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Research Article

Non-Follow-Up of Pulmonary Tuberculosis Patients in Health Facilities and Associated Factors, Hoima, Uganda

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Abstract

Introduction: The World Health Organization and Ministry of Health recommend monitoring of tuberculosis patients that are on treatment to assess for healing progress. Tuberculosis treatment success in Hoima district was only 68% in 2017 compared to the national target of 85%. About 55% of the smear positive tuberculosis patients remain positive at the end of two months of medication. Failure to examine sputum at the end of 2 months during treatment reduces chances of early detection of treatment failure.

Objective: The main objective of the study was to determine prevalence and factors associated with non-follow-up of pulmonary tuberculosis patients for the 2 months' sputum examination in health facilities in Hoima, Uganda.

Methods: We conducted a cross sectional study of 435 pulmonary tuberculosis patients' records from 1st January 2017 to 31st December 2018. The dependent variable was absence of 2 Months' sputum results and the independent variables included HIV status, directly observed treatment, facility location, facility ownership, distance and baseline sensitivity. The prevalence and it's 95% confidence interval was determined. Logistic regression was used to determine associated factors.

Results: The prevalence of two months' sputum non-follow-up was found to be 26.9% (95%CI = 7.0 - 64.4). The factors associated with sputum non-follow-up included: positive versus negative HIV status (aPR = 1.48, P < 0.001), not on versus being on directly observed treatment (aPR = 1.31 P = 0.002), rural versus urban health facilities (aPR = 1.79, P = 0.006), private versus government health facilities (aPR = 2.05, P = 0.015), distance > 5 km versus ≤ 5 km (aPR = 1.38, P = 0.021) and baseline tuberculosis drug sensitivity (aPR = 1.44, P = 0.318) which confounded health facility location.

Conclusion: We found a high prevalence of sputum non-follow-up. Tuberculosis patients that were HIV positive, not on directly observed treatment, staying in a distance greater than 5km from the health facility and patients attending rural and private health facilities were likely to miss 2 months' sputum follow-up.

Keywords: Factors; Associated; Sputum; Non-follow-up; Uganda

Abbreviations

PTB: Pulmonary Tuberculosis; TB: Tuberculosis; aPR: Adjusted Prevalence Ratio; HIV: Human Immune Virus

Introduction

Tuberculosis(TB) is one of the leading 10 causes of death worldwide and accounts for about 1.7 million deaths annually [1]. Uganda is among the 30 countries highly affected by TB with 201 cases per 100,000 persons [1]. Sputum for some pulmonary tuberculosis patients is not examined at two months of tuberculosis treatment in Hoima district, mid-Western Uganda. In Uganda, the prevalence of two months' sputum non examination has ranged from 16% in Kiboga and Kyankwanzi [2] and 46% in the Eastern part of the country [3]. Only 68% of bacteriologically confirmed tuberculosis patients in Hoima were successfully treated as opposed to the national target of 85% [4]. About 55% of the smear positive tuberculosis patients remain positive at the end of the intensive phase [5].

Our study aimed at answering two research questions, one of which was on the prevalence of non-follow up of PTB patients for the two months' sputum examination from January 2017 to December 2018 in health facilities of Hoima district, mid-Western Uganda. The second was on factors associated with non-follow up of PTB patients for the two months' sputum examination from January 2017 to December 2018 in health facilities of Hoima district, Mid-western Uganda.

Objective of the Study

Our main objective was to determine the prevalence and associated factors of non-follow up of PTB patients for the two months' sputum examination from January 2017 to December 2018 in health facilities of Hoima district, Mid-western Uganda.

Methods

Study design

We used a cross sectional study design.

Study setting

The study was conducted in Hoima district located approximately 230 kilometres by road, Northwest of Kampala, the capital city of Uganda**.** The study was done in thirteen government and two private health facilities that were offering tuberculosis services. Hoima district has one government aided regional referral hospital, two health centre IVs (one is private) and 9 health centre IIIs (8 government and 1 private) that offer tuberculosis services. The regional referral hospital is located in Hoima municipality and offers both inpatient and outpatient services to people from Hoima. It also receives referrals from other health facilities and neighbouring districts. The departments of Hoima regional referral hospital are: outpatient department, tuberculosis unit (including multidrug resistant ward), emergency, obstetrics and gynaecology, laboratory, surgical, medical, paediatric, theatre and nutrition. Th is hospital has a private wing where patients are required to pay for the services. The health centre IV departments include: out-patient department, in-patient department wards, laboratory, theatre and maternity ward. They offer services to the catchment population and referrals from health centre IIIs. The health centre III departments include: outpatient department, laboratory and maternity. The health centre IIIs offer services to populations in their catchment areas.

On average, the hospital receives over 170 tuberculosis patients per year. Health centre IVs and IIIs receive about 45 and 5 patients per year respectively.

The district medical department is headed by a district health officer under whom there is a district health team. There is a subdistrict in charge who heads the health centre IV and oversees the health centre IIIs. The health centre IIIs are headed by clinical officers. Below the health centre IIIs are health centre IIs headed by enrolled nurses. Below health centre IIs are health centre Is headed by Village Health Teams (VHTs). The health facility tuberculosis clinics are headed by tuberculosis unit focal persons who oversee facility tuberculosis related activities.

There are a number of private health facilities in Hoima and only Azur health centre IV and Bujumbura health centre III offer tuberculosis services. Tuberculosis drugs are offered at no cost. However, testing services including sputum follow-up tests are offered at a cost of about five thousand Ugandan shillings (approximately 1.5 US dollars) per test.

Population

- **Target population:** All confirmed tuberculosis patients who were on tuberculosis treatment.
- **Accessible population:** Confirmed pulmonary tuberculosis patients on tuberculosis treatment in Hoima followed-up from 1st January 2017 to 31st December 2018.
- **Study population**: Confirmed pulmonary TB patients that had received tuberculosis treatment for at least two months from 1st January 2017 to 31st December 2018 in Hoima district government and private health facilities offering tuber-

culosis services.

- **Inclusion criteria:** We included records of bacteriologically confirmed pulmonary TB patients on TB treatment for at least two months from 1st January 2017 to 31st December 2018 in Hoima district government and private health facilities.
- **Exclusion criteria:** We excluded records of patients that had died and or had been transferred to other health facilities outside the study area before completing the 2 months of TB treatment.

Sample size

Sample size calculation for objective one

To determine the appropriate sample size to establish prevalence of sputum non-follow-up among pulmonary bacteriologically confirmed tuberculosis patients in Hoima district, Kish Leslie formulae was used:

$$N = \left(\frac{Z^2 p(1-p)}{d^2}\right) DE$$

N was the required sample size.

DE is design effect (since more than one health facilities were be considered) = 2

d was precision (tolerable sampling error) = 5%.

p was estimated proportion of sputum non-follow-up = 16% [2].

z was the standard normal value at 95% confidence level =1.96.

$$N = \left(\frac{1.96^2 0.16(1-0.16)}{0.05^2}\right) * 2$$

N = 414 pulmonary bacteriologically confirmed tuberculosis patients.

Sample size calculation for objective two

The sample size was estimated using formula for comparison of two proportions:

$$N = \left[\frac{z_\alpha \sqrt{P(1-P)\left(\frac{1}{Q_1}+\frac{1}{Q_2}\right)} + z_\beta \sqrt{P_1(1-P_1)\left(\frac{1}{Q_1}\right) + P_2(1-P_2)\frac{1}{Q_2}}}{P_1 - P_2}\right]^2 DE$$

N was the required sample size.

Q1 was the proportion of male tuberculosis patients = 66.5% [6].

Q2 was the proportion female of tuberculosis patients = 33.5% [6].

Zα was the standard normal value corresponding to 5% level of significance = 1.96.

Zβ was the power of the study to detect a difference for 80% power = 0.84.

DE was the design effect = 2

Proportion of male tuberculosis patients that got lost to follow-up (P1) = 22.9% [7].

Proportion of female tuberculosis patients that got lost to follow-up (P2) = 58% [8].

p = p1q1+p2q2.

p = (0.229 x 0.665) + (0.58 x 0.335) = 0.347.

$$N = \left[\frac{1.96\sqrt{0.347(1-0.347)\left(\frac{1}{0.665}+\frac{1}{0.335}\right)} + 0.84_x\sqrt{0.229(1-0.229)\left(\frac{1}{0.665}\right) + 0.58(1-0.58)\frac{1}{0.335}}}{0.229-0.58}\right]^2 x2$$

N = 129 pulmonary bacteriologically confirmed tuberculosis patients' records.

Since the first formula gave the largest sample size (414), it was taken as the minimum sample size for the study.

Sampling procedure

Consecutive sampling was used and all eligible patient records were selected for the study to avoid selection bias. We got 435 patient records as our study sample from the pool of 502 tuberculosis patients' records.

Variables

- **Dependent variable for the study:** The dependent variable was status of sputum results at two months. Sputum results were either absent (sputum non-follow-up) or present (sputum follow-up) in the tuberculosis unit register or the tuberculosis laboratory register at the end of two months of tuberculosis treatment.
- **Independent variables for the study:** Age, sex, weight, distance from facility (within 5km or above 5km), HIV status, availability of treatment supporter (DOT), facility level (V, IV

or III), antiretroviral treatment (ART), patient type (new or retreatment), type of facility (private or government), presence of a counsellor, health facility setting (facilities in sub counties were taken to be rural and urban for facilities that were in town councils or municipality) and whether drug sensitivity was done at baseline (yes or no).

Data collection methods

We used data abstraction forms to collect data from the registers. Two research assistants were recruited and trained for two days on how to abstract data from the registers and research ethics. Data abstraction forms were pretested in Kyangwali health centre III, Kikuube district. We got permission from the Hoima District Health Officer to access the registers with required patients' records in health facilities that were offering tuberculosis treatment services during the study period. We then went to specific health facilities, approached the health facility in charges for permission and provision of the registers including presumptive TB registers, unit TB registers, TB laboratory registers, antiretroviral registers (to cross check ART status). Health facility related information was got from health facility in charges. Data collection was done for two months from 4th March to 30th April 2019.

Data management

The principal investigator cross-checked data collected for correctness and completeness on a daily basis. We used unique identifiers during data collection to ensure privacy. We kept data under lock and key system. We set up a database using Epi data version 3.2 and data were double entered by principal investigator and research assistants then exported to STATA version 15 for analysis.

Data analysis

Descriptive analysis

We used patients' records of smear positive tuberculosis patients who attended Hoima district health facilities from 1st January 2017 to 31st December 2018. Factors associated with sputum non-follow-up were described using percentages for categorical variables. Normally distributed numerical factors were summarized as means and standard deviations. Prevalence of two months' sputum non-follow-up among pulmonary bacteriologically confirmed tuberculosis patients was computed using STATA version 15 as the ratio of pulmonary bacteriologically confirmed tuberculosis patients without two months' sputum follow-up results to those diagnosed with pulmonary bacteriologically confirmed tuberculosis between 1st January 2017 and 31st December 2018.

Bivariate and multivariate analysis

We carried out modified Poisson regression via the generalized linear models using STATA version 15 after testing for the assumptions. Bivariate modified Poisson regression and multivariable Poisson regression were used. We adjusted for clustering using health facility levels and used robust standard errors. We first checked for the association between the dependent variable and independent variables. Independent factors with a p-value less than 0.2 and those suggested by literature were considered for multivariable analysis. Assumptions of multi collinearity and outliers were then assessed before fitting the multivariable modified Poisson model. During model building we assessed for significant interaction terms and confounders. To test for interaction, since we did not have a main factor, we ran a modified Poisson model of all the factors that had a p value less than 0.2 at the bivariate analysis. We formed interaction terms with the significant variables (with probability of less than 0.05), ran the model with the basic variables added and saved it as a full model. We also ran and saved the reduced model which contained only the basic variables. A chunk test comparing the full and reduced model was ran and it was significant at p value < 0.05. The non-significant interaction terms were removed, starting with the least significant. Factors with significant interaction terms and those supported by literature were retained in the model. Other factors were dropped one by one starting with least significant until we got significant factors. Variables were considered as statistically significant if the p value was less than 0.05. We continued to assess for confounding and a factor was considered a confounder if it caused a change of greater than or equal to 10% to prevalence ratio. Goodness of fit of the model was assessed which showed that the independent variables were adequately associated with the outcome.

Results

Study profile

This study was carried out in Hoima district located in mid-Western part of Uganda. Records of 435 pulmonary tuberculosis patients treated in selected health facilities in Hoima district between 1st January 2017 and 31st December 2018 were sampled for the study.

Social demographic, clinical and health facility characteristics

Of the 435 patients' records reviewed, 309(71%) were for males. Most of the records (n=277,63.7%) were for patients who were from distances longer than 5km from the health centres they went to. Social demographic, clinical and health facility characteristics of the study population are summarized in table 1 below.

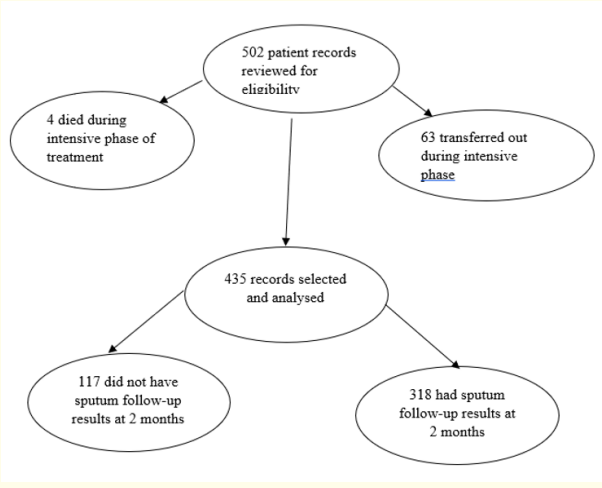

Figure 1: Study profile for the quantitative study.

Prevalence of sputum non-follow-up among 435 smear positive patients in Hoima

The overall prevalence of two month's sputum non-follow-up was 26.9% (95% CI = 7.0 - 64.4). Sputum non-follow-up prevalence was highest among patients not on directly observed treatment with 52.4% and lowest among patients staying within 5 kilometres with 20.3%. The prevalence of sputum non-follow-up are summarized in table 2 above.

Characteristic	Category	Frequency(n)	Percentage (%)
DOT	Yes	414	95.2
	No	21	4.8
HIV status	Negative	293	67.4
	Positive	142	32.6
Health facility location	Rural	62	14.3
	Urban	373	85.7
Patient type	Retreatment	21	4.8
	New	414	95.2
Health facility levels	HC III	114	26.2
	HC IV	75	17.2
	Hospital	246	56.6
Health facility type	Private	28	6.4
	Government	407	93.6
Baseline TB drug sensitivity	Done	297	68.1
	Not done	138	31.7
Age at start of treatment /years (median, lower q, upper q)		36, 28,47	
Weight at start of treatment/ kg (mean, sd)		50.7, 9.3	

Table 1: Social demographic, clinical and health facility characteristics for 435 smear positive TB patients attending health facilities in Hoima from 1st January 2017 to 31st December 2018.

DOT stands for directly observed therapy, TB for tuberculosis, HC for health centre, sd for standard deviation and q for quartile.

Characteristic	Category	Frequency(n)	Non-follow up n (%)	95%CI
Smear positive patients		**435**	**117 (26.9)**	**7.0-64.4**
Sex	Female	126	38 (30.2)	13.0-54.9
	Male	309	79 (25.6)	5.0-69.1
Distance	≤5 km	158	32 (20.3)	3.9-61.7
	>5km	277	85 (30.7)	9.6-64.9
DOT	Yes	414	106 (25.6)	7.7-58.5
	No	21	11 (52.4)	22.1-81.0
HIV status	Negative	293	66 (22.5)	5.2-60.7
	Positive	142	50 (35.2)	12.3-67.8
ART status	On ART	142	50 (35.2)	12.3-67.8
Health facility location	Rural	114	32 (51.6)	
	Urban	373	85 (22.8)	11.7-39.7
Patient type	Retreatment	21	5 (23.8)	0.0-100.0

	New	414	112 (27.1)	7.1-64.4
Health facility type	Private	28	14 (50.0)	0.4-99.6
	Government	407	103 (25.3)	5.7-65.5
Baseline tuberculosis drug sensitivity	Done	297	62 (20.9)	5.7-53.4
	Not done	138	55 (39.9)	26.3-55.2

Table 2: Prevalence of sputum non-follow-up among 435 smear positive patients from 1st January 2017 to 31st December 2018 in Hoima district.

DOT stands for directly observed therapy, TB for tuberculosis and ART for antiretral viral therapy.

Bivariate analysis between factors and sputum non-follow-up

Factors that had a p value of < 0.2 those suggested by literature were considered for Multivariate analysis. The bivariate analysis between predictors and sputum non-follow-up are summarized in table 3 below.

Multivariate analysis of factors associated with sputum non-follow-up

Baseline TB drug sensitivity testing was left in the final model because it confounded health facility location. Results of multivariate analysis are summarized in table 4 below.

Factors	Non-follow-up n (%)	Follow-up n (%)	Prevalence ratio (PR)	95% CI	P-value
Sex					
Male	79 (25.6)	230 (74.4)	0.85	0.61 - 1.17	0.318
Female	38 (30.2)	88 (69.8)	1.00		
Age			1.00	0.99 - 1.02	0.475
Distance > 5km	85 (30.7)	192 (69.3)	1.52	1.07 - 2.14	0.019*
≤ 5 km	32 (20.2)	126 (79.8)	1.00		
DOT					
No	11 (52.4)	10 (47.6)	2.05	1.60 - 2.62	<0.001*
Yes	106 (25.6)	308 (74.4)	1.00		
HIV status					
Positive	50 (35.2)	92 (64.8)	1.56	1.23 - 1.98	0.001*
Negative	66 (22.5)	227 (77.5)	1.00		
Weight			1.00	0.99 - 1.00	0.011*
ART status					
On ART	50 (35.2)	92 (64.8)	1.56	1.23 - 1.98	0.001*
Not on ART	66 (22.6)	226 (77.4)	1.00		
HF type					
Gov't	103 (25.3)	304 (74.7)	1.00		
Private	14 (50.0)	14 (50.0)	1.97	0.82 - 4.78	0.131*
Health facility location					
Urban	85 (22.8)	288 (77.2)	1.00		
Rural	49 (43.0)	65 (57.0)	2.26	1.71 - 3.00	<0.001*

Patient type New	112 (27.0)	302 (73.0)	1.14	0.43 - 2.99	0.796
Retreatment	5 (23.8)	16 (76.2)	1.00		
Baseline TB drug sensitivity Not done	55 (40.9)	83 (60.1)	1.91	1.12 - 3.25	0.017*
Done	62 (20.9)	235 (79.1)	1.00		

Table 3: Unadjusted association between factors and sputum non-follow-up for 435 smear positive TB patients from 1st January 2017 to 31st December 2018 attending Hoima district health facilities.

We took age and weight at the start of tuberculosis treatment. HF stands for health facility, Gov't is government *means p-value < 0.2.

Factors	Category	Prevalence Ratio (PR)	[95% Confidence Interval]	P-value
HIV-status	Positive	1.48	1.23 - 1.77	< 0.001
	Negative	1.00		
DOT	No	1.31	1.11 - 1.55	0.002
	Yes	1.00		
Health facility location	Rural	1.79	1.19 - 2.72	0.006
	Urban	1.00		
Health facility type	Private	2.05	1.15 - 3.66	0.015
	Government	1.00		
Distance	>5km	1.38	1.05 - 1.81	0.021
	<5km	1.00		
Sex	Female	1.20	0.83 - 1.75	0.329
	Male	1.00		
Age		1.00	0.99 - 1.01	0.583
Baseline TB drug sensitivity	Not done	1.44	0.70 - 2.95	0.318*
	Done	1.00		

Table 4: Multivariate analysis of factors associated with two months' sputum non-follow-up for smear positive patients from 1st January 2017 to 31st December 2018 in Hoima district.

DOT stands for directly observed therapy, TB for Tuberculosis, statistically significant p-value is in bold and * shows a cofounder.

Discussion

We sought to determine the prevalence and factors associated with non-follow up of PTB patients for the two months' sputum examination from January 2017 to December 2018 in health facilities of Hoima district, Uganda. We found the prevalence of two months' sputum non-follow-up at 26.9% (95% CI, 7.0 - 64.4) for bacteriologically confirmed tuberculosis patients from 1st January 2017 to 31st December 2018 in Hoima health facilities. This is far above the 0% recommended by World Health Organization [9] and National Tuberculosis and Leprosy Program (MOH, 2014). The prevalence of two months' sputum non-follow-up is not different from 26.2% that was found out in a retrospective study carried out in South Af-

rica [14]. In previous studies conducted in Uganda, the prevalence of sputum non-follow-up has ranged from 16% in Kiboga and Kyankwanzi [2] and 46% in the Eastern part of the country [3]. This high prevalence of two months sputum non-follow-up could have been caused by high patient volume and lack of reliable patient contacts as explained by a study in India [10]. The high prevalence of two months' sputum non-follow-up in Hoima implies that some TB patients are not assessed which could lead to an increase in multidrug resistant tuberculosis, increased tuberculosis spread, morbidity and mortality. We assessed two months' sputum non-follow-up as absence of two months' sputum results in the health unit tuberculosis register and laboratory register which could have led an over estimate of prevalence. There was a stronger clustering than was anticipated during sample size estimation resulting in inadequate sample size hence wide confidence intervals.

Patients that were not on DOT in comparison to those on DOT (aPR = 1.31, P = 0.002), were 1.3 times more likely to miss two months' sputum follow-up. This could have been due to lack of social support that could have been provided by a treatment supporter including reminding the patient about the sputum follow-up. This result is consistent with the study done in Kiboga and Kyankwanzi which found out that not being on directly observed treatment was associated with loss to follow-up (aOR = 1.7) [2]. The two studies were conducted in similar study settings which could have led to consistence in the results. This result is inconsistent with [17,19-21]. This inconsistence could be as a result of difference in the study settings.

A patient that is HIV positive versus negative one (aPR =1.48, P < 0.001), was 1.5 times more likely to miss sputum follow-up. This result could been due to social stigma influencing HIV Positive patients to miss appointments [11]. This result is consistent with studies where positive HIV-status was associated with loss to follow-up (aOR = 7.67, 95%CI 1.00 - 59.0, P = 0.05) [12], studies in Uganda (a OR 2.91, 95%CI 1.71 - 4.96) [15], (a OR 1.83; 95%CI 1.09 - 3.26), (OR 3.35, 95%CI 1.41 - 7.92, P = 0.01) [16] and a study in Haiti [21]. Tuberculosis and HIV are disease conditions which require a patient to go through a process and in some health facilities, patients are handled in different clinics and patients prioritize HIV clinics. This could be the cause of an increased likelihood of missing sputum follow-up among patients with both conditions. The result is inconsistent with studies done in South Africa [17], Pakistan [18], Georgia [19], France [20] US and Canada [25]. The inconsistence of results could be due to the difference in the study settings.

A patient travelling more than 5 km in comparison to that one travelling less than 5km (aPR =1.38, P = 0.021), was 1.4 times more likely to miss sputum follow-up. This could be due to lack of transport to travel the long distances to the health facilities [11]. This result is consistent with a study done in Cameroon where travelling long distances was associated with loss to follow-up (aOR = 2.31, 95% CI 1.63 - 3.27) [13], (p value = 0.029) [18], (OR 1.3, 95%CI 1.1 - 1.5) [23,24]. The results are similar possibly due to the fact that the studies were carried out in low-income countries. This result is inconsistent with the findings of a study that was done in Uganda, where travelling long distances was found not to be associated with loss to follow-up [15].

Limitations

The study was reliant on routinely collected tuberculosis data (secondary data) which was not originally designed for study purposes, hence some data elements required for the study, were found lacking especially weight of 14 participants. However, weight was not found to be significant and no study has been found to contradict this finding. Record keeping did not seem to be good as most health unit tuberculosis registers did not have cover pages and some pages were torn. The study was done in Hoima district and the findings were not necessarily a reflection of the overall picture of the country. The 95% confidence intervals for incidences were very wide meaning that more clustering than what was anticipated occurred at the analysis level.

Conclusion

The prevalence of two months' sputum non-follow-up was high 26.9% [95%CI 7.0 - 64.4]. For every ten patients, 3 patients did not submit sputum for examination at two months during Treatment. The factors associated with sputum non-follow-up included positive HIV status, patients not on directly observed therapy, rural health facility location, patients staying in more than 5km from the health facility and private health facility.

Recommendations

Health workers at health facilities should intensify health education and offer adequate counselling to tuberculosis patients such that they can be empowered to ask for tuberculosis care services. Health workers should give due attention to tuberculosis patients living with HIV/AIDS, patients attending urban health facilities, patients not on DOT and patients not done baseline sensitivity.

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