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REVIEW

The excess burden of trachomatous trichiasis in women: a systematic review and meta-analysis

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Summary It is widely accepted that women carry an increased burden of trachomatous trichiasis compared with men, but there is no systematic review of the available prevalence surveys in the peer-reviewed literature. A literature search was conducted to identify population-based trachoma prevalence surveys utilising the WHO simplified grading system that included data for trichiasis. Of 53 identified studies, 24 studies from 12 different countries met the inclusion criteria. Prevalence data were pooled in a meta-analysis to estimate an overall odds ratio (OR). The overall odds of trichiasis in women compared with men was 1.82 (95% CI 1.61–2.07). Individual survey ORs ranged from 0.83 (95% CI 0.40–1.73) in Myanmar to 3.82 (95% CI 2.36–6.19) in Ethiopia. There were statistically significant differences in odds of trichiasis by gender in 17 of 24 studies, all of which showed increased odds of trichiasis in women compared with men. These data confirm the perception that women have a greater burden of trichiasis, and this burden persists across all populations studied. Women must be specifically and deliberately targeted for trichiasis surgery if the aim of eliminating blindness from trachoma is to be achieved.
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1. Introduction

Trachoma is a disease of the eye that causes blindness. Previously endemic worldwide, the disease is now believed to be confined to 57 countries across South and Central America, Africa, the Middle East, Southeast Asia and Australia.[1] The majority of blindness from trachoma is currently reported from sub-Saharan Africa, with the greatest burden in Ethiopia.[2,3] Globally it is estimated that approximately 500 million people are at risk of trachoma. There are approximately 40 million people with active ocular *Chlamydia* infection and 8.2 million with severe blinding trachoma (trichiasis).[1]

Trachoma has been classified into discrete grades that correspond to stages of the disease.[4] Active disease in which

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there is a biologically active and reproducing infection with ocular *Chlamydia trachomatis* is more commonly seen in children from the ages of 3 months to 10 years than in adults, and children in this age group, particularly those aged under 5 years, can have very productive infections in which the copy number of chlamydial DNA is frequently up to four orders of magnitude greater than the mean copy number in infected adults.[5] Children are therefore considered the reservoir of infection. Transmission of infection from infected to susceptible individuals takes place through direct contact with fingers and fomites such as bed sheets, cloths and towels, as well as carriage by eye-seeking flies.[6] Severe blinding trachoma [trachomatous trichiasis (TT)] is a result of many frequent infections throughout life.

Many studies have found excess trichiasis in women compared with men, which is often explained in terms of the excess exposure to ocular *Chlamydia* infection in women because of their childcare responsibilities and proximity to children throughout the day and when sleeping at night.[7]

Although many studies have estimated the sex-specific risk of trichiasis among women compared with men in the context of individual surveys conducted in many countries across four continents, there has been no attempt to review the data systematically. This meta-analysis was conducted to calculate a single odds ratio (OR) to describe the excess burden of trichiasis in women compared with men.

2. Methods

2.1. Literature search

A systematic literature search of online databases (PubMed, Medline, OVID and Cochrane) was conducted in July 2008 using the following keywords: trachoma; trichiasis; prevalence; epidemiology; survey; and assessment. The search identified peer-reviewed trachoma prevalence surveys published in English or French and was repeated in December 2008 to identify any new additions to the literature. The reference lists of retrieved articles were hand-searched to identify other studies that may have qualified for inclusion in the review.

Studies were included if they met the following criteria: (i) published in a peer-reviewed journal; (ii) used a population-based sampling methodology to determine the prevalence of trichiasis; (iii) used the WHO simplified grading system; and (iv) the survey reported either sex-specific trichiasis prevalence or provided sufficient information to allow back-calculation of the number of TT cases (numerator) and the number of people screened (denominator) for both sexes. At the time of publication of this review, one unpublished study from Nigeria was included; the authors were able to verify the survey methodology and were given access to the full data set (J.D. King et al., unpublished data).

Only population-based prevalence surveys were considered for inclusion since they provide a prevalence estimate applicable to the population from which the random sample is taken. The population-based prevalence surveys identified in the search had several different sampling methodologies. Sampling methodologies for population-based prevalence surveys were not subject to additional review beyond the original peer-review process. Papers presenting data collected using the 'Trachoma Rapid Assessment' (TRA) and 'Acceptance-based Sampling for Trachoma Rapid Assessment' (ASTRA) methodologies were excluded as these methods do not provide a prevalence estimate that can be generalised to the population from which the sample is taken.

2.2. Calculation of numerators and denominators

Both the number of females and males with trichiasis (numerators) and the total number of females and males surveyed (denominators) were required for the analysis. This was determined in four separate ways.

- Method 1: numerators and denominators given explicitly in text or tables—no calculation required.
- Method 2: sex-specific denominators and TT prevalence given, but no numerators/denominators—the sex-specific numerators were calculated as the product of the sex-specific denominator and prevalence. Where the number of TT cases and TT prevalence were presented, the denominator was calculated by dividing the number of cases by the prevalence for each sex.
- Method 3: sex-specific TT prevalence and proportion of one sex given for the sample population—the denominators were calculated as the product of the sex-specific proportion of the sample and the sample population. The numerator was the product of the sex-specific prevalence and the denominator.
- Method 4: sex-specific TT prevalence, total number of TT cases and sample population given—sex-specific denominators were calculated by algebraic manipulation where the unknown sex-specific population was eliminated in the equation by substitution with the algebraic expression of the sex-specific population. The numerators were the product of the sex-specific prevalence and denominators. Example: Dolin et al.[8] report a prevalence of TT of 3.9% for women and 2.5% for men; there were 107 TT cases in total and a sample population of 3288. To calculate the denominator and numerator for women, we assumed that the total population consisted of y females and x males:

$$x = 3288 - y, \text{ and } y = 3288 - x$$

Given that the total number of TT cases was 2.5% of x and 3.9% of y, we can state:

$$107 = 0.025x + 0.039y$$

We can eliminate x (men in this example) to calculate the denominator of women by substitution:

$$107 = 0.039y + 0.025(3288 - y)$$

$$107 = 0.039y + 82.2 - 0.025y$$

$$24.8 = 0.014y$$

$$y = 1771 \text{ women surveyed}$$

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Table 1 Studies excluded from the meta-analysis

Country/location	Year of survey	Survey method	Reason for exclusion
Australia			
Anangu and Pitjantjatjara[10]	2001	PBPS	Males and females examined, insufficient data presented
Brazil			
Olimpia, Guaraci and Cajobi; Sao Paulo[11]	1992	PBPS	Only children examined
Upper Rio Negro Basin[12]	2002	PBPS	Males and females examined, insufficient data presented
Botucatu, Sao Paulo State[13]	2002	PBPS	Only children examined
Yanomami Indians[14]	2002	PBPS	Males and females examined, insufficient data presented
Upper Rio Negro Basin[15]	2008	PBPS	Males and females examined, insufficient data presented
Burkina Faso			
National survey[16]	2003	PBPS	Only children examined
Chad			
Ouaddaï-Biltine and Lac-Kanem-Chari Baguirmi Regions[17]	2003	PBPS	Only females examined
China			
Hainan Province[18]	2002	PBPS	Only children examined
Ethiopia			
Jimma Zone[19]	1997	PBPS	Males and females examined, insufficient data presented
Jangua Mariam locality[20]	2000	PBPS	Males and females examined, insufficient data presented
South Gondar Zone[21]	2001	TRA	TRA or ASTRA methodology
Gurage, Oromia and South Welo[22]	2005	PBPS	Only children examined
The Gambia			
20 villages[23]	2001	TRA	TRA or ASTRA methodology
Kenya			
6 districts[24]	2006	PBPS	Males and females examined, insufficient data presented
Mali			
National survey[25]	1998	PBPS	Only females examined
Mopti Region[26]	2000	TRA	TRA or ASTRA methodology
Malawi			
Salima District[27]	2003	ASTRA	TRA or ASTRA methodology
Nepal			
Sarlahi District[28]	1996	PBPS	Only children examined
Niger			
Maradi[29]	2007	PBPS	Only children examined
Senegal			
National survey[30]	2003	PBPS	Only females examined
Kaolack Region[31]	2005	ASTRA	TRA or ASTRA methodology
Tanzania			
Kongwa District[32]	1991	PBPS	Males and females examined, insufficient data presented
Singida[33]	2001	PBPS	Only females examined
50 districts[34]	2007	PBPS	Only children examined
Vietnam			
18 provinces[35]	2005	ASTRA	TRA or ASTRA methodology
Yemen			
9 governates[36]	2006	TRA	TRA or ASTRA methodology
Zambia			
Luapula Valley[37]	1992	PBPS	Males and females examined, insufficient data presented
Gwembe District[38]	2006	PBPS	Males and females examined, insufficient data presented

PBPS: population-based prevalence survey; TRA: Trachoma Rapid Assessment; ASTRA: Acceptance Sampling Trachoma Rapid Assessment.

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Table 2 Studies included in the meta-analysis

Country	Setting (reference)	Year	Ages examined	Method used to derive numerator and denominator [a]	Females		Males		OR	95% CI
					TT	*N*	TT	*N*		
Brazil	Bebedouro State[39]	1992	≥10 years	4	3	490	2	490	1.50	0.25–9.02
Ethiopia	Dalocha District[40]	2001	≥10 years	1	11	199	7	170	1.34	0.51–3.54
	Alaba District[41]	2003	≥10 years	2	83	1976	21	1909	3.82*	2.36–6.19
	Damot Gale District[42]	2004	≥15 years	1	59	450	17	405	3.12*	1.79–5.45
	Tigray Region[43]	2006	≥10 years	1	99	2488	33	1412	1.70*	1.14–2.54
	Amhara Region[44]	2008	≥15 years	1	408	10 056	137	9613	2.85*	2.34–3.46
	Amhara TCP–baseline[45]	2009 [b]	≥15 years	1	187	2094	58	1825	2.81*	2.08–3.80
	Amhara TCP–3 year evaluation[45]	2009	≥15 years	1	54	1304	15	973	2.69*	1.51–4.79
Egypt	Nile Delta[46]	1989	≥15 years	1	59	79	45	79	1.31	0.80–2.16
	Menofiya Governate[47]	2001	≥50 years	1	54	1082	41	1344	1.64*	1.08–2.47
The Gambia	National survey[8]	1998	≥30 years	4	69	1771	38	2051	2.10*	1.41–3.14
Ghana	National survey[48]	2009	≥15 years	1	83	20 997	35	16 967	1.92*	1.29–2.85
Morocco	Ouarzazate[49]	1992	≥15 years	3	18	370	8	321	1.95	0.84–4.55
Myanmar	Mandalay Division[50]	2007	≥40 years	1	16	1240	13	836	0.83	0.40–1.73
Nigeria	Kaita LGA[51]	2001	All ages	4	75	1660	26	1233	2.14*	1.36–3.37
	Katsina State[52]	2008	≥15 years	1	236	4721	108	4169	1.93*	1.53–2.43
	Yobe State[53]	2008	≥15 years	2	47	1237	21	840	1.52	0.90–2.56
	Plateau and Nassarawa State [c]	2009	≥15 years	1	64	13 218	18	9220	2.48*	1.47–4.19
Oman	National survey[54]	2007	≥40 years	1	66	1360	32	990	1.50	0.98–2.31
Sudan	Southern Sudan, 5 districts[55]	2005	≥15 years	2	537	5424	220	2821	1.27*	1.08–1.49
	Mankien District[56]	2006	≥15 years	1	186	991	112	559	0.94	0.72–1.21
	Ayod County[57]	2008	≥15 years	1	114	698	41	403	1.61*	1.10–2.34
	Southern Sudan, children[58]	2008	≥15 years	1	98	5570	68	5585	1.45*	1.06–1.97
Tanzania	National survey[59]	2008	≥15 years	2	1946	57 235	673	39 588	2.00*	1.83–2.19
Vietnam	12 districts[60]	2006	≥35 years	2	2166	24 285	1037	19 392	1.67*	1.55–1.80

TT: number with trachomatous trichiasis; *N*: total number examined; OR: odds ratio; TCP: trachoma control programme; LGA: local government area.

[a] Method 1, no calculation necessary; Method 2, sex-specific denominators and TT prevalence given; Method 3, sex-specific TT prevalence and proportion of one sex given; Method 4, sex-specific TT prevalence, total number of TT cases and sample population presented.

[b] The baseline results presented in this paper were not published until 2009. The baseline survey was conducted in 2003.

[c] Unpublished data.

* Statistically significant difference between prevalence of trichiasis in men and women.

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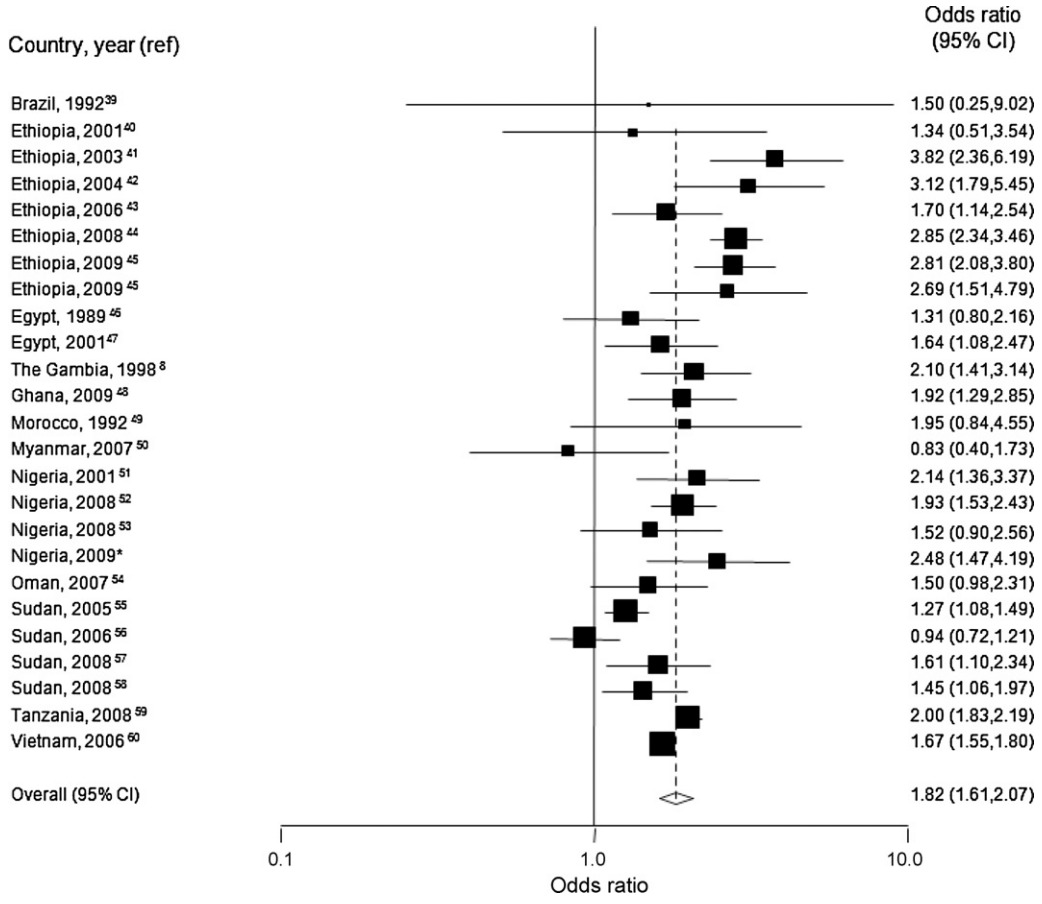

Figure 1 Forest plot of the odds ratios of trichiasis for all the included studies. * Unpublished data.

The sex-specific prevalence was 3.9% of women, so the numerator is the product of the prevalence and the denominator (method 2).

Female TT cases $= 0.039 \times 1771$

69 cases of TT among 1771 women

2.3. Statistical analysis

Statistical analysis was conducted using Stata 10.0 (Stata Corp., College Station, TX, USA). Data from all the included studies were pooled and the OR of the overall effect estimate was calculated using the METAN routine in Stata.[9] Owing to expected heterogeneity between the studies as a result of the underlying differences in geographical location, cultural context and age range of study participants, a random effects model was used to weight the studies in the summary statistic. Separate pooled analyses were conducted for the 20 surveys performed in Africa, the 18 studies conducted as baseline prevalence surveys and the 8 studies conducted in settings where trachoma control programme interventions were actively operating trichiasis cases.

3. Results

A total of 53 studies were identified, of which 24 were found to meet the inclusion criteria. Table 1 shows the country and location of the excluded studies and the reason for exclusion. Studies were excluded because: (i) they only surveyed women and did not present data for men (4 studies); (ii) they only surveyed children and did not report TT in adults (8 studies); (iii) men and women were surveyed for TT, but insufficient data were presented to calculate the sex-specific numerators and denominators (10 studies); or (iv) data did not yield true sex-specific prevalence data (survey methodology was TRA or ASTRA) (7 studies).

The 24 studies that met the inclusion criteria are shown in Table 2. The studies were conducted in 12 countries between 1989 and 2008; 23 were published in English and 1 in French. All studies, with the exception of the surveys in Brazil, Myanmar, Oman and Vietnam, were conducted in Africa. One study,[45] conducted in Amhara Region of Ethiopia, presented prevalence of TT at baseline and after 3 years of implementation of the SAFE strategy (Surgery, Antibiotics, Facial cleanliness and Environmental improvement); these two estimates of TT prevalence were included in the analysis separately. The individual OR for trichiasis in women compared with men was statistically significant in 17 of the 24 studies, with a range of effect from 1.27 (95% CI 1.08—1.49) to 3.82 (2.36—6.19). Among the surveys that met the inclusion criteria, there were no studies that demonstrated a statistically significant increased risk of trichiasis in men compared with women. Where statistically significant, the excess odds of trichiasis were universally against women regardless of the survey country or continent.

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Figure 1 presents a forest plot of the ORs for all included studies. Including all 24 surveys, the pooled OR was 1.82 (95% CI 1.61—2.07). When the 20 studies conducted in Africa are analysed separately, the pooled OR was 1.90 (95% CI 1.63—2.20). The meta-analysis was also stratified to compare the pooled ORs between settings with and without trachoma control interventions. In 18 surveys primarily conducted as baseline surveys prior to implementation of trachoma control interventions, the pooled OR was 1.80 (95% CI 1.5—2.2), whilst in 8 surveys conducted in settings where trachoma control programmes were actively operating trichiasis cases the pooled OR was 1.80 (95% CI 1.6—2.1).

4. Discussion

The analysis presented estimates of a summary OR for the excess risk of TT from population-based prevalence surveys of trachoma in eight African, two Asian, one Middle Eastern and one South American country. The pooled odds of trichiasis in women compared with men was 1.82 (95% CI 1.61—2.07). A statistically significant increased odds of trichiasis in women was seen in 17 of the 24 studies that met the inclusion criteria, including those from Ethiopia, Egypt, The Gambia, Ghana, Nigeria, Sudan, Tanzania and Vietnam. There were no studies identified that showed a statistically significant increased odds of trichiasis in men compared with women. The magnitude of the effect varied between 0.83 (95% CI 0.40—1.73) in a study from Myanmar to 3.82 (95% CI 2.36—6.19) in a study from Alaba District in Ethiopia. In studies where the OR was statistically significant, the effect was consistently shown to be a greater odds of trichiasis in women than men.

The geographical location was different in all studies that met the inclusion criteria, and the age range included in the sample population ranged from all ages in one study in Nigeria[51] to age $\geq$50 years in the Menofiya study in Egypt.[47] Although the biological difference between men and women is constant, the cultural differences are entirely context-specific and varied between the studies so as to effectively be random effects. Given the wide variation between studies, the summary OR should not be considered by the overall OR (1.82) alone but in the context of the range demonstrated by the 95% CI (1.61—2.07). It is highly likely that as additional prevalence surveys are conducted in trachoma-endemic countries, the mean summary OR will vary slightly although it is unlikely to go beyond the 95% CI calculated here. A sub-analysis of the 20 African studies (5 of which were from Ethiopia) showed a summary OR of 1.90 with the range (95% CI) being 1.63—2.20. This should not be interpreted to mean the risk is greater for African women compared with women in any other non-African endemic country. The odds of developing trichiasis are higher for women than men irrespective of their country of residence.

The estimation of a summary OR to demonstrate the increased odds of developing trichiasis in women does not provide new information on why women are at greater risk. The possible explanations (a sex-linked predisposition to trichiasis, increased exposure to children who form the reservoir of infection, and gender-linked behavioural differences) have been discussed and reviewed by Courtright and West.[7]

Programmatically, the summary OR is a stark reminder that it will simply not be possible for trachoma-endemic countries to reach the goal of elimination of blinding trachoma (currently the definition includes reduction of TT in the whole population to $\leq$0.1%) without paying particular attention to gender bias and without specifically and deliberately targeting women for trichiasis surgery.

This study has a number of potential limitations. Surveys were included in the meta-analysis if they had been peer-reviewed and provided sufficient gender-specific data to allow calculation of a numerator and denominator for trichiasis in both men and women. There were 29 surveys in the peer-reviewed literature that did not meet the criteria. In each of the included studies, there is a possibility of bias in the sample selection. This may have been introduced by guides steering survey teams to the visually impaired in the random walk surveys, oversampling of sick or visually impaired people who were more likely to be at home during the survey, or undersampling of adult males who were healthy migrant workers and not present during surveys. However, it is difficult to hypothesise a source of systematic bias across the 24 studies that would consistently result in increased odds of trichiasis in women compared with men. Eleven of the 24 studies were conducted in areas in which trachoma control interventions were being employed. There is some concern that where surgical services for trichiasis are offered, uptake is greater among men than women[61] and therefore the timing of the survey in relation to SAFE activities may explain gender differences. This is argued on the grounds that men have greater access to financial resources to pay for travel to surgery, are less tolerant of coping strategies for living with trichiasis and have fewer domestic responsibilities that tie them to the home on a day-to-day basis. However, the evidence from the field (Tanzania and Vietnam) is that uptake of surgical services is proportionate to the prevalence of trichiasis in both men and women.[62] Our analysis suggests that there were no differences in the excess risk of TT among women after stratifying the meta-analysis to compare the pooled ORs for surveys where trachoma control had not taken place with surveys where trachoma control had been implemented. In addition, a study in five trachoma-hyperendemic districts of Amhara Region of Ethiopia that provided TT prevalence data at baseline and at evaluation of SAFE suggests that women continued to experience greater odds of TT even after 3 years of implementing the full SAFE strategy.[61] Therefore, whether surveys were conducted at baseline or after implementation of SAFE interventions is unlikely to have significantly affected the summary OR.

In conclusion, the overall summary OR of 24 population-based trachoma prevalence surveys conducted in 12 countries demonstrates that the odds of trichiasis in women is 1.82 times of that of men (95% CI 1.61—2.07). The summary OR does not provide information for any specific country, yet since 17 of the 24 studies show significantly higher odds of trichiasis in women than men, this indicates that women in all trachoma-endemic countries and contexts are at increased risk of trichiasis. If the aim of the global alliance to eliminate blindness from trachoma by 2020 (GET 2020) is to be achieved, programmes must provide surgical services that specifically and deliberately target women.

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