

What is already known on this topic

Clinical trials of anthelmintic treatments have shown increased linear growth in young people up to age 16 years, whereas in younger people the increase is mainly in weight

Little evidence exists of the benefits of giving periodic mass treatment through public health programmes, and none is targeted at preschool children

What this study adds

Giving anthelmintic treatments routinely as a part of periodic child health days can lead to extra weight gain in preschool children in Uganda

The weight gain of children who attended child health days every six months was 10% greater than in untreated controls

reported benefits in ponderal growth, as in our study. The meta-analysis pointed out that most studies have been done in populations infected with *Ascaris lumbricoides*, but the largest effect on weight gain in preschool children has been in those infected predominantly with hookworm, as in our study.

Deworming has benefits beyond those measured in our study, such as reducing anaemia.^{6,7} Moreover, treating children alone can reduce the prevalence of worms among untreated people.⁸

On average, each child health day costs between \$500 and \$600, exclusive of the costs of volunteers. Each event reaches about 450 children, suggesting a cost of about \$1 to \$1.33 per child. A dose of albendazole added \$0.21 (US\$ 385) to the costs of materials at child health days (2002 prices) but added little to the costs of staff since they were already dispensing

vitamin A. This cost could be reduced to \$0.03 by bulk purchase of the drug. But even when applying the prices in 2002 and ignoring the other benefits of deworming, the 10% increase in weight gain with twice yearly treatment at a cost of \$0.42, or a 5% increase at a cost of \$0.21, represents an attractive return.

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- 1 Awasthi S, Bundy DAP, Savioli L. Helminthic infections. *BMJ* 2003; 327:431-3.
- 2 Kabatereine N, Tukahebwa E, Brooker S, Alderman H, Hall A. Epidemiology of intestinal helminth infections among schoolchildren in southern Uganda. *East Afr Med J* 2001;78:283-6.
- 3 World Health Organization. *Prevention and control of schistosomiasis and soil-transmitted helminthiasis*. Report of a WHO expert committee. WHO technical report series 912. Geneva: WHO, 2002.
- 4 Dickson R, Awasthi S, Williamson P, Demellweek C, Garner P. Effect of treatment for intestinal helminth infection on growth and cognitive performance in children: systematic review of randomized trials. *BMJ* 2000;320:1697-701.
- 5 Stoltzfus RJ, Chway H, Montresor A, Tielsch JM, Jape JK, Albonico M, et al. Low dose daily iron supplementation improves iron status and appetite but not anemia, whereas quarterly anthelmintic treatment improves growth, appetite and anemia in Zanzibari preschool children. *J Nutr* 2004;134:348-56.
- 6 Bundy DAP, Shaeffer S, Jukes M, Beegle K, Gillespie A, Drake L, et al. School based health and nutrition programs. Chapter 61. *Disease control priorities for developing countries*. In: Jamison D, Claeson M, Breman J, Meacham A, eds. Oxford: Oxford University Press, 2005.
- 7 Jalal F, Neisheim M, Agus Z, Sanjur D, Habicht J-P. Serum retinol concentrations in children are affected by food sources of β -carotene, fat intake, and anthelmintic drug treatment. *Am J Clin Nutr* 1998;68:623-9.
- 8 Bundy DAP, Wong MS, Horton J. Control of geohelminths by delivery of targeted chemotherapy through schools. *Trans R Soc Trop Med Hyg* 1990;84:115-20.

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Reliability of self reported form of female genital mutilation and WHO classification: cross sectional study

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Abstract

Objective To assess the reliability of self reported form of female genital mutilation (FGM) and to compare the extent of cutting verified by clinical examination with the corresponding World Health Organization classification.

Design Cross sectional study.

Settings One paediatric hospital and one gynaecological outpatient clinic in Khartoum, Sudan, 2003-4.

Participants 255 girls aged 4-9 and 282 women aged 17-35.

Main outcome measures The women's reports of FGM, the actual anatomical extent of the mutilation, and the corresponding types according to the WHO classification.

Results All girls and women reported to have undergone FGM had this verified by genital inspection. None of those who said they had not undergone FGM were found to have it. Many said to have undergone "sunna circumcision" (excision of prepuce and part or all of clitoris, equivalent to WHO type I) had a form of FGM extending beyond the clitoris (10/23 (43%) girls and 20/35 (57%) women). Of those who said they had undergone this form, nine girls (39%) and 19 women (54%) actually had WHO type III (infibulation and excision of part or all of external genitalia). The anatomical extent of forms classified as WHO type III varies widely. In 12/32 girls

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(38%) and 27/245 women (11%) classified as having WHO type III, the labia majora were not involved. Thus there is a substantial overlap, in an anatomical sense, between WHO types II and III.

Conclusion The reliability of reported form of FGM is low. There is considerable under-reporting of the extent. The WHO classification fails to relate the defined forms to the severity of the operation. It is important to be aware of these aspects in the conduct and interpretation of epidemiological and clinical studies. WHO should revise its classification.

Introduction

Despite many decades of campaigns and legislation, female genital mutilation (FGM) is still highly prevalent in the areas where it has traditionally been practised. Even though many people re-evaluate and abandon it when they emigrate,¹ there is evidence that it continues in Europe.²⁻⁵ In the United Kingdom, though data on prevalence are scarce, there are thought to be 3000-4000 new cases every year.⁶ Almost all studies about the prevalence and trends of FGM are based on women's reports. It is not known how this reported form corresponds to reality. We used clinical examination to assess the reliability of self reported form of FGM in Sudan and compared these reports with the extent of cutting verified by clinical examination classified according to the World Health Organization system (table 1).

Methods

Data were obtained from two different hospital based studies.^{8,9} Cases were women aged ≤ 35 with primary infertility ($n=102$). Controls were women aged ≤ 35 who were having their first baby and had no history of infertility ($n=180$). The study took place at Khartoum Teaching Hospital and Soba University Hospital from March 2003 to June 2004.

Girls were recruited as part of another study looking into paediatric complications of genital mutilation with special reference to urogenital symptoms, signs, and diagnoses in a public hospital emergency ward in Khartoum, Sudan.⁸ We consecutively recruited girls aged 4-9 ($n=255$) who presented to the emergency ward and asked their guardians whether the girls had undergone FGM.

For both groups, those who reported having undergone genital mutilation were then asked at what age and what form of FGM had been done. After obtaining informed consent from the woman or guardian, the doctor conducted a full physical examination, including genital inspection, to verify the exact anatomical extent of the operation. All doctors had received special training so they classified FGM in

the same way. Particular efforts were made to avoid observer bias concerning the extent of vulval damage.

We used the Mann-Whitney test to analyse continuous variables and χ^2 to test for differences between proportions, with $P < 0.05$ indicating significance unless otherwise stated.

Results

Altogether we included 537 participants in the study, 255 girls aged 4-9 and 282 women aged 17-35. Of these, 52 girls and 275 women had undergone FGM. We had no data on the anatomical extent of FGM (clinical inspection of genitals) for two women and four girls. For one girl and one woman information was missing on reported form. Ten women did not know their form of FGM. Genital inspection verified FGM in all women and girls reported to have undergone the procedure. None of those who said they did not have any form of FGM were found to have it.

Table 2 shows the anatomical features of the different traditional terms used to describe forms of FGM. Many who said they had undergone "sunna" (which should correspond to WHO type I) had a form of FGM extending beyond the clitoris (10 (43%) girls and 20 (57%) women). Nine (39% girls) and 19 (54%) women reported to have undergone "sunna" actually had WHO type III. Out of those who reported that they had undergone the "intermediate" form, four (80%) girls and 14 (82%) women had WHO type III, as classified by the doctor on inspection. The form of FGM was reported incorrectly in one in four respondents. Out of the 10 women who did not know their form of FGM, seven had type III. In 12 (38%) girls and 27 (11%) women classified as having WHO type III, the labia minora were stitched but the labia majora were not involved. Thus there is a substantial overlap, in an anatomical sense, between WHO types II and III.

Discussion

The reliability of reported form of FGM is low, and the WHO classification fails to relate the defined forms to the severity of the operation. It is important to be aware of these aspects in the design and interpretation of epidemiological and clinical studies.

Strengths and limitations

There are a few methodological limitations with our study. As a hospital based study, it was not designed to obtain a representative sample of girls and women in the area, though our observed prevalence among women was similar to that seen in the last community based survey (97% and 91%).¹⁰ The doctors who examined the women and girls and classified the form of FGM knew what form the women or guardians had reported.

Recall bias in the women and guardians might have affected the results. For adult women there was no difference in the time since the procedure between those who reported correctly and incorrectly, but for girls there was. It is difficult to explain this difference, but it probably has more to do with a tendency to justify what has been done by using the religious term "sunna" than the time passed. In the past few years there has been an intense debate in Sudan on the legal and

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Table 1 WHO classification of female genital mutilation⁷

Type	Detail
I	Excision of prepuce and part or all of clitoris
II	Excision of prepuce and clitoris together with partial or total excision of labia minora
III	Infibulation and excision of part or all of external genitalia
IV	Pricking, piercing, incision, stretching, scraping, or other harming procedures on clitoris and/or labia

Table 2 Correlation between anatomical extent of FGM and reported form in 47 girls and 262 women* who had reported a form of circumcision and had genital inspection done

Anatomical extent of genital mutilation	Reported form of genital mutilation					
	Sunna		Intermediate		Pharaonic	
	Girls	Women	Girls	Women	Girls	Women
Prepuce only	—†	—†	—‡	—‡	—‡	—‡
Part or whole clitoris	13†	15†	—‡	2‡	—‡	1‡
Clitoris + labia minora without stitching	1§	1§	1†	—†	1‡	1‡
Clitoris + labia minora with stitching	5§	7§	—†	3†	7‡	16‡
Clitoris + labia majora without stitching	—§	—§	—§	—§	1‡	6‡
Clitoris + labia majora with stitching	4§	12§	4§	11§	10†	187†

Sunna should correspond to WHO type I; pharaonic should correspond to WHO type III.

*Information missing on reported form for one girl and one woman; 10 women did not know their form of FGM; data missing on anatomical extent of FGM (clinical inspection of genitals) for two women and four girls.

†Expected extent of operation.

‡Over-reporting of extent of FGM.

§Under-reporting of extent of FGM.

religious status of “sunna circumcision.” This has given FGM a religious context, which traditionally it did not have.

There was complete agreement between reporting having undergone FGM or not and what was found by inspection of genitals, in both girls and women. In this regard our findings differ from previous studies. In urban and rural Tanzania there was inconsistency between self reported and clinically determined FGM in more than 20% of women (women tend to say they had not undergone FGM when they had).^{11 12} These studies investigated the reporting of having undergone FGM or not and did not comment on the reliability of reporting of different forms. A study from Nigeria showed that self reporting was reliable in 79% of women.¹³ In rural Gambia a community based study showed 97% agreement between reported status of FGM and what was found on examination. Our study shows that the self reporting of different forms of FGM is not reliable.

Our results indicate an extensive over-reporting of the “sunna” form. The word “sunna” refers to what the prophet Muhammed has said or done. By using the term “sunna” the practice is associated with Islam and given a religious value. Thus, one possible reason for the widespread under-reporting of form of FGM could be to justify the practice by referring it to a religious term. It could also be that the practitioner who performed the operation called it “sunna,” even though she did a more extensive form. It is, however, important to note that FGM is not a religious practice as it

predates the arrival of both Christianity and Islam in Africa,^{3 14} and FGM is not known in many Muslim countries.³

Most of those who promote what they call “sunna circumcision” say it entails only the removal of the prepuce of the clitoris (S A Khalid, personal communication).¹⁵ Our results, on the contrary, show a tendency to use “sunna” for different forms of FGM. Among the 27 girls and 35 women with alleged “sunna” in our study, there was not a single case of removal of the prepuce only. This is in accordance with previous experience from Sudan¹⁵ and Tanzania.¹²

WHO classifies all forms that involve suturing as type III, regardless of whether the labia minora or majora have been cut. Therefore classification as type III does not indicate the extent of the mutilation that has been done. This is important, especially in investigations of FGM and complications. It is rarely pointed out that the frequency and severity of complications are a function of the extent of the operation.¹⁶

Many studies have failed to find associations between FGM and morbidity when they have used the WHO definitions. In our recent study from Sudan on the association between FGM and infertility there was a highly significant association between the anatomical extent and primary infertility, but when we used the WHO classification on the same material we found no association.⁹

Recommendations

In studies to estimate the prevalence of FGM and its different forms by interviews, women should be asked to explain what they mean by the different terms, including the extent of cutting. The use of visual aids might facilitate this. Clinical studies on FGM and its relation to morbidity and complications should classify forms of FGM according to the anatomical extent of FGM rather than use the WHO classification. The WHO should revise its classifications to relate the different forms more to the anatomical extent of the operation.

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What is already known on this topic

Almost all studies about the prevalence and trends of female genital mutilation (FGM) have been based on women self reporting their form of FGM

How this reported form corresponds to reality is unknown

What this study adds

The reliability of reported form of FGM is low, and there is considerable under-reporting of the extent of FGM

The WHO classification fails to relate the defined forms of FGM to the severity of the operation

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- 1 Johnsdotter S. Created by God: how Somalis in Swedish exile reassess the practice of female circumcision [dissertation]. Lund, Sweden: Department of Sociology, Lund University, 2002.
- 2 Dorkenoo E. *Cutting the rose: female genital mutilation: the practice and its prevention*. London: Minority Rights Publications, 1994.
- 3 Rahman A, Toubia N. *Female genital mutilation: a guide to laws and policies worldwide*. London: Zed, 2000.
- 4 Holmgren H, Almroth L, Berggren V, Bergstrom S. [Genital mutilation of children is an offence. Do health services have a sufficient knowledge to see the problem?] *Lakartidningen* 2005;102:1637-43.
- 5 Morison LA, Dirir A, Elmi S, Warsame J, Dirir S. How experiences and attitudes relating to female circumcision vary according to age on arrival in Britain: a study among young Somalis in London. *Ethn Health* 2004;9:75-100.
- 6 Bosch X. Female genital mutilation in developed countries. *Lancet* 2001;358:1177-9.
- 7 WHO Technical Working Group. *Female genital mutilation*. Geneva: WHO, 1996.

- 8 Almroth L, Bedri HA, Elmusharaf S, Satti A, Idris T, Hashim MSK, et al. Urogenital complications among girls with genital mutilation: a hospital based study in Khartoum. *Afr J Reprod Health* 2005;9:127-33.
- 9 Almroth L, Elmusharaf S, El Hadi N, Obeid A, El Sheikh MA, Elfadil SM, et al. Primary infertility after genital mutilation in girlhood in Sudan: a case-control study. *Lancet* 2005;366:385-91.
- 10 Department of Statistics and Institute for Resource Development/Macro International. *Sudan demographic and health survey 1989/1990*. Columbia, MD: Department of Statistics and Institute for Resource Development/Macro International, 1991.
- 11 Msuya SE, Mbitvo E, Hussain A, Sundby J, Sam NE, Stray-Pedersen B. Female genital cutting in Kilimanjaro, Tanzania: changing attitudes? *Trop Med Int Health* 2002;7:159-65.
- 12 Klouman E, Manongi R, Klepp K-I. Self-reported and observed female genital cutting in rural Tanzania: associated demographic factors, HIV and sexually transmitted infections. *Trop Med Int Health* 2005;10:105-15.
- 13 Snow RC, Slangor TE, Okonofua FE, Oronsaye F, Wacker J. Female genital cutting in southern urban and peri-urban Nigeria: self-reported validity, social determinants and secular decline. *Trop Med Int Health* 2002;7:91-100.
- 14 Lockhat H. *Female genital mutilation: treating the tears*. London: Middlesex University Press, 2004.
- 15 Toubia N. Female circumcision as a public health issue. *N Engl J Med* 1994;331:712-6.
- 16 Obermeyer CM. Female genital surgeries: the known, the unknown, and the unknowable. *Med Anthropol Q* 1999;13:79-106.

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Rare diseases, orphan drugs, and orphan diseases

Rare comes from the Latin *rarus* (loosely spaced or sparse) and eventually from the putative Indo-European root *ERE*, denoting separation, as in hermits and eremites and the net-like structures *rete*, *retinaculum*, and *retina*.

Orphan comes from the Greek *orphanos* (a child deprived of one parent or both, or an adult deprived of a child). Metaphorically it denoted poverty and unspiced food. Its Indo-European root was *ORBH* (bereft) giving the Latin *orbis* and the obsolete English words *orbatum* and *orbity* (orphanhood or childlessness). One bereft of freedom is a slave, forced into hard work, as in the German *Arbeit* and the Czech *robota*. Karel Čapek coined the word *robot* (female *robotka*) in his play *R.U.R. (Rossum's Universal Robots, 1920)* to denote an imagined race of mechanical people. And the etymology reflects the link between orphans and the workhouse.

Modern metaphorical meanings of orphan include a discontinued model of a motor vehicle and a line of type beginning a new paragraph at the bottom of a column or page. An orphan virus, such as hepatitis G, is one without a recognised associated disease. Orphan enzymes have catalytic sites that can be occupied by millimolar concentrations of ethanol but have no known physiological roles. Orphan receptors, such as the opioid *OP4* receptor identified from gene sequences, have no known endogenous ligands or physiological functions.

Rare diseases—The National Institutes of Health Office of Rare Diseases lists more than 6000, from Aagenaes syndrome to Zuska's disease. The US definition of a rare disease is one that affects less than 200 000 individuals; the corresponding number in Japan is 50 000 and in Australia 2000. These numbers translate to prevalences of 1-8 in 10 000. The European Community definition is less than 5 in 10 000, and the World Health Organization has suggested less than 6.5-10 in 10 000. Below I suggest an alternative.

Orphan drugs—The US Orphan Drug Act (1984) defines an orphan drug as one with "efficacy against a disease affecting fewer than 200 000 people ... or one that ... will not be profitable for seven years." So,

orphan drugs are either drugs that are used to treat rare diseases (such as haem arginate for porphyrias) or drugs that are too costly to develop. Of course, they are often both, but one does not necessarily imply the other. For example, ibuprofen is an orphan drug when used to treat the rare disease patent ductus arteriosus in neonates (orphans or not). Conversely, drug companies have not thought it profitable to seek authorisation for amitriptyline in post-herpetic neuralgia, making it an orphan drug.

Orphan diseases—This term has been used to denote neglected diseases—for example, Fabry's disease, alveolar echinococcosis, and even some common conditions such as endometrial cancer and diabetes in preschool children. However, it is more often used as a synonym for rare diseases, although some rare diseases respond to drugs that are not orphans.

Now the main criterion currently used by the National Institute for Health and Clinical Excellence (NICE) for approving drugs for use in the United Kingdom is that cost should be below about £30 000 per quality adjusted life year (QALY). This suggests a different method of defining a rare disease. If an orphan drug is one that costs over (say) £30 000 per QALY, and if a disease is a rare disease if an orphan drug is used to treat it, then a rare disease could be defined as one whose treatment costs more than £30 000 per QALY. Or perhaps we should distinguish rare diseases (defined by prevalence) from orphan diseases (defined by cost). And while we're at it, we might call orphan drugs, unQALYfied drugs.

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