Risky behaviour and psychosocial correlates in adolescents – is there a link with tuberculosis?

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Abstract
Objective: Reasons for the increase in incidence of Tuberculosis (TB) in late adolescence are poorly understood. One hypothesis is that psychological and behavioural variables associated with adolescence may increase risk of developing TB. The study aimed to determine whether psychosocial and behavioural variables affect incidence of TB disease in adolescents. **Methods:** A case-control study design was used in adolescents who were participants in a TB epidemiological study. Cases were adolescents diagnosed with TB disease. Approximately half of the controls had no TB disease but a positive TST indicative of latent TB. Half had neither TB disease nor latent TB. A self-administered questionnaire was completed by participants. The questionnaire consisted of a combination of standardised psychosocial instruments. **Results:** Of 292 participants, 62 were cases, 112 had latent TB and 118 neither TB disease nor latent TB. There were no significant differences in instrument scores between cases and controls. There was a trend for certain adverse life events to be more common in the TB-disease group. **Conclusion:** In adolescents, a trend for association between TB incidence and psychosocial and behavioural variables was not statistically significant. Given the trend, research with larger samples, and more comprehensive assessment of the relationship between stressors and TB, is warranted.

Keywords: Tuberculosis; Adolescents; Self-injurious behaviour; Psychosocial factors

Introduction

Tuberculosis (TB) is a major public health concern for children and adults globally.[1] As shown in data from Cape Town, the incidence of TB is typically high during early childhood. It decreases during later childhood and increases in later adolescence and early adulthood (Figure 1). The reasons for the increase during late adolescence are poorly understood and have not received much attention in the medical literature.

A proportion of people who have been exposed to the Mycobacterium tuberculosis (Mtb) organism develop latent TB infection and a proportion of those with latent infection
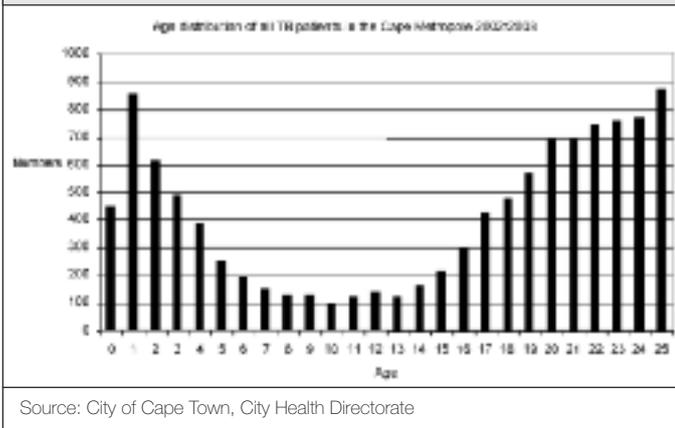
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develop active TB disease.[2] Various factors determine this disease progression. Some of these factors are related to an individual's biological risk factors and disease susceptibility, such as HIV, malnutrition, smoking and co-morbid illness.[2] Social and environmental conditions on a household and community level have also been shown to be independent risk factors for TB disease.[3]

A further hypothesis especially relevant to the adolescent period is that psychological and behavioural variables may play a role in the spread and progression of TB disease. These variables may include substance abuse, antisocial behaviour, risk-seeking behaviour, psychopathology, and reactions to significant life-events. Little research has been done to link these variables to the spread and progression of TB, although they have been shown to influence infectious diseases in general.[4-7] They may have a direct effect on disease progression by alteration of the immune response through exposure to stress.[4,5] They may influence spread of disease

Figure 1: Age distribution of all TB patients notified in the Cape Metropole July 2002 to June 2003 (N=5039). Incidence is high in early childhood, decreases in older children, and increases again in late adolescence

Source: City of Cape Town, City Health Directorate

indirectly through behaviours that place people in settings where infection is more likely.[7] Social support, on the other hand, may reduce susceptibility to infectious disease.[6]

Our objective therefore, was to determine whether, in adolescents in a population with a high burden of TB, psychosocial and behavioural variables affect the incidence of TB disease.

Methods

Setting and study population
Adolescents were recruited from the greater Worcester area in the Western Cape Province of South Africa. The area has a high burden of TB disease with a reported all-age TB disease incidence of 1400 per 100 000.[8] This study was nested within a larger epidemiological study conducted at high schools in the area to determine TB incidence in adolescents.[9,10] Participants were between 12 and 18 years of age at the time of enrolment into the epidemiological study. They were enrolled into this nested study towards the end of their 2 year follow-up period. All participants were literate. Ethics approval for this study was given by the University Of Cape Town Faculty Of Health Sciences Human Research Ethics Committee.

Study design and sampling
A case-control study design was used. Cases were drawn from a group of adolescents who had been diagnosed with TB disease (n=107) in the epidemiological study. The control group consisted of 2 sub-groups. One sub-group (n=112) consisted of participants without a diagnosis of TB disease but with a positive Tuberculin Skin Test (TST) indicative of latent TB infection. The other sub-group (n=118) was comprised of participants who had not been diagnosed with TB and had a negative TST. A TST was considered positive if the result was equal to or greater than 10 mm.

Cases and controls were drawn from the epidemiological study within which this study was nested. All cases available at the time this study was conducted were approached to participate. For the purposes of this study, any adolescent placed on TB treatment by a clinician was regarded as having active TB. Some cases were confirmed by microbiological

testing of sputum and others by x-ray examination. Active TB was excluded in participants with a positive TST by means of a directed medical history, microbiological testing on 2 sputum specimens, and a chest X-ray.

Most of the participants were seen at their school during school hours.

Inclusion into the control groups was determined by compiling a random list of participants from the main study database who did not have TB disease. This list was sorted according to TST result and school. Within this random list participants in each control group were selected. This selection was based on which schools the study team were visiting on study days for the main epidemiological study. For the control groups, if a selected participant was unavailable on that day or did not wish to take part, the next participant on the list from that school was selected for inclusion (Figure 2). The control group was not matched to the case group. More participants in the control groups were included to maximise the study power, but the numbers were ultimately limited by the amount of time available to study staff to do the study.

Study procedures and instrumentation
Participants were asked to fill out a self-administered study questionnaire. It was completed in a single session without a time-limit. Instructions were given by a study team member on how to complete the questionnaire. Each study questionnaire consisted of a set of 5 sub-questionnaires. These sub-questionnaires were standard instruments designed to gather data on psychosocial correlates. The Masten Life Events Questionnaire[11], Harvard Trauma Scale adapted to South Africa[12], K-10[13], Multidimensional Scale of Perceived Support[14], and the ASSIST hazardous substance test[15] were used. These instruments are summarized in more detail in Table I. The questionnaire was developed in English, translated into the local languages, and checked through back-translation. Each participant was required to answer all questions. The questionnaire was piloted on 20 randomly selected adolescents not participating in the main study to ensure comprehensibility and ease of use of the questionnaire. No changes to the study questionnaire were deemed necessary to be made before implementation after piloting. All questionnaires were completed within a period of 4 weeks.

Data Management & Analysis
All statistical analyses were performed with SPSS Version 16.0. A direct comparison of instrument scores was made between cases who had been diagnosed with TB disease, controls with TB infection as determined by a positive TST, and controls with neither TB disease diagnosis nor latent TB infection. Chi-square analysis or analyses of variance (ANOVA), as appropriate, were used to detect differences in mean scores between any of the 3 analysis groups per sub- scale. The significance level was set at $p < 0.01$, given the multiple simultaneous comparisons that were utilised.[16]
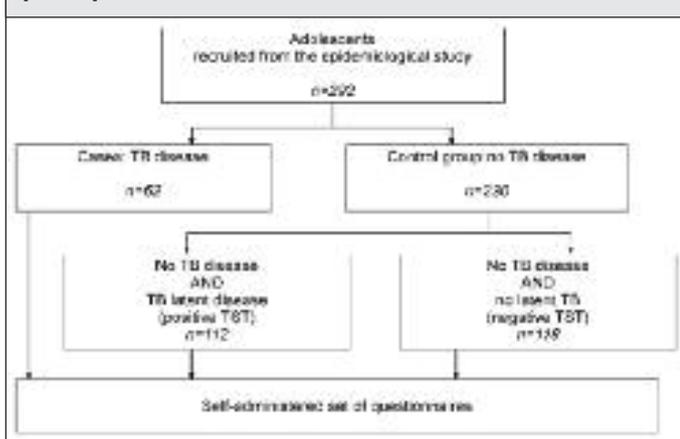
Results
Two-hundred and ninety-two (292) adolescents participated in the study. Of the possible 107 TB disease cases detected in the main epidemiological study, 62 were included in this sub-

Table I: Summary of questionnaire instruments used in the study questionnaire		
Questionnaire and Sub-Parts	*Purpose of Instrument*	*Scale*
Masten Life Events Questionnaire Discrete Onset-Ambiguous-Independent life events Discrete Onset-Negative-Nonindependent life events Discrete Onset-Negative-Nonindependent life events Chronic-Negative-Nonindependent life events Discrete-Positive-Nonindependent life events	Determines which of 51 pre-determined life-events occurred in preceding year. Each event is categorized on 3 characteristics: independence from behaviour, desirability (positive or negative experience), and duration (chronic or discrete)	Yes/No response on each of 51 items.
Harvard Trauma Scale Exposure to violence sub-scale PTSD symptoms sub-scale	Determines exposure to traumatic life events such as violence and rape, and the occurrence of post-traumatic symptoms. A version adapted to South Africa was used.	Yes/No response to 49 exposure items and 29 symptom items
K-10	Assesses presence of psychopathology by how often certain pre-defined psychiatric symptoms occurred in preceding 4 weeks	5-item Likert scale for each of 10 symptoms. Total score of 10 likely to be well, 50 likely severe mental disorder.
Multidimensional Scale of Perceived Support Family sub-scale Friends sub-scale Significant other sub-scale	Assessment of social support received. For each sub-scale 4 questions are asked that require 1 of 4 responses indicating how often support was perceived to have been given	4-item Likert scale for each of 4 questions per sub-scale. Range of total score is 0-36.
ASSIST hazardous substance abuse Test	Used to assess problematic substance abuse. Scores were calculated for each substance where use was reported in the preceding 3 months. Scores are categorized as low-, medium-and high risk. Medium risk indicates problematic use, high risk indicates probable dependence.	For each reported substance, risk was dichotomized at the threshold of hazardous risk so that medium and high risk was coded "1" and low and no risk was coded "0."

study. The remainder were either not available to complete the questionnaires or were not willing to do so. There were 230 controls: 112 with latent TB infection but no history of TB disease; and 118 with no TB disease nor latent TB infection

(Figure 2). The mean age of participants was 17 years (range 15-20). There was no significant difference in gender proportion or mean age between the 3 groups (Table II).

There were no statistically significant differences between the case and control groups on any of the psychosocial measures investigated in this study (Table III). However, there was a trend, which was not statistically significant, for lower scores in the control groups on two of the Masten life events subscales. These subscales were for discrete-onset independent events of ambiguous or indistinct desirability, and for chronic negative independent events. Life events elicited in these subscales are shown in Table IV.

Discussion
In this study, psychosocial correlates did not differ significantly in adolescents who had a recent history of TB disease from controls who did not. These correlates included the occurrence of significant life events, exposure to trauma, psychopathology, perceived social support, and correlates of risky behaviour and substance abuse. These findings offer only partial support for the hypothesis that psychosocial

Figure 2: Schematic of study design and number of participants

Table II: Baseline Characteristics by group. P-values for a statistical difference across the groups are given				
	Group 1 TB disease	*Group 2 TB infected only*	*Group 3 no disease or infection*	*p-value for difference between groups*
Mean age in years (standard deviation)	17.94 (1.51)	17.97 (1.48)	17.73 (1.48)	P=0.430

Gender
  Male
  Female
	41 (66%)
	21 (34%)
		60 (51%)
		58 (49%)
			55 (49%)
			57 (51%)
				p=0.082

Table III: Comparison of instrument scores across the case group and the 2 control groups.					
	Group 1 *TB disease*	*Group 2* *latent TB no TB disease*	*Group 3* *no latent TB no TB disease*		
	Mean Score *(Standard deviation)*	*Mean Score* *(Standard deviation)*	*Mean Score* *(Standard deviation)*	*F-value (df)*	*p-value*
Masten Life Events Discrete Onset-Negative-Independent Chronic-Negative-Independent Discrete Onset-Ambiguous-Independent Discrete Onset-Negative-Nonindependent Chronic-Negative-Nonindependent Discrete-Positive-Nonindependent	2.4 (1.56) 0.35 (0.43) 1.34 (1.19) 1.17 (0.94) 1.65 (1.54) 1.42 (1.34)	2.33 (2.15) 0.36 (0.26) 1.22 (1.17) 0.94 (0.68) 1.78 (1.63) 1.57 (1.24)	1.9 (2.2) 0.23 (0.27) 0.87 (0.96) 2.88 (5.52) 1.62 (1.56) 1.44 (1.24)	1.09 (2) 2.77 (2) 3.79 (2) 1.50 (2) 0.30 (2) 0.43 (2)	0.340 0.065 0.024 0.234 0.743 0.648
K-10	23.47 (7.70)	22.33 (8.0)	21.21 (8.13)	1.65 (2)	0.195
Social Support Family subscale Friend subscale Significant other subscale	12.31 (3.21) 10.71 (3.59) 11.77 (3.12)	12.05 (3.97) 10.98 (3.44) 11.80 (3.13)	11.55 (3.42) 11.20 (3.75) 12.40 (3.16)	1.25 (2) 0.36 (2) 1.30 (2)	0.287 0.698 0.273
Harvard Trauma Scale Exposure to violence PTSD symptoms	6.12 (5.25) 8.54 (7.20)	5.40 (5.90) 6.42 (6.47)	5.35 (5.67) 6.98 (6.64)	0.35 (2) 1.56 (2)	0.703 0.213
Risk for Substance Use	14.5 (9)	17.8 (21)	16.1 (18)	0.17 (2)	0.847
*A significance level of p<0.01 was applied					

Table IV: Items in 2 of the Masten sub-scales for life events that are independent of the participant's behaviour. A yes-no response was required for each of these events and the total sub-scale score was determined per participant by assigning a value of 1 to a YES answer and 0 to a NO answer

Discrete Onset-Ambiguous-Independent Life Events
• I have a new brother or sister who was born during this past year
• Our family moved to a new home or apartment during this past year
• Another adult has come to live with my family during this past year
• One of my parents remarried during this past year
• An unmarried family member became pregnant during this past year
• My mother began to work some time during this past year

Chronic- Negative-Independent Life Events
• One of my parents had problems at work (demotion, trouble with boss or co-workers, change in working hours)
• The family financial situation was difficult
• There were many arguments between adults living in the house
• There were many arguments between a parent and a former or separated spouse
• A member of my family developed severe emotional problems
• A brother or sister became involved with drugs or alcohol
• A parent had trouble with alcohol or drugs

factors can explain the increase in TB incidence during late adolescence.

Research on non-biological risk-factors for TB has focused mainly on social and economic variables.[3] Although our study is exploratory, it is the first to explore a potential link between TB incidence and psychosocial factors. The absence of an association between psychosocial factors and TB incidence in our study may be due to the small sample

size or limitations of the research design. It may also be that the psychosocial factors are overshadowed by other stronger, undetermined variables.

Although not statistically significant, there was a trend for lower scores on two of the Masten sub-scales for the control groups. The Masten scale determines the occurrence of significant life events, for example deaths in the family, divorce, moving house. It characterises these life events on 3 characteristics: independence from behaviour (whether an event could be the secondary result of behaviour), desirability (whether it was a positive or negative experience), and duration (chronic or discrete).[11] Life events that were independent of behaviour and of ambiguous or negative desirability tended to occur more frequently in the TB diseased group. The reason for the trend in these particular sub-scales is unclear. It may be that such events are linked to socio-economic factors rather than psychosocial factors in the context of TB epidemiology e.g. forced relocation or an increase in size of the household. These events may lead to additional strain on limited household income and resources. Further differentiation and exploration was not possible within these sub-scales, and represents an opportunity for further research.

There were limitations to this study. Sample size was limited by the number of TB disease cases available within the larger epidemiological study. The small sample size may limit the representivity of the findings to the wider population. However, the findings do highlight some important signals of note even though the study is exploratory in nature. Sampling of the control groups was not completely random due to logistic considerations. Staff time was limited and study visits needed to coincide with

scheduled visits in the epidemiological study. Matching of the control and case groups was not practical in this setting. There was no control nor data collection for possible confounders such as race or income. However, if these confounders were a factor, it is more likely that differences in psychosocial correlates between groups would be inflated rather than hidden. This study was conducted in an area with a high burden of TB disease and in a population of adolescents only. Our findings may not necessarily be generalizable to low or medium TB burden populations where biological transmission factors such as the large number of infective contacts are not as overwhelming; or in communities where adolescents leave school early or are not literate. Findings might also be different for an adult population as opposed to an adolescent population with different social and psychological characteristics. This exploratory research relied on the completion of self-administered questionnaires. An additional study tool may be the use of qualitative data-collection methods such as focus groups or participant interviews.

Conclusion

In a population of adolescents in an area with a high burden of TB, there was no statistically significant association between the incidence of TB and psychosocial variables. These variables included exposure to stressors, symptoms of distress, psychopathology, risky behaviour, and perceived social support. Given the trend towards significance, research with larger samples, and a more comprehensive assessment of the relationship between stressors and TB, is warranted.

Acknowledgements

References

1. WHO. Global tuberculosis control 2009 : Epidemiology, Strategy and Financing: World Health Organization (WHO); 2009.
2. Reider H. Epidemiologic basis of Tuberculosis Control: Paris: International Union Against Tuberculosis and Lung Disease (IUATLD); 1999.
3. Harling G, Ehrlich R, Myer,L The social epidemiology of tuberculosis in South Africa: a Multilevel analysis. Social Science & Medicine 2008;66:492-505.
4. Glaser R, Rabin B, Chesney M, Cohen S, Natelson B. Stress-induced immunomodulation: implications for infectious diseases? Jama 1999;281(24):2268-70.
5. Marsland AL, Bachen EA, Cohen S, Rabin B, Manuck SB. Stress, immune reactivity and susceptibility to infectious disease. Physiol Behav 2002;77(4-5):711-6.
6. House JS, Landis KR, Umberson D. Social relationships and health. Science 1988;241(4865):540-5.
7. Biondi M, Zannino LG. Psychological stress, neuroimmunomodulation, and susceptibility to infectious diseases in animals and man: a review. Psychother Psychosom 1997;66(1):3-26.
8. Groenewald P. Boland/Overberg Annual Health Status Report 2006: Department of Health, Boland-Overberg Region; 2007.
9. Mahomed H, Hawkridge T, Verver S, Geiter L, Hatherill M, Abrahams DA, et al. Predictive factors for latent tuberculosis infection among adolescents in a high-burden area in South Africa. Int J Tuberc Lung Dis 2011;15(3):331-6.
10. Mahomed H HA, Verver S, Abrahams D, Geiter L, Hatherill M, Ehrlich R, Hanekom WA, Hussey G. The Tuberculin Skin Test Versus QuantiFERON TB Gold® in Predicting Tuberculosis Disease in an Adolescent Cohort Study in South Africa. . Plos One 2011;in press.
11. Masten AS NJ, Andenas S. Life Events and Adjustment in Adolescents: The Significance of Event Independence, Desirability, and Chronicity. Journal of Research on Adolescence 1994;4(1):71-97.
12. Mollica RF C-YY, Bollini P, et al. The Harvard Trauma Questionnaire: Validating a Cross-Cultural Instrument for Measuring Torture, Trauma, and Posttraumatic Stress Disorder in Indochinese Refugees. Journal of Nervous & Mental Disease 1992;180(2):111-116.
13. Kessler RC AG, Colpe LJ, Hiripe E, Mroczek DK, Normans SLT, Walters EE, Zaslavsky AM. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychological Medicine 2002;32(6):959-976.
14. Zimet GD DN, Zimet SG, Farley GK The Multidimensional Scale of Perceived Social Support Journal of Personality Assessment 1988;52(1):30-41.
15. Group WAW. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): development, reliability and feasibility. Addiction 2002;97(9):1183-94.
16. Bland JM, Altman DG. Multiple significance tests: the Bonferroni method. Bmj 1995;310(6973):170.