

Prevalence and associations of active trachoma among rural preschool children in Wadla district, northern Ethiopia

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Abstract

Background Trachoma is a neglected eye problem and an important cause of preventable corneal blindness. In endemic areas, initial infection can occur in early childhood, and following recurrent episodes of infection, it progresses to scarring and blindness. In past decades, trachoma disappeared from developed countries through enhancements of hygiene and sanitation but the disease is still a problem in developing countries. In Ethiopia, data indicate that Amhara is the region with the highest prevalence of active trachoma. The aim of this study was to assess prevalence and association of active trachoma among rural preschool children in Wadla district, north Wollo zone, Amhara. **Methods:** A total of 596 children aged 1–5 years living in 30 of Wadla's 150 rural villages were screened for signs of active trachoma using a cluster sampling technique. Following pre-testing of the survey instrument in a different district, questions about socio-demographic status were asked of heads of households by health informatics professionals. Integrated eye care workers, previously trained to undertake trachoma screening over one month, performed eye examination. Logistic regression was used to look for associations of active trachoma. **Results:** The prevalence of active trachoma among rural pre-school age children in Wadla district was 22%. Low economic status (adjusted odds ratio [AOR] 3.8 (95% CI 1.3–11.4), being 37–48 months old (4.2;1.5–12.0), living in a house with thatched roof (4.4;1.4–13.6), presence of flies in the home (4.6;2.1–9.9), once-weekly face-washing frequency (8.6;2.5–29.3), having a face that had not been washed for longer than a week (10.6;2.9–37.7), and not using soap when washing hands (4.5;1.8–11.3) were associated with active trachoma. **Conclusion:** The prevalence of active trachoma among rural pre-school children was high and it is still a major public health problem in Wadla. Thus, the woreda health office should create awareness for Wadla woreda communities. **Keywords :** Active Trachoma, Associations, Water, Sanitation, Hygiene

Background

Trachoma is a neglected eye problem and an important cause of preventable corneal blindness (1, 2). It can be categorized into active trachoma and cicatricial trachoma (2,3) In endemic areas, cycles of infection with ocular strains of *Chlamydia trachomatis* progress to scarring, trichomatous trichiasis and corneal opacity (4, 5,6). Trachoma is a disease of poverty and poor hygiene (7). The infection found primarily in children (4), with the late-stage disease more frequently seen in adult women than adult men, possibly because of women's greater time spent in proximity to children. Preschool children hold the main pool of ocular *C. trachomatis* infection (8, 9). Active trachoma can be an extremely common problem in children, with prevalence estimates of 60-90% in some areas (10). Ocular *C. trachomatous* believed to be transmitted through hand-to-hand contact, sharing of towels, fomites, pillows, and eye-seeking flies (11).

Globally in 2019, an estimated 2.5 million people were had trichomatous trichiasis, needing surgery (S) to prevent ongoing visual impairment. Others nearly 142 million people were lived in districts in which the prevalence of active trachoma met WHO-defined criteria for intervention with antibiotics (A) and interventions to promote facial cleanliness (F) and improve the environment (E), in order to prevent future trichiasis. Ethiopia is the most affected country: more than half of the 142 million people needing the A, F

and E components of the “SAFE strategy” in 2019 lived here, Ethiopia (12). Within Ethiopia, Amhara has the highest trachoma burden (13), although, the prevalence and associations of active trachoma vary from setting to setting. Hence, studying these variables may help to tailor local control approaches. This is why we undertook investigations in Wadla district, North Wollo zone, Amhara after 5 successive years of mass drug administration in order to re-estimate the prevalence of active trachoma and examine its associations.

Methods

A community-based cross-sectional study design was used. Fieldwork was undertaken from March 11, 2017 to April 26, 2017. The estimated population of Wadla district was 128,170 with 64,574 males and 63,596 females. There were 28,414 households in this district with an average of 4.5 persons per house. The district had 1 general hospital, 7 health centers, and 20 health posts.

Population

The sampling frame was children aged 1–5 years in 150 rural villages of Wadla district. The study units were rural households that had preschool-age children.

Sample size determination

We estimated the required sample size using the single population proportion formula. We assumed, based on previous surveys, an observed prevalence of active trachoma (12.1%) (14), which we wished to estimate with 95% confidence within $\pm 5\%$. We used a design effect of 1.5, and allowed for 10% non-response rate. By multiplying by the design effect of 1.5 and incorporating a 10% non-response rate, we estimated 273 children needed to be framed in selected households.

Sampling technique

A multistage cluster sampling technique was applied. Wadla district had 20 kebeles (sub-districts) with 247 villages. Twelve of the kebeles were rural, whereas eight of the kebeles were urban. Totally, 150 of the 247 villages were rural. We used simple random sampling to select 30 of the 150 rural villages. There were 967 households in the selected 30 villages, but only 499 of those households had preschool children. Thus, those 499 households were visited. Heads of households were interviewed for socio-demographic and economic information, plus housing and environmental conditions, and all children aged between 1 and 5 years who had been resident in the district for at least six months were invited to be examined. Graders used the WHO simplified trachoma grading scheme to grade signs of trachoma (15) (Figure1).

Definitions

Clean face: A face free of eye discharges, nose discharges and flies at the time of examination

Preschool: Children aged greater than, equal to 1 year and less than, or equal to five years

Village: A grouping of homes that contained at least 30 households organized as one peasant association

Fly in the house: When there was observable fly in the house during data collection by observation

Active trachoma: at least one of the two signs of active trachoma in the WHO simplified trachoma grading scheme (TF or TI) in at least one eye (16).

Trachomatous inflammation—follicular (TF): Five or more follicles each having a diameter of at least 0.5mm in the central part of the upper tarsal conjunctiva (16).

Trachomatous inflammation—intense (TI): a pronounced inflammatory thickening of the upper tarsal conjunctiva that obscures more than half of the normal deep tarsal blood vessels (16).

Trachomatous scarring (TS): easily visible scarring in the upper tarsal conjunctiva (16)

Trachomatous trichiasis (TT): at least one eyelash rubs on the eyeball or evidence of removal of in-turned eyelashes in the two weeks before examination (16).

Corneal opacity (CO): easily visible corneal opacity over the pupil (16)

Exclusion and Inclusion Criteria

All children in the appropriate age range who had lived in the district for at least 6 months, who were resident in selected villages and available at the time of study were invited to be included. Children who were seriously ill or for whom informed consent was not given by parents or guardians were excluded.

Data collection tools and procedures

Face to face interviews, observation using a checklist and clinical eye examination were used. Experienced health informatics professionals using structured interview questions that prepared from literatures (17, 18) collected data on socio-demographic status, environmental, and housing conditions. All questionnaires on socio-demographic status, housing, and environmental condition, observation checklist, and eye examination tools were pretested and validated before data collection in Kosomender, Meket district, a district bordering Wadla to the north. A household wealth index was developed using composite indicators for rural residents' assets: livestock ownership, size of agricultural land and quantity of crop production.

Two integrated eye care workers performed eye examination. Those integrated eye care workers were ophthalmic nurses who had been previously trained for a total duration of one month for the purposes of contributing to the 2013–2014 national trachoma survey. The Carter Center delivered that previous training using both pictures and live patients as media of instruction. For this survey, the trachoma

graders undertook refreshment training for 5 days. This involved examination of 58 live patients and 100 pictures of different trachoma signs. Trainers, whose grades were used as the gold-standard assessment assessed graders. The training was also delivered for interviewers. Interviewers assisted graders by recording clinical grades, and data related to each household's socio-demographic status and environmental situation. The training was emphasized on the objectives and procedures of data collection, and mode of communication between graders and interviewers.

When undertaking the actual fieldwork for the study, graders initially observed the eyelashes and cornea of study subjects, looking for TT and CO, then everted the upper lid and inspected the upper tarsal conjunctiva for TF, TI, and TS. Binocular lenses ($\times 2.5$) and penlight torches were used (4) to magnify the examined eye.

Data analysis and presentation

The data were checked for completeness, coded, and entered into Epi-info version 7, and then transferred to SPSS version 23 for analysis. The data were checked for normality using Hosmer-Lemeshow-goodness-of-fit. A univariable analysis model were carried out, and variables that had p-value < 0.25 in a binary logistic regression model were included in the multivariable logistic regression analysis. Potential co-linearity was also considered and tested using multi co-linearity in considering tolerance and variance inflation factor (VIF). Variables with a p-value < 0.05 in the multivariable logistic regression analysis were considered statistically significant. A principal component analysis was performed to categorize households' wealth into poorer, poorest, middle, richer, and richest. However, for the presentation of the variables, the wealth index grouped into three; lowest, middle, and highest. Both active trachoma and cicatricial trachoma were modelled as outcome variables (Figure 2).

Data Quality Assurance

The questionnaire was prepared in English and translated to Amharic, then re-translated to English (to check for accuracy) by individuals fluent in both English and Amharic. Both graders and one of the researchers had participated previously in a community-based trachoma survey. The interviewers also had previous experience in community-based data collection.

Results

In the study villages, there were 610 preschool children. However, 596 preschool children from 499 households were examined that gave a response rate of 100%. The remain 14 children were not involved in the screening phase because of the exclusion criteria and absentism after repeated household visit. More than three-fourths (383, 77%) of households had male heads. The range in the number of residents per household was 2–10 with a median of five. The range in the number of 1–5-years old children per household was 1–3 with a median of one. All 499 families were Amhara in ethnicity and followed Ethiopian orthodox Christianity, and 325 (65%) of fathers, and 380 (76%) of mothers were unable to read and write. Four hundred and sixty-six (93%) of fathers were farmers and 16 (3%) of fathers were

government employees (Table 1). In addition to the socio-demographic characteristics, the environmental characteristics of households are shown in Table 2 (Table 2).

Among children examined, 301 (51%) were males, and 295 (49%) were females. The median age was 36 months (**Table 3**). Of those 596 screened children for Trachoma 56.2% of female children were had trachoma. One hundred and thirty children had active trachoma, giving a prevalence of 22% [95% CI, 18–25%]. One hundred and six children had TF, 13 had TI, and 11 had both TF and TI. There was no TS, TT or CO in these 1–5-years old children. Two hundred and eighty (47% of the) children had a clean face, 89 (15%) had ocular discharge, 75 (13%) had nasal discharge, 34 (6%) had both ocular and nasal discharge and 55 (9%) of the children had nasal discharge, ocular discharge, and fly on the face.

Factors associated with active trachoma

On binary logistic regression analysis, lowest economic status, being in the age group of 24-36 months, the father being unable to read and write, the mother being unable to read and write, living in a house with a thatched grass roof, fly in the house, and MUAC of children <13.9cm were associated with active trachoma (Table 4). However, on multivariable logistic regression analysis, only lowest economic status (AOR (95% CI), (3.80 (1.27-11.42)), being 37–48 months old (4.21 (1.47-12.03)), living in a house with a thatched grass roof (4.40 (1.42-13.59)), and the presence of fly in the home (4.6 (2.1-9.9)) increased the odds of active trachoma (**Table 4**).

Discussion

The objective of this study was to assess the current prevalence of active trachoma and to identify its associations among children aged 1–5 years in rural communities of Wadla district. The prevalence of active trachoma in this age group was 22%, [95% CI, 18–25%], whereas the prevalence of TF was 21%. Although the usual indicator age group for determining the need or otherwise for the A, F and E components of the SAFE strategy is the prevalence of TF in 1–9 years-old children, the prevalence that we estimate here suggests that three further years of antibiotic mass drug administration is likely to be required, according to WHO recommendations (19). However, a study in northern Ethiopia reported that the azithromycin mass treatment coverage in 2012 was 92.9% (20). That reported mass azithromycin coverage was greater than the minimum coverage set by WHO, 80% (21). The prevalence agreed with a review that indicated 70 million people in Ethiopia required MDA, this was the largest need of any country in the world (22).

The prevalence of TI in 1–5-years old children here was 3.4%. Severe inflammatory trachoma is a risk factor for later cicatricial disease, particularly when the sign is observed repeatedly over time (23).

In our subjects, reportedly face washing once weekly and having a face that had remained unwashed for longer than a week were associated with active trachoma. Similar associations have been seen elsewhere (18, 24). We also found that the absence of a toilet or presence of human excreta near to the home increased the odds of there being active trachoma. Recent multi-country observational data support the

link between inadequate access to sanitation and the likelihood of active trachoma (25). In general, the associations that we found agreed with the previous published literature, which suggest strong links between trachoma and environmental factors related to water, sanitation, and hygiene. Some of these associations implicate the fly *Musca sorbens*, which oviposits in human excreta left exposed on the soil, as an important vector (26-28). In this study grassed thatched house roof (AOR (95% CI), 4.402 (1.425-13.597)) were increasing the risk of active trachoma. This association evidenced from central Ethiopia (29). In this study, not using soap was increasing the risk of trachoma [(AOR (95% CI), 4.49 (1.79-11.29))]. This agreed with studies that were conducted in Dessie city, and Gonder (30, 31).

Unfortunately, we did not have any entomological data for this site.

Other limitations of our analyses include our reliance on self-report for many of the exposure variables, and the exclusion of children aged 6–9 years. Yet, this research estimates the prevalence of active trachoma in preschool children, and its associations, for the attention of policymakers interested in trachoma elimination in Wadala district.

Conclusions

The prevalence of active trachoma among rural preschool children was high, suggesting that active trachoma is still a major public health problem in Wadla district. Environmental factors were found to be associated with active trachoma. This might suggest an ongoing need for implementation of the F&E components of the SAFE strategy for trachoma elimination in this district.

Abbreviations

COR – Crude odds ratio, AOR- Adjusted odds ratio, CI – Confidence interval, AT-Active Trachoma, SAFE- Surgery, Antibiotics, Facial cleanliness, Environmental improvement, GET2020- Global elimination of Trachoma by 2020, WHO- World Health Organization, TT- trachomatous trichiasis, TF- trachomatous inflammation—follicular, TI- trachomatous inflammation—intense, TT- trachomatous trichiasis, CO- corneal opacity, MUAC-Mid upper arm circumference, MDA-mass drug administration

Declarations

Ethics approval and consent to participate

The study was approved by the Health Research Ethics Review Committee [HRERC0917/2017], College of Health Sciences, Mekelle University. A written permission to implement the study was obtained from Woldia zonal health department and Wadla District health office. A written informed consent was obtained from children's parents or guardians for interview and examination. Confidentiality was maintained by omitting the name and personal identification of respondents within datasets used for analyses.

Consent for publication

The participants were requested their consent for publication of the outcomes, and agreed on the publication of the outcome in international reputable, and a peer-reviewed journal.

Availability of data and materials

The data generated in this study will be available to researchers wishing to use them for non-commercial purposes.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Conceived the title and designed the study: AMA, MAG, MWK, KDT, and WBT. Field study: MWK, KDT, WBT, MAG, and AMA. Analyzed the data: MWK, AMA, KDT, MAG, and WBT. Critically revising the work: WBT, MWK, AMA, KDT, and MAG. All authors had read and approved the final version of this manuscript with consideration of full accountability.

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Tables

Table 1: The socio-demographic status of households in assessing prevalence and risk factors of active trachoma among rural preschool children in Wadla district, Amhara region, Northern Ethiopia, 2017

Variables	Frequency (n=499)	Percent (%)
Sex of the head of the Household		
Male	383	76.8
Female	116	23.2
Marital status of the head of the household		
Married	492	98.6
Divorce	7	1.4
Wealth index		
Poor	144	28.9
Medium	279	55.9
Rich	76	15.2
Occupation of the head of the house hold		
Farmer	466	93.4
Merchant	17	3.4
Government employee	16	3.2
Educational status of the head of the household		
Unable to read and write	325	65.1
Able to read and write	109	21.8
Up to grade 8	35	7
Grade 9-12	19	3.8
Diploma and above	11	2.2
Educational status of mothers		
Unable to read and write	380	76.2
Able to read and write	55	11
Up to grade 8	23	4.6
Grade 9-12	35	7
Diploma	6	1.2
Number of rooms in the house (observation)		
One	424	85
Two and More	75	15
Family Size		
Less than 6	286	57.3
Greater than and equal to 6	213	42.7
Total number of children less than five years in the house		
One	424	85
Two	69	13.8
Three	6	1.2
Number of children less than ten years in the house		
One	132	26.5
Two	240	48.1
Three	102	20.4
Four	25	5
Adult Face washing habit (self report)		
At least one times per a day	417	83.6
Less than 7 times per week	82	16.4

Table 2: The environmental situations of households in assessing prevalence and risk factors of active trachoma among rural preschool children in Wadla district, Amhara region, northern Ethiopia, 2017

Variables	Frequency (n=499)	Percent (%)
Presence of fly in or around house (observation)		
Present	242	48.5
Absent	257	51.5
Source of water (self-report)		
River	30	6.0
Unprotected well	12	2.4
Protected well	56	11.2
Pipe	401	80.4
Amount of water in litter (self-report)		
Less than 20	180	36.1
20-40	162	32.5
40-60	92	18.4
60-80	49	9.8
Greater than 80	16	3.2
Total time taken to reach to water source (self-report)		
Less than and equal to 1/2 hr.	459	92
Greater than 1/2 hr.	40	8
Place of cooking (observation)		
In the same room of living house	157	31.7
In the same house but in a kitchen	166	33.3
A kitchen constructed against outside wall of the house	3	.6
Isolated kitchen	173	34.7
Presence of window in a kitchen (observation)		
Yes	248	49.7
No	251	50.3
Household waste removal (self-report)		
Burn it	312	62.5
Bury it	90	18
Dispose in the farm	93	18.8
Dispose in another place	4	.8
Presence of latrine (observation)		
Present	371	74.3
Absent	128	25.7
Presence of feces at open field in nearby house (observation)		
Present	243	48.7
Absent	256	51.3
Presence of cattle in the household (observation)		
Present	439	87.9
Absent	60	12.1
Cattle sheltering (n=439) (observation)		
In the same room where family lives	128	29.1
In the same living house but in a separate room	203	46.2
Attached shelter against outside of the house	6	1.6
Isolated shelter far from the house	102	23.1

Table 3: The socio-demographic status of children in assessing prevalence and risk factors of active trachoma among rural preschool children in Wadla district, Amhara region, northern Ethiopia, 2017

Variables	Frequency (n=596)	Percent
Sex of children		
Male	301	50.5
Female	295	49.5
Age of children in months (kebele registration book)		
12 - 24	208	34.9
25 - 36	102	17.10
37 - 48	129	21.6
49 - 59	157	26.3
Current breast-feeding status of children		
Yes	239	40.1
No	357	59.9
Face washing frequency of children (self-report)		
2 or more times per a day	108	18.1
Once daily	79	13.3
2 to 6 times per week	149	25
Once weekly	167	28
Stays unwashed for longer than a week.	93	15.6
Habit of child bathing for at least one times per a week (self-report)		
Yes	445	74.7
No	151	25.3
Use of soap for face washing (self-report)		
Yes	264	44.3
No	332	55.7
Use of soap for hand washing (self-report)		
Yes	254	42.6
No	342	57.4
Face of children on observation (observation)		
Clean face	280	47
Ocular discharge	89	14.9
Nasal discharge	75	12.6
Flies on the face of child		10.6
Ocular and nasal discharge	34	5.7
Ocular & nasal discharge & flies on the face	55	9.2
Presence of another eye problem (self-report)		
Yes	146	24.5
No	450	75.5
Type of eye problem (n=146)		
Discharge	96	65.6
Itching	8	5.3
Excessive tear	25	17.1
Redness of eye	18	12.2
Took drug during mass drug administration in the last year (self-report)		
Yes	515	86.4
No	81	13.6

Table 3: The bivariable and multivariable logistic regression analysis in assessing prevalence and risk factors of active trachoma among rural preschool children in Wadla district, Amhara region, northern Ethiopia, 2017

Variables	Trachoma (n=596)		OR (95% CI)	
	Presence (%)	Absence (%)	COR	AOR
Type of House roof (observation)				
Clean iron	15 (11.5)	82 (17.6)	1.00	1.00
Thatch iron	24 (18.5)	141 (30.3)	0.9(0.5-1.9)	0.9 (0.3-2.8)
Clean grass	27 (20.8)	144 (30.9)	1.0(0.5-2.0)	0.7 (0.2-2.2)
Thatch grass	64 (49.2)	99 (21.2)	3.5 (1.9-6.7) *	4.4 (1.4-13.6) *
Fly in the house or in nearby (observation)				
Yes	96(73.8)	206 (44.2)	3.6 (2.3-5.5)	4.6 (2.1-9.9) *
No	34 (26.2)	260 (55.8)	1.00	1.00
Face washing frequency (self-report)				
Two and more times	9 (6.9)	99 (21.2)	1.00	1.00
Once daily	2 (1.5)	77 (16.5)	0.3 (0.1-1.4)	0.2 (0.03-1.3)
2-6 times per week	15 (11.5)	134 (28.8)	1.2 (0.5-2.9)	1.366 (.365-5.114)
Once weekly	63 (48.5)	104 (22.3)	6.7 (3.1-14.1) *	8.7 (2.6-29.3) *
Unwashed for a week.	41(31.5)	52 (11.2)	8.7 (3.9-19.2) *	10.6 (2.9-37.7) *
Soap for face washing (self-report)				
Used	26 (20)	238 (51.1)	1.00	1.00
Not used	104 (80)	228 (48.9)	4.2 (2.6-6.7) *	4.5 (1.8-11.3) *
Soap for hand washing (self-report)				
Used	35 (26.9)	219 (47.0)	1.00	1.00
Not used	95(73.1)	247 (53.0)	2.4 (1.6-3.7) *	1.6 (0.8-3.6)
Household Latrine (observation)				
Present		364 (78.1)	1.00	1.00
Absent		102 (21.9)	2.0 (1.3-3.0) *	5.0 (2.0-12.9) *
Household waste around the house (observation)				
Exist	80(61.5)	214 (45.9)	1.9 (1.3-2.8) *	3.4 (1.6-7.6) *
Not exist	50 (38.5)	252 (54.1)	1.00	1.00
Mothers educational status				
Unable to read and write	111 (85.4)	348 (74.7)	2.9 (1.3-6.6) *	0.8 (0.2-3.2)
Able to read and write	12 (9.2)	53 (11.4)	2.1 (0.8-5.7)	0.3 (0.1-1.6)
Attend formal education	7 (5.4)	65 (13.9)	1.00	1.00
Wealth index				
Poor	73 (56.2%)	101 (21.7)	4.6 (2.3-9.1) *	4.2 (1.5-12.0)
Medium	45 (34.6%)	288 (61.8)	1.003 (.506-1.988)	0.5(0.2-1.4)
Rich	12 (9.2%)	77(16.5)	1.000	1.00
MUAC of children				
Less than 13.9	81(62.3)	230 (49.4)	1.7 (1.1-2.52) *	1.3 (0.6-2.6)

Greater than 14	49(37.7)	236 (50.6)	1.00	1.00
Age of children				
12-24	42	166 (35.6)	0.8 (0.5-1.3)	0.7 (0.3-1.8)
25-36	(32.3)	88 (18.9)	0.5 (0.3-0.9) **	0.7(0.2- 2.1)
37-48	14 (10.8)	93 (20)	1.2 (0.7-2.1)	2.7(.1.0-7.2)
49-59	36 (27.7)	119 (25.5)	1,00	1.00
Fathers education	38 (29.2)			
Unable to read & write		299 (64.2)	2.3 (1.1-4.7) **	1.4 (0.3-6.2)
Able to read & write	93 (71.5)	102 (21.9)	1.9(0.9-4.5)	2.1 (0.5-9.7)
Formal education	28 (21.5)	65 (13.9)	1.00	1.00
	9 (6.9)			

Note: "*" = P - value less than 0.001 and "***" = P - value less than 0.05

Figures

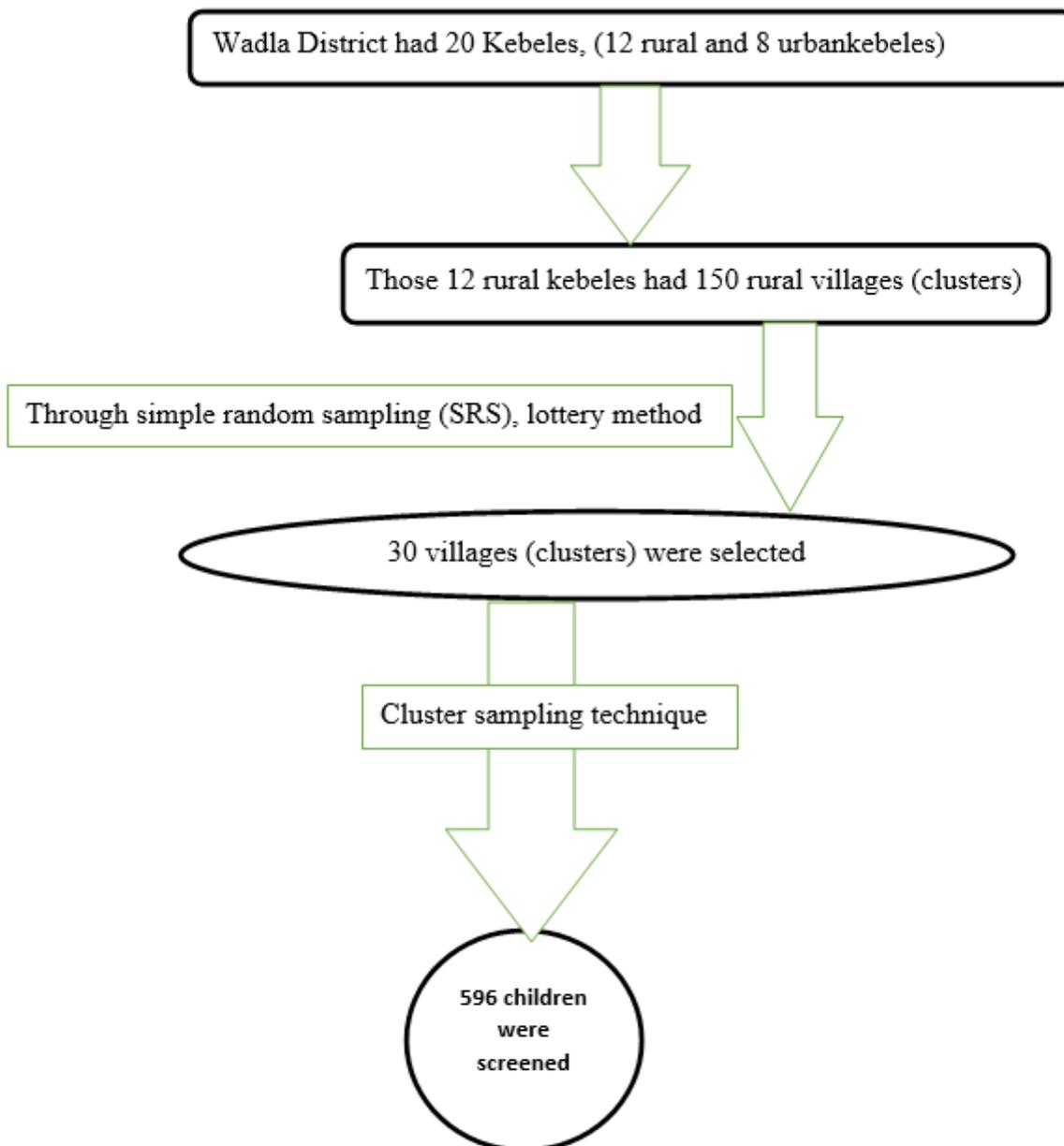


Figure 1: The schematic diagram of sampling procedure in assessing prevalence and risk factors of active trachoma among rural pre-school children in Wadla district, 2017

The sample size calculated was 583 using single population proportion formula, but as the sampling procedure was cluster sampling, the screening was included 596 pre-school children.

Figure 1

The schematic diagram of sampling procedure in assessing prevalence and risk factors of active trachoma among rural pre-school children in Wadla district, 2017 The sample size calculated was 583 using single population proportion formula, but as the sampling procedure was cluster sampling, the screening was included 596 pre-school children.

Procedure of eye examination and results reporting

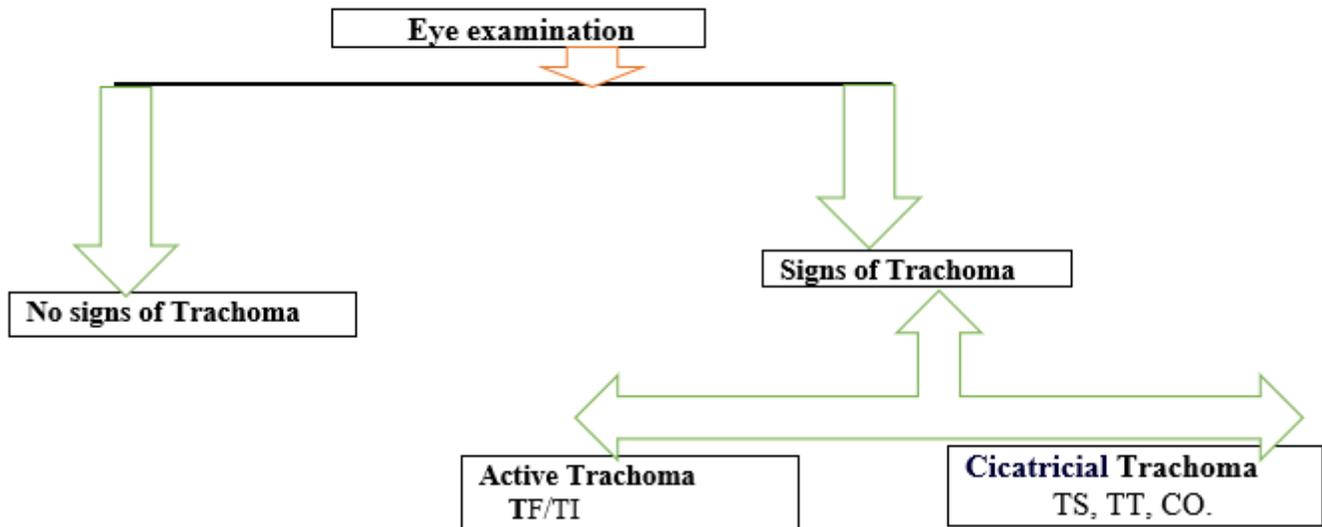


Figure 2

The schematic presentation of eye examination and result reporting procedure in assessing prevalence and risk factors of active trachoma among rural preschool children in Wadla district, Amhara region, northern Ethiopia, 2017. Key: TF- Trachomatous inflammation follicular, TI- Trachomatous Inflammation intense, TS- trachomatous scarring, TT- trachomatous trichiasis, and CO- corneal opacity

Supplementary Files

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

- [formula.docx](#)
- [TableS1.docx](#)
- [TableS2.docx](#)
- [STROBEOPT.pdf](#)