A Comparative Analysis of Tuberculosis Treatment Success between Hunan Province of China and Eastern Ghana

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Key Words

Tuberculosis • Comparative analysis • Treatment success

Abstract

Objective: To assess the differences in tuberculosis (TB) treatment success between Hunan and Eastern Ghana. **Subjects and Methods:** The study was a retrospective comparative study using 2005–2006 surveillance data from the Hunan province of China and the Eastern region of Ghana. Data analyzed were from the provincial/regional capital and a randomly selected city of lower economic status. χ^2 test and Fisher's exact test were used to do general and stratified comparison of treatment success rates within/between the two areas. Multivariate logistic regression was used to analyze the independent effect of explanatory variables on treatment success. **Results:** Generally, the treatment success rate was significantly higher in Hunan (93.1 vs. 60.7%, $p = 0.000$). Stratified analyses showed a similar pattern for almost all the group-specific rates. Key predictors of TB treatment success in Hunan were gender, age group, and type of city of residence whilst in Eastern Ghana treatment success was associated with only age group. Odds ratios for treatment success in Hunan were significantly lower for males

(OR = 0.78; 95% CI = 0.63, 0.97), and higher for patients resident in the provincial capital (OR = 1.35; 95% CI = 1.12, 1.62). In both countries treatment success rates decreased with increasing age. **Conclusion:** TB treatment success in Hunan was comparatively better than that in Eastern Ghana. Gender, age group, and type of city of residence were the key predictors of treatment success in Hunan whilst in Eastern Ghana age group was the key predictor.

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Introduction

Tuberculosis (TB), caused by the *Mycobacterium tuberculosis* bacillus, remains a major public health problem in the world affecting over 8 million people, and causing about 2 million deaths in a year [1]. It is estimated that over 90% of global TB cases and deaths occur in developing countries, and it affects mainly people within the economically productive age group (15–54 years) [1]. Co-infection with the human immunodeficiency virus (HIV) has increased the risk of developing active TB thereby making TB the leading cause of death among people with HIV [2]. Furthermore, the emergence and

spread of multidrug-resistant *M. tuberculosis* have compounded the seriousness of the TB problem [2].

Globally, there are 22 high-burden countries accounting for approximately 80% of all estimated new TB cases each year [2]. Of these, 9 are in Africa, 5 in Southeast Asia, 4 in the Western Pacific region, 2 in the Eastern Mediterranean region, 1 in Latin America and 1 in Eastern Europe. China, belonging to the Western Pacific region, is listed among the high-burden countries, and together with India accounts for 35% of the annual new cases in the world [2]. This notwithstanding, China by the end of the year 2005 had attained a treatment success rate of 94% (above the global target of 85%). Although not among the high-burden countries, Ghana by the end of 2005 had achieved a lower treatment success rate of 72% [3].

The objective of our study was to comprehensively assess TB treatment success differences between Hunan and Eastern Ghana with a view of providing useful information for TB control.

Subjects and Methods

Study Area and Population

The study was conducted in the Hunan Province of China and the Eastern region of Ghana. The Hunan province is located in South Central China along the middle reaches of the Yangtze River with Changsha, which is about 1,640 km away from Beijing, as its capital. The province covers a total area of 211,800 km² and has a human population of 66,977,000 (population density of 316 persons/km²). The climatic conditions in Hunan are subtropical in nature with an annual rainfall of 1,250–1,750 mm and an average annual temperature of 15–18°C. The main occupation in the province is farming. The population is made up of 52% males and 48% females. About 22% of the population is aged 0–14 years, and 7% aged 65 years and above. HIV prevalence for 2005 was estimated to be 0.1% [4, 5].

The Eastern region of Ghana covers a total area of 19,323 km² and has a human population of 2,108,852 (population density of 109/km²). The region has Koforidua, about 85 km from Accra, as its capital. The climatic conditions are tropical in nature with an annual rainfall of 750–1,750 mm and an average annual temperature of 26–30°C. The main occupation in the region is farming. The population is made up of 49% males and 51% females. About 42% of the population is aged 0–14 years, and 6% aged 65 years and above. HIV prevalence for 2005 was estimated to be 4.7% [3, 6, 7].

Study Design

The study was a retrospective comparative study of TB treatment success using the 2005–2006 surveillance data from Hunan and Eastern Ghana. Two cities were selected from each province/region. These were the provincial/regional capital (referred to as primary city) and a randomly selected city of lower economic status (referred to as secondary city).

Using WHO classifications, successfully treated patients included those who were cured or completed their treatment. Briefly, an outcome was classified as 'cured' when an initially smear-positive patient was smear-negative in the last month of treatment, and on at least one previous occasion. An outcome was classified as 'completed' when a patient who had completed treatment did not meet the criteria for 'cured' or 'failure'. A treatment was classified as 'failure' when a patient who was smear-positive remained smear-positive or became smear-positive again at least 5 months after the start of treatment or later during treatment [3].

Treatment Regimen

Patients included in our study had been treated in reference to three WHO diagnostic categories. Briefly, category I referred to new smear-positive pulmonary TB, new smear-negative pulmonary TB with extensive parenchymal involvement, and severe forms of extrapulmonary TB or concomitant HIV disease. Category II referred to previously treated smear-positive pulmonary TB. Category III referred to new smear-negative pulmonary TB and less severe forms of extrapulmonary TB [1]. Drugs used in Hunan and Eastern Ghana were isoniazide (H), rifampicin (R), pyrazinamide (Z), ethambutol (E), thioacetazone (T), and streptomycin (S).

In Hunan, the treatment regimens were given as follows: (I) 2-month initial phase of HRZE given 3 times a week, followed by 4-month continuation phase of HR given 3 times a week (2H3R3Z3E3/4H3R3). (II) 2-month initial phase of HRZES given 3 times a week, followed by 6-month continuation phase of HRE given 3 times a week (2H3R3Z3E3S3/6H3R3E3). (III) 2-month initial phase of HRZ given 3 times a week, followed by 4-month continuation phase of HR given 3 times a week (2H3R3Z3/4H3R3).

In Eastern Ghana, the treatment regimens were given as follows: (I) Daily 2-month initial phase of SHRZ, followed by daily 6-month continuation phase of HT (2SHRZ/6HT). (II) Daily 3-month initial phase of HRZE supplemented with S during the first 2 months followed by continuation phase involving 5 months of HRE given 3 times a week (2SHRZE/1HRZE/5H3R3E3). (III) Daily 2-month initial phase of SHT, followed by daily 10-month continuation phase of (HT2SHT/10HT) [8].

Data Analyses

Data from the 2005 and 2006 TB registers were captured using Microsoft Excel and analyses done using Statistical Package for Social Sciences (SPSS version 15.0). The outcome variable was treatment success. Explanatory variables common to the TB registers in Hunan and Eastern Ghana were gender, age group, patient classification, place of residence, and treatment regimen. χ^2 test and Fisher's exact test were used to do general and stratified comparison of treatment success rates within/between the two areas. Trend analyses were also done for age-specific rates. Treatment outcomes for the different treatment regimens (categories I, II, and III) were compared with each other. Furthermore, multivariate logistic regression was used to analyze the independent effect of explanatory variables on treatment success (yes = 1, no = 0). The explanatory variables were: gender (male: 1, female: 2); age group (0–14 years: 1, 15–44 years: 2, 45–64 years: 3, 65 years and above: 4, 65 years and above as referent); patient classification (new case: 1, previously treated case: 0); place of residence (primary city: 1, secondary city: 0); and treatment regimen (category

ry I: 1, category II: 2, category III: 3, category I as referent). To confirm the role of area of study in determining treatment success, area of study was added to the explanatory variables in a combined data from the 2 areas (Hunan: 1, Eastern Ghana: 0) and used in the multivariate logistic regression.

Data quality was checked by using cross-tabulations to identify misclassified treatment outcomes.

Results

General Characteristics of TB Patients

The selection of primary and secondary cities yielded a total of 7,867 patients (7,384 cases from Hunan and 483 cases from Eastern Ghana). The majorities of patients in the two study areas were males (64.8–73.0%), aged 15–44 years (42.7–52.7%), new cases (87.8–93.9%), resident in the primary city (66.9–77.0%), and received category I treatment regimen (85.1–93.5%) (table 1).

Treatment Success Rates within/between Hunan and Eastern Ghana

In Hunan, treatment success was associated with all the variables analyzed ($p < 0.05$). Treatment success rates were significantly higher among females (94.3%), new patients (93.2%), and patients resident in the primary city (93.6%). Between-group comparisons showed that there were no significant differences in success rates between treatment regimens I and III, and II and III. However, patients receiving the category I treatment regimen had a significantly higher success rate compared with those receiving the category II treatment regimen (93.2 vs. 90.5%, $p = 0.036$). Treatment success rates were highest among patients aged 0–14 years (98.0%), and significantly decreased with increasing age (table 2).

In Eastern Ghana, treatment success was associated with only age group. As in Hunan, treatment success rates were highest among patients aged 0–14 years (86.7%) and decreased with increasing age. There were no significant associations between treatment success and gender, patient classification, type of city of residence, and treatment regimen (table 2).

Between study area analyses showed that overall treatment success rates were significantly higher in Hunan compared with Eastern Ghana (93.1 vs. 60.7%). Stratified analyses showed that treatment success rates were significantly higher in Hunan with respect to almost all group-specific rates. There was no significant difference in success rates between Hunan and Eastern Ghana with respect to patients aged 0–14 years ($p > 0.05$) (table 2).

Table 1. General characteristics of TB patients in selected cities in Hunan and Eastern Ghana (2005–2006)

Characteristic	Hunan (n = 7,384)	Eastern Ghana (n = 483)
Gender		
Male	5,389 (73.0)	313 (64.8)
Female	1,995 (27.0)	170 (35.2)
Age group, years		
0–14	50 (0.7)	30 (6.2)
15–44	3,487 (42.7)	253 (52.7)
45–64	2,448 (33.2)	143 (29.6)
≥ 65	1,399 (18.9)	57 (11.8)
Patient classification		
New case	6,934 (93.9)	424 (87.8)
Previously treated case	450 (6.1)	59 (12.2)
Type of city of residence		
Primary	4,940 (66.9)	372 (77.0)
Secondary	2,444 (33.1)	111 (23.0)
Treatment regimen		
Category I	6,905 (93.5)	411 (85.1)
Category II	453 (6.1)	41 (8.5)
Category III	26 (0.4)	31 (6.4)
Treatment outcome		
Cured	4,281 (58.0)	210 (43.5)
Completed	2,590 (35.1)	83 (17.2)
Treatment failure	57 (0.8)	8 (1.7)
Defaulted	309 (4.2)	123 (25.5)
Deaths	147 (2.0)	59 (12.2)

Figures in parentheses indicate percentages.

Factors Influencing Treatment Success in Hunan and Eastern Ghana

The results of multivariate logistic regression showed that the odds ratios for treatment success were lower among males (OR = 0.78), highest among patients aged 0–14 years (OR = 5.53), and decreased with increasing age; they were higher among patients resident in the primary city (OR = 1.35) in Hunan and higher among patients aged 0–14 years compared with patients aged 65 years and above (OR = 7.16) for Eastern Ghana. In the combined data, the odds ratios were significantly higher in Hunan (OR = 9.84), highest among patients aged 0–14 years (OR = 6.60), and decreased with increasing age, and they were higher among patients resident in the primary city (OR = 1.23) (table 3).

Table 2. Comparison of treatment success rates between TB patients in Hunan and Eastern Ghana

Factor	Hunan (n = 7,384)			Eastern Ghana (n = 483)			p value ^a
	n	cases	p value	n	cases	p value	
Overall success	–	6,875 (93.1)	–	–	293 (60.7)	–	0.000
Gender							
Male	5,389	4,989 (92.6)		313	190 (60.7)		0.000
Female	1,995	1,882 (94.3)	0.009	170	103 (60.6)	1.000	0.000
Age group, years							
0–14	50	49 (98.0)		30	26 (86.7)		0.120
15–44	3,487	3,290 (94.4)		253	155 (61.3)		0.000
45–64	2,448	2,275 (92.9)		143	84 (58.7)		0.000
≥ 65	1,399	1,257 (89.8)	0.000	57	28 (49.1)	0.008	0.000
Patient classification							
New case	6,934	6,465 (93.2)		424	258 (60.8)		0.000
Previously treated case	450	406 (90.2)	0.021	59	35 (59.3)	0.887	0.000
Type of city of residence							
Primary	4,940	4,622 (93.6)		372	221 (59.4)		0.000
Secondary	2,444	2,249 (92.0)	0.015	111	72 (64.9)	0.321	0.000
Treatment regimen							
Category I	6,905	6,435 (93.2)		412	251 (60.9)		0.000
Category II	453	410 (90.5)	0.036 ^b	31	22 (71.0)	0.356 ^b	0.002
Category III	26	26 (100)	0.324 ^b 0.195 ^c	40	20 (50.0)	0.240 ^b 0.123 ^c	0.000

Figures in parentheses indicate percentages. n = Total number of patients. Trend analyses for age group were significant for both countries. ^a p value for between-country comparisons. ^b Compared with category I. ^c Compared with category II.

Discussion

We did a large sample comparative study of TB treatment success between Hunan and Eastern Ghana. The study showed that in Hunan TB treatment success was associated with gender, age group, and type of city of residence in both univariate and multivariate logistic regression analyses but in Eastern Ghana, treatment success was associated only with age group.

Males in Hunan showed significantly lower rates of treatment success than females, similar to findings in other parts of Asia, Europe, and South Africa [9–15]. Males are often not considered as vulnerable groups in most health intervention programs. It is, however, vital to consider them as a potentially vulnerable group requiring special interventions to improve TB treatment outcomes. The detailed mechanism may need further investigations. Increasing age of patients in both Hunan and Eastern Ghana was a challenge to positive treatment outcomes. This observation, which may be due to the declining protective efficacy of TB immunizations given at birth, compares well with several studies [10, 12, 13],

thereby stressing the importance of developing strategies to enhance positive treatment outcomes among older TB patients. Although patient classification in Hunan was associated with treatment success in the univariate analyses and not the multivariate logistic regression, it is worth mentioning that our observation of a higher treatment success rate among new TB cases (compared with previously treated cases) is consistent with findings in other parts of Asia and Europe [10, 16, 17]. Previously treated TB cases, who are often treated as cases of relapse, treatment default and failure, need special attention to improve their treatment outcomes. The observation that treatment success rate in Hunan was significantly higher among patients resident in the primary city confirmed previous reports [18, 19] that treatment success among TB patients is often associated with high income levels coupled with good health systems, a characteristic of urban communities.

Comparisons between the two areas of study further showed that treatment success rates were significantly higher in Hunan. This observation was evident among virtually all groups of patients analyzed, and therefore

Table 3. Results of logistic regression analysis of factors influencing treatment success among TB patients in Hunan and Eastern Ghana

Variable	Hunan		Eastern Ghana		Combined	
	OR	95% CI	OR	95% CI	OR	95% CI
Study area						
Hunan					9.84	7.89, 12.28
Eastern Ghana ¹						
Gender						
Male	0.78	0.63, 0.97	1.10	0.74, 1.65	0.85	0.70, 1.02
Female ¹						
Age group, years						
0–14	5.53	0.76, 40.47	7.16	2.20, 23.31	6.60	2.52, 17.27
15–44	1.90	1.51, 2.38	1.65	0.92, 2.96	1.85	1.50, 2.28
45–64	1.50	1.19, 1.89	1.48	0.79, 2.77	1.51	1.21, 1.89
≥ 65 ¹						
Patient classification						
New case	1.70	0.54, 5.35	1.53	0.77, 3.03	1.62	0.91, 2.86
Previously treated case ¹						
Type of city of residence						
Primary	1.35	1.12, 1.62	0.70	0.45, 1.10	1.23	1.03, 1.46
Secondary ¹						
Treatment regimen						
Category III	0	0, –	0.64	0.33, 1.26	0.87	0.48, 1.59
Category II	1.25	0.39, 3.98	2.35	0.89, 6.17	1.31	0.71, 2.42
Category I ¹						

¹ Referent.

suggests that the TB control program in Hunan is comparatively better than that of Eastern Ghana. Indeed, the odds ratio for treatment success in Hunan was almost 10 times higher compared with Eastern Ghana. This observation could be attributed to a number of factors. These include political commitment to public health in general and TB control in particular, human resources for health, treatment regimen, and HIV. Whilst per capita government expenditure on health is estimated to be USD 204 in China, that for Ghana is estimated to be USD 10 [20]. The funding gap for TB control in China in 2005 was estimated to be 23% of total funds needed whilst the gap for Ghana was estimated to be 70% of total funds needed [3, 21]. In addition to the higher government expenditure on public health in China there is also an internet-based communicable disease reporting system for tracing patients with TB thereby ensuring proper diagnosis and treatment [22]. In terms of human resources for health, which greatly affects the performance of health systems and consequently affects the achievement of disease-specific (including TB) targets, the Chinese health system appears to be better than the Ghanaian health system. It

is estimated that in China there are 14 physicians per 10,000 population whilst in Ghana there are 2 physicians per 10,000 population. With regards to laboratory staff, the densities for China and Ghana are 2 and less than 1 per 10,000 population, respectively. For pharmaceutical personnel, the densities for China and Ghana are 3 and less than 1 per 10,000 population, respectively [20, 23]. These differences obviously place a heavier burden on the Ghanaian health workforce thereby negatively affecting the performance of the TB control program. Although the treatment regimen in both study areas followed WHO recommendations, the inclusion of streptomycin in the regimen for Eastern Ghana, particularly for treatment category I and III patients, may have contributed to the lower success rates. The category I and III patients, who together formed over 90% of TB cases in each study area, were mainly new patients, and may have had great challenges enduring the painful injections of streptomycin, which was given daily for 2 months. The high toxicity of thioacetazone may also have affected treatment success in Eastern Ghana [1]. Additionally, the high 2005 HIV prevalence in Eastern Ghana (4.7%) may have contribut-

ed to the lower treatment success rates. HIV infection has been associated with TB treatment outcomes, among others [24]. Other factors that need to be studied are human genetic factors in the two populations. This is because host genetic factors such as human leukocyte antigens (HLA) and non-HLA genes have been associated with TB susceptibility and may throw more light on determinants of treatment outcomes in the two populations [25].

Conclusion

The study showed that TB treatment success rates are significantly higher in Hunan, suggesting that TB control in the province is relatively better than in Eastern Ghana.

Gender, age group, and type of city of residence are key predictors of treatment success in Hunan whilst in Eastern Ghana age group is the key predictor. Useful lessons from China, in the area of health financing, training and retaining of health personnel, an internet-based reporting system, and treatment regimen may help improve Eastern Ghana's situation.

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