Original Research

The differences in tuberculosis notifications and outcomes among males and females in Colombo, Sri Lanka

Chandima Hemachandra[1]*, Sudath Samaraweera[1], Arunasalam Pathmeswaran[2]

[1]Ministry of Health, Sri Lanka; [2]Department of Public Health, Faculty of Medicine, University of Kelaniya, Sri Lanka

*Correspondence: chandimadh@gmail.com

https://orcid.org/0000-0002-5590-5806

DOI: https://doi.org/10.4038/jccpsl.v29i3.8614

Received on 28 May 2023
Accepted on 12 Aug 2023

Abstract

Introduction: More males than females are reported with tuberculosis (TB). Assessment of disparities between the two groups would permit adopting targeted interventions.

Objectives: To describe the differences in notification rates, sputum investigations and treatment outcomes of male and female TB patients

Methods: A descriptive follow-up study was conducted among 2169 adult TB patients registered in the Colombo District Tuberculosis Register using registry data. Comparisons were made between males and females using Chi-squared test and risk ratio (RR).

Results: Males had a higher TB notification rate (161 per 100 000) than females (79 per 100 000) and the highest notification rates were observed in 65-74-year-old age category in both groups. A higher proportion of males than females had pulmonary TB (78.2% in males and 59.7% in females; $p<0.05$). More males than females had a positive (RR=1.09; 95% CI: 1.05, 1.13) or high-grade sputum smear result (RR=1.15; 95% CI: 1.01, 1.31). Both groups had similar sputum conversion rates at the end of acute phase (80.4% vs. 84.1%). More males were lost to follow up compared to females (10.7% vs. 3.1%, $p<0.05$).

Conclusions & Recommendations: The observed differences between males and females highlight the need to examine TB data disaggregated by sex and to have more sensitive diagnostics for females.

Keywords: *gender, notification rates, sputum investigations, treatment outcomes, tuberculosis*

Introduction

Tuberculosis is a global public health problem mostly affecting people in Southeast Asia, Africa and Western Pacific Regions. An estimated 10.6 million people, predominantly males, developed ill health due to TB in 2021 (1). The male: female ratio of incident TB cases was observed to range from 1.3 in the Eastern Mediterranean Region to 2.1 in the European and Western Pacific Region in 2019. The figures for children were close to one in all World Health Organization (WHO) regions (2), implying a factor that begins to exert its influence around 15 years to be responsible for the observed gender differences.

Sri Lanka reported a total of 3918 new male (62.7%) and 2331 female (37.3%) TB cases in 2021 (3). Similar observations were made in several studies (4-5). Disparities were observed among males and females in seeking outpatient care, submitting sputum for testing, and becoming sputum smear-positive with a male predominance (6-7). The sputum smear examination with Ziehl Neelsen (ZN) staining, the conventional method of diagnosing TB was observed to be less sensitive in diagnosing TB in females compared with auramine staining and culture studies (8). More females than males were declared cured at the end of the treatment course in several studies (4, 6) while a reverse pattern was observed in some countries (9).

The absence of a comprehensive analysis of routine data disaggregated by sex prompted the authors to undertake the present study to describe the differences in notifications, clinical forms, investigations, and outcomes of TB among males and females in Sri Lanka.

Methods

A descriptive follow-up study was conducted at the District Chest Clinic Colombo, using routine data of TB patients registered in the Colombo District Tuberculosis Register. All the patients diagnosed at public or private institutions are required to be registered at the chest clinic. District Chest Clinic Colombo caters to 2.3 million people, of whom 77.6% live in urban areas, 22.1% in rural areas and 0.3% in estates (10). Twenty-five percent of the total case burden in the country are treated at this clinic (3).

The study population consisted of a one-year cohort of TB patients 15 years or above registered in the District Tuberculosis Register of Colombo District. The patients transferred in from other districts were excluded. With anticipated population proportions of 0.28 and 0.09 of non-compliance to treatment among male and female TB patients (11) and a precision of 0.03, the estimated sample size was 2420 (12). There were a total of 2169 TB cases fulfilling the inclusion and exclusion criteria, registered in the register and thus included in the present study.

A pretested data collection form was used to extract data from the register. To assess the validity of register data, a random sample of 10% (n=217) of cases from the register was cross-checked with source documents. Percentage agreement was more than 95% for age, sex, history of previous treatment, sputum microscopy results at diagnosis and treatment outcome. Whenever the information in the District TB Register was found to be incomplete or incompatible, relevant source records were referred. The principal investigator with the assistance of a trained pre-intern medical officer retrieved data from the register in the second quarter of 2017. Data collection was anonymized, and no personally identifiable data were extracted from the TB register. The standard WHO definitions were used to categorize patients, disease and treatment outcomes (13).

Data analysis

Coding, data entry and analysis were done using Statistical Package for Social Sciences (SPSS) version 21.0. Five percent of the entered data was

rechecked, and frequency distributions were examined to screen for errors in data entry. Sociodemographic characteristics**,** notifications, investigation findings, and outcomes of disease were compared between male and female groups. The sputum conversion rate was expressed as the percentage of bacteriologically confirmed pulmonary TB (PTB) cases registered in a specified period that were smear-negative at the end of the initial phase of treatment. TB notification rates by sex and age groups were calculated per 100 000 populations in Colombo District based on the population tables, Census of Population and Housing of Sri Lanka 2012, the last census conducted (14). Chi-squared test and independent-sample t-test were used for comparison of categorical and numerical variables respectively. A p value less than 0.05 was taken as a significant association. To assess the strength of association, RR with 95% confidence interval (CI) was calculated. The trend for notification rates by sex and age categories was calculated using linear regression.

Results

The study included TB patients aged 15 years or above registered in the District TB Register. The sample included 1427 (65.8%) male patients. The female patients were younger (mean age=44.5; SD=17.7) than the male patients (mean=49.1; SD=15.6) ($p<0.05$).

Table 1: Distribution of the TB notification rates by sex and age group in Colombo District

Age groups (years)	TB notification rates per 100 000 male, female or total population			Notification rate ratio (M: F)	TB incidence (new & relapse cases) rates per 100 000 male, female or total population			Incidence rate ratio
	Male	Female	Total		Male	Female	Total	
15 - 24	61	73	67	0.8	59	70	65	0.8
25 - 34	86	64	75	1.3	83	61	72	1.4
35 - 44	153	69	111	2.2	143	67	105	2.1
45 - 54	246	88	164	2.8	227	85	153	2.7
55 - 64	266	99	177	2.7	257	93	170	2.8
65 - 74	306	112	220	2.8	296	101	187	2.9
≥ 75	251	68	139	3.7	247	66	136	3.7
Total	**161**	**79**	**119**	**2.0**	**153**	**76**	**113**	**2.0**

M: F=male: female; TB=tuberculosis

p for trend with increasing age: for TB notification rate and incidence rate in males $p<0.01$; for notification rate ratio and incidence rate ratio $p<0.01$; for TB notification rate in females $p=0.02$ (only up to age group 65-74); TB incidence rate in females $p=0.01$ (only up to age group 65-74)

TB notification rates

The notification rate of TB among males was 161 per 100 000, whereas it was 79 per 100 000 among females (Table 1). The highest rates were observed in the 65–74-year age group in both males and females. The male to female notification rate ratio was lowest in the 15-24 years age group (0.8:1) and the highest in 75 years or above age group (3.7:1). The trend was statistically significant with increasing age. The male: female notification rate ratio increased ($p<0.01$), and there was an increase in notification rates for males ($p<0.01$). For females, the trend was only significant up to the age of 74 ($p=0.02$). The calculation of rates for both male and female incident cases (new and relapse) showed a similar trend across age groups.

Table 2: Distribution of sputum examination grading of bacteriologically confirmed pulmonary tuberculosis patients at diagnosis by sex

Characteristic		Male No. (%)	Female No. (%)	Total No. (%)
Sputum smear microscopy grading at diagnosis (n=1214)	No AFB	23 (2.6)	34 (10.4)	57 (4.7)
	Scanty*	99 (11.2)	39 (11.9)	138 (11.3)
	+**	203 (22.9)	87 (26.5)	290 (23.8)
	2+***	160 (18.1)	48 (14.6)	208 (17.1)
	3+****	258 (29.1)	81 (24.7)	339 (27.9)
	Positive*****	143 (16.1)	39 (11.9)	182 (15.0)
	Sub Total	886 (100.0)	328 (100.0)	1214 (100.0)
Sputum culture grading (n=1216)	1-9 colonies	7 (0.8)	9 (2.7)	16 (1.3)
	+#	18 (2.1)	12 (3.7)	30 (2.5)
	2+##	19 (2.1)	14 (4.3)	33 (2.7)
	3+###	35 (3.9)	18 (5.5)	53 (4.3)
	Positive*****	4 (0.5)	3 (0.9)	7 (0.6)
	Contaminated	2 (0.2)	0 (0.0)	2 (0.2)
	Not available/ not done	803 (90.4)	272 (82.9)	1075 (88.4)
	Sub Total	888 (100.0)	328 (100.0)	1216 (100.0)
Sputum WHO Recommended Rapid Diagnostic grading (n=1216)	T	25 (2.8)	10 (3.0)	35 (2.8)
	RR	1 (0.1)	0 (0.0)	1 (0.1)
	N	5 (0.6)	2 (0.6)	7 (0.6)
	Positive*****	1 (0.1)	0 (0.0)	1 (0.1)
	Not available/ not done	856 (96.4)	316 (96.3)	1172 (96.4)
	Total	888 (100.0)	328 (100.0)	1216 (100.0)

AFB=Acid Fast Bacilli; N=Mycobacterium tuberculosis not detected; RR=Mycobacterium tuberculosis, Rifampicin resistance detected; T=Mycobacterium tuberculosis detected; Rifampicin resistance not detected

*Scanty: 1-9 AFB/100 high power field (HPF); **+: 10-99 AFB/100 HPF; ***++: 1-10 AFB/HPF; ****+++: >10 AFB/HPF; *****Positive: grading not given and only "positive" was marked in the investigation results; #+: 10 -100 colonies; ##2+: >100 colonies; ###3+: innumerable or confluent growth

Most of the reported cases had no history of treatment for TB thus were categorized as new cases (90.7% in males and 92.3% in females; p=0.2). Among the cases with a history of previous treatment, a higher proportion of males (21.8%) than females (8.8%) had ended up as lost to follow-up in their most recent course of TB treatment (p=0.03). The two groups did not significantly differ from each other based on whether they were treatment failures (6.0% in males vs. 12.3% in females; p=0.15) or relapses (51.1% in males vs. 43.8% in females; p=0.36). The comparison of TB cases by the site of the disease showed that males (78.2%) were more likely than females (59.7%) to present with PTB. Of the male patients, 21.8% had extrapulmonary TB (EPTB), whereas of the female patients, 40.3% had EPTB (p<0.05). The notification rate of PTB was 126 per 100 000 in males, while it was 47 per 100 000 in females. For EPTB, it was 35 per 100 000 and 32 per 100 000, respectively in males and females.

Among the PTB, more males (79.6%) were diagnosed with bacteriologically confirmed PTB than females (74.0%) (p=0.02).

Table 3: Treatment outcomes of bacteriologically confirmed PTB, clinically diagnosed PTB and EPTB cases by sex

Characteristic		Unsuccessful* outcome No. (%)	Successful* outcome No. (%)	Total	RR	95% CI
Bacteriologically confirmed PTB cases	Male	208 (23.4)	680 (76.6)	888	1.92	1.4, 2.63
	Female	40 (12.2)	288.8 (87.8)	328	1.0	
	Sub total	248 (20.4)	968 (79.6)	1216		
Clinically diagnosed PTB cases	Male	54 (23.7)	174 (76.3)	228	1.43	0.89, 2.3
	Female	19 (16.5)	96 (83.5)	115	1.0	
	Sub total	73 (21.3)	270 (78.7)	343		
EPTB cases	Male	50 (16.1)	261 (83.9)	311	1.17	0.8, 1.71
	Female	41 (13.7)	258 (86.3)	299	1.0	
	Sub total	91 (14.9)	519 (85.1)	610		

CI=confidence interval; EPTB=extrapulmonary tuberculosis; PTB=pulmonary tuberculosis; RR=risk ratio

*Cured and treatment completed categories were amalgamated to "successful outcome" (Treatment success) whereas all other categories were amalgamated to "unsuccessful outcome"

TB and investigations

Among the bacteriologically confirmed PTB patients, most of the males had a smear microscopy grading of 3+ (29.1%), followed by 22.9% having 1+ grading at the time of diagnosis (Table 2). Most of the females had a grading of 1+ (26.5%) followed by a grading of 3+ by 24.7%. Examining the sputum culture results of the same group found, 3.9% of male patients and 5.5% of female patients to have a culture grading of 3+ followed by 2+ by 2.1% and 4.3%, respectively. The majority of the cases were not offered a sputum culture or WHO-recommended rapid diagnostic at the time of diagnosis which was consistent with the policy during the period where only the prioritised patients were offered a sputum culture (15). Nearly equal proportion of male (2.8%) and female cases (3%) were detected to have tubercle bacilli in sputum with no resistance to rifampicin when examined by the WHO-recommended rapid diagnostic method.

Males were likely to get a positive result at microscopy compared to females (RR=1.09; 95% CI: 1.05, 1.13) though such association was not observed when tested with WHO recommended rapid diagnostics (RR=1.01; 95% CI: 0.75, 1.36). Males were observed to get a higher grading of smear microscopy results (a test result of scanty or 1+ categorised as 'low grade' and 2+ or 3+ categorised as 'high grade') compared to females (RR=1.15; 95% CI: 1.01, 1.31) but not with culture grading (RR=1.13; 95% CI: 0.87, 1.47) (1–9 colonies or 1+ result categorised as 'low grade' and 2+ or 3+ result categorised as 'high grade').

Outcomes of TB patients

At the end of the intensive phase of treatment, 84.1% of females and 80.4% of males had converted from sputum positivity to negativity (p=0.14). At the end of the treatment period, the most recorded outcome of new TB among males (43.3%) was 'cured', while it was 'treatment completed' (50.4%) among the females. Among retreatment cases, 38.3% of males were declared 'cured', while 45.5% of females were

declared 'treatment completed'.

Among the bacteriologically confirmed PTB patients, males were at 1.92 times (95% CI: 1.4, 2.63) higher risk of unsuccessful outcome compared to females, but a significant association with unsuccessful outcome was not observed in clinically diagnosed and EPTB cases (Table 3). The loss to follow-up rate of all TB patients was 10.7% among males while it was 3.1% among females (RR=3.44; 95% CI: 2.24, 5.28). The death rates (7.3% in males and 6.1% in females) and treatment failure rates (2.0% in males and 1.5% in females) were similar in both groups.

Discussion

The present study findings showed a male: female ratio of almost 2:1 among patients with TB, while the female patients were relatively younger than the male patients; females were almost twice as more likely to be diagnosed with EPTB; males were more likely to have a positive or high-grade sputum smear result; unsuccessful treatment outcomes were relatively higher among males. Sputum conversion rates were similar among both males and females.

The TB notification rate for males was nearly twice the rate for the female population. This difference in notification rate was reflected mainly in the PTB rates rather than in EPTB. This is on par with the more male patients reported around the world with a ratio of 1.6:1 (2). The differences in biological factors among males and females; differences in X linked chromosomes, immune responses and steroid hormonal effects on immunity could be partly responsible for the higher number of TB cases observed among males (16). On the other hand, a ten-year trend showing higher female case notification rates in one province and higher male case notification rates in the other in a cross sectional analysis of secondary data from the National Tuberculosis Programme of Pakistan suggests the possibility of the involvement of environmental factors (17). The highest incidence rates in the 65–74 years age category in both groups in the present study suggest the presence of disease in older age groups. This could be the result of a cohort effect where older people had higher exposures when they were young. The incidence of TB had been over 80 per 100 000 population in 1962 and reduced close to 30 per 100 000 by 1996 (18) in Sri Lanka and was 29.1 per 100 000 in the year 2021 (3). The similar notification rates observed up to about 35 years among males and females suggests similar exposures to risks in these age groups. An education level of secondary or above of 78.5% among males and 75.7% among females (10) and, reasonably high participation in the labour force by young females (19) could lead to similar exposures in these groups.

A comparison of PTB with EPTB found a significantly higher proportion of males to have PTB compared to females and vice versa for EPTB. More males being diagnosed with bacteriologically confirmed PTB compared to females resemble the findings of the record-based study in West Bengal (4) and Thorrur (5) which showed newer smear-positive cases ($p<0.05$) among males. The higher rates of EPTB among females could be the involvement of endocrine factors in females, suggested in a study where females aged 45-64 years had an increased likelihood to develop EPTB (20).

Males reporting a higher grading in sputum microscopy than females and males being at risk of getting a positive smear result indicates the possibility of missing more female cases if the diagnosis was based only on the sputum smear microscopy. The higher rate of sputum positivity or higher grading could be that males were likely to have a severe form of the disease with more cavities or females fail to produce a quality sample of sputum for examination. These findings were similar to the observations made in other studies; in Bangladesh, among the patients above 15 years with cough for more than 21 days, more males were diagnosed with

positive sputum microscopy ($p<0.05$) (21). During 1995 - 1996 in Malawi 53% of males and 47% of females had a positive test result in smear microscopy (6). A study found males to have more cavities in X-rays than females ($p<0.05$) and to have a higher sputum volume ($p<0.01$) though the latter did not show any association with smear or culture positivity. An increase in the number of cases diagnosed after examination of repeated samples (7) suggests whether sputum microscopy depends on the quality of the sample produced. The absence of a clear statistical difference among males and females in respect of sputum culture grading and WRD results unlike in sputum microscopy in the present study rationalizes the use of these investigations in the diagnosis of TB in females. Since the sputum microscopy depends on the quality of the sputum sample produced, Xpert MTB/RIF which detects organisms at lower concentrations (15) as a diagnostic test in patients with negative smear results, would increase the case detection (22). Further to that, Ziehl Neelsen staining microscopy in diagnosing female TB patients was found less sensitive compared to culture studies (7)**.**

Fairly equal sputum conversion rates observed among males and females at the end of the intensive treatment period in the present study contrary to other study findings where being a male was identified as an independent risk factor for non-conversion of sputum when sputum was tested at the end of two months (23-24). The mean duration of sputum conversion in males in Iran was calculated to be 2.29 months (SD=1.23) compared to 1.74 months (SD=0.85) in females ($p=0.05$) (25). The observed results in the current study could be a result of testing sputum at the end of the intensive phase i.e., end of the second or third month in new cases and end of the third or fourth month in retreatment cases during which period the combination of all drugs was continued.

Higher treatment success rates observed in females than in males among bacteriologically confirmed PTB cases may reflect females' higher motivation or favorable circumstances for adherence to treatment or males' barriers to treatment. A significant higher rate of loss to follow up among males as compared to females points towards the possible barriers to regular treatment by male patients. Unemployment, illiteracy, smoking, alcohol, etc., that have been linked to non-adherence among TB patients in other studies (26-28), were not explored in the present study. Patients ended up as lost to follow up are likely to present as retreatment cases, thereby contributing to more male numbers than females. Yet the comparison of male and female cases based on previous treatment history failed to identify any difference between males and females by the fact whether they are new or retreatment cases. However, this was reflected in the retreatment cases registered for treatment; 21.8% of males had been lost to follow up in the previous treatment course while it was 8.8% for females. Males' association with an unsuccessful treatment outcome in bacteriologically confirmed PTB patients is on par with the findings observed among new smear positives, where more female patients were cured than males (4, 6). The contrasting findings in some countries in which the treatment success rate of all forms in males was higher than in females might reflect differences in access to treatment (9).

We conducted our study using registry based secondary data of one-year cohort similar to the routine one-year surveillance by the National Tuberculosis Programme. The differences of sputum investigations, sputum conversion and treatment outcomes were presented based on bivariate analysis only.

Conclusions & Recommendations

The findings confirm the existence of substantial sex differentials in TB notification rates, sputum examinations, and treatment outcomes warranting sex-disaggregated indicators for identification of gaps, implementing health interventions, measuring

the impact of control programmes, and more sensitive diagnostics for females. Men must be identified as a high-risk group for TB and targeted screening and treatment adherence interventions need to be implemented to lessens the overall burden.

Public Health Implications

- Globally, more males are diagnosed and reported with TB than females. Both biological and socio-cultural attributes have gained recognition in health research as important factors.
- The findings of this study confirm the existence of sex differentials in disease type, sputum examination findings and treatment outcomes in a TB high burden district of Sri Lanka.
- Epidemiologically guided sex-disaggregated data enables the identification of gaps and can be utilized to facilitate strategic planning in health care.

Author Declarations

Competing interests: The authors declare that they have no competing interests.

Ethics approval and consent to participate: Ethics clearance was granted by the Ethics Review Committee of the of the Faculty of Medicine, University of Colombo.

Funding: Self-funded

Acknowledgements: We wish to acknowledge the National Programme for Tuberculosis Control and Chest Diseases and all the staff at the District Chest Clinic Colombo.

Author contributions: CH - concept and design of the study; collection, analysis, and interpretation of data; preparation of the manuscript. SS and AP- concept and design of the study; interpretation of data; critical revision of the manuscript. All authors read and approved the final manuscript.

References

1. World Health Organization. *Global Tuberculosis Report 2022*. Geneva: World Health Organization, 2022. Available from: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022.
2. World Health Organization. *Global Tuberculosis Report, 2020*. Geneva: World Health Organization, 2020. Available from: https://www.who.int/publications/i/item/9789240013131.
3. National Programme for Tuberculosis Control and Chest Diseases. *Annual Report 2021*. Colombo: National Programme for Tuberculosis and Chest Diseases, 2021. Available from: https://www.nptccd.health.gov.lk/wp-content/uploads/2022/03/NPTCCD-Annual-Report-2020.pdf.
4. Mukherjee A, Sarkar A, Saha I, Chowdhury R. Gender differences in notification rates, clinical forms and treatment outcome of tuberculosis patients under the RNTCP. *Lung India* 2012; 29(2): 120-122. https://doi.org/10.4103%2F0970-2113.95302.
5. Rajarao P & Anjanamma TC. Gender differences in treatment outcome of tuberculosis patients under the Revised National Tuberculosis Control Programme. *Ann Int Med Den Res* 2019; 5(5): FM7-10.
6. Karim F, Ahmed F, Begum I, Johansson E, Diwan VK. Female-male differences at various clinical steps of tuberculosis management in rural Bangladesh. *Int J Tuberc lung Dis* 2008; 12(11): 1336-1339. PMID 18926047.
7. Boeree MJ, Harries AD, Godschalk P, Demast Q, Upindi B, Mwale A, Nyirenda TE, Banerjee A, Salaniponi FML. Gender differences in relation to sputum submission and smear-positive pulmonary tuberculosis in Malawi. *Int J Tuberc Lung Dis* 2000; 4(9): 882-884. PMID 10985659.

8. Kivihya-Ndugga LEA, van Cleeff MRA, Ng'ang'a LW, Meme H, Odhiambo JA, Klatser PR. Sex-specific performance of routine TB diagnostic tests. *Int J Tuberc lung Dis* 2005; 9(3): 294-300. PMID 15786893.
9. Getahun B, Ameni G, Medhin G, Biadgilign S. Treatment outcome of tuberculosis patients under directly observed treatment in Addis Ababa, Ethiopia. *Brazilian J Infect Dis* 2013; 17(5): 521-528. https://doi.org/10.1016/j.bjid.2012.12.010.
10. Department of Census & Statistics. *Census of Population and Housing 2012.* Colombo: Department of Census & Statistics, 2012.
11. Janakan, N. *Epidemiological pattern of tuberculosis and selected aspects of case management in the district of Colombo, Sri Lanka*. MD Thesis (Community Medicine). Colombo: Postgraduate Institute of Medicine, 2005.
12. Lawanga, SK & Lameshow S. *Sample size determination in health studies: a practical manual.* Geneva: World Health Organization, 1991. Available from: https://apps.who.int/iris/handle/10665/40062.
13. World Health Organization. *Definitions and reporting framework for tuberculosis – 2013 Revision.* Geneva: World Health Organization, 2013.
14. Department of Census and Statistics. *Census of Population and Housing – 2012 Sri Lanka POPULATION TABLES*. Colombo: Department of Census and Statistics, 2012. Available from: www.statistics.gov.lk/PopHouSat/CPH2011/index.php?fileName=FinalPopulation&gp=Activities&tpl=3.
15. National Programme for Tuberculosis Control and Chest Diseases. *National Manual for Tuberculosis Control.* Colombo: National Programme for Tuberculosis Control and Chest Diseases, 2016.
16. Nhamoyebonde S & Leslie A. Biological differences between the sexes and susceptibility to tuberculosis. *J Infect Dis* 2014; 209(Suppl. 3): S100-S106. https://doi.org/10.1093/infdis/jiu147.
17. Dogar OF, Shah SK, Chughtai AA, Qadeer E. Gender disparity in tuberculosis cases in eastern and western provinces of Pakistan. *BMC Infect Dis* 2012; 12(244): 1-7. https://doi.org/10.1186/1471-2334-12-244.
18. Respiratory Disease Control Programme. *Administration Report Respiratory Disease Control Programme 1996*. Colombo: Respiratory Disease Control Programme, 1996.
19. Department of Census and Statistics. *Sri Lanka Labour Force Survey Annual Report - 2016.* Colombo: Department of Census and Statistics, 2017. Available from: http://www.statistics.gov.lk/Resource/en/LabourForce/Annual_Reports/2016.pdf.
20. Forssbohm M, Zwahlen M, Loddenkemper R, Rieder HL. Demographic characteristics of patients with extrapulmonary tuberculosis in Germany. *Eur Respir J* 2008; 31(1): 99-105. https://doi.org/10.1183/09031936.00020607.
21. Zaman K, Yunus M, Arifeen SE, Baqui AH, Sack DA, Hossain S, Rahim Z, Ali M, Banu S, Islam MA, Begum N, Begum V, Breiman RF, Black RE. Prevalence of sputum smear-positive tuberculosis in a rural area in Bangladesh. *Epidemiol Infect* 2006; 134(5): 1052-1059. https://doi.org/10.1017/S0950268806006108.
22. Wu Z, Rueda ZV, Li T, Zhang Z, Jiang Z, Jiang Y, Sha W, Yu F, Chen J, Pan Q, Shen X, Yuan Z. Effect of the Xpert MTB/RIF on the detection of pulmonary tuberculosis cases and rifampicin resistance in Shanghai, China. *BMC Infect Dis* 2020; 20(1): 153. https://doi.org/10.1186/s12879-020-4871-9.
23. Feng J, Huang S, Ting W, Chen Y, Lin Y, Huang R, Lin C, Hwang J, Lee J, Yu M, Yu K, Lee Y, Su W. Gender differences in treatment outcomes of tuberculosis patients in Taiwan: a prospective observational study. *Clin Microbiol Infect* 2012; 18(9): E331337. https://doi.org/10.1111/j.1469-0691.2012.03931.x.
24. Gunda DW, Nkandala I, Kavishe GA, Kilonzo SB, Kabangila R, Mpondo BC. Prevalence and risk factors of delayed sputum conversion among patients treated for smear positive PTB in Northwestern Rural Tanzania: a retrospective cohort study. *J Trop Med* 2017; 2017: 5352906. https://doi.org/10.1155/2017/5352906.

25. Azarkar Z, Sharifzadeh G, Ebrahimzadeh A, Olumi S. Time to sputum smear conversion in smear-positive pulmonary tuberculosis patients and factors for delayed conversion. *Iran J Med Sci* 2016; 41(1): 44-47. https://pubmed.ncbi.nlm.nih.gov/26722144.

26. Belilovsky EM, Borisov SE, Cook EF, Shaykevich S, Jakubowiak WM, Kourbatova EV. Treatment interruptions among patients with tuberculosis in Russian TB hospitals. *Int J Infect Dis* 2010; 14(8): e698-e703. https://doi.org/10.1016/j.ijid.2010.03.001.

27. Leung CC, Yew WW, Chan CK, Chang KC, Law WS, Lee SN, Tai LB, Leung ECC, AU RK, Huang SS, Tam CM. Smoking adversely affects treatment response, outcome and relapse in tuberculosis. *Eur Respir J* 2015; 45(3): 738-745. https://doi.org/10.1183/09031936.00114214.

28. Xu W, Lu W, Zhou Y, Zhu L, Shen H, Wang J. Adherence to anti-tuberculosis treatment among pulmonary tuberculosis patients: a qualitative and quantitative study. *BMC Health Serv Res* 2009; 9: 169. https://doi.org/10.1186/1472 6963 9 169.