregnancy Test, and the resulting performances (sensitivity, specificity, Positive Predictive Value and Negative Predictive Value).

Table 4: Prevalence of pregnancy based on rapid pregnancy test in relation to reported pregnant and symptoms in the questionnaire

Table 5: Sensitivity and specificity of reported pregnancy in different sub-groups of participants

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FirstTrimesterResearchProposalQUESTIONNAIRE.pdf
- Table2.pdf
- Table4.pdf
- Table1.pdf
- Table5.pdf
- Table3.pdf
- QuestionnaireRationaleQxP.pdf