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SEROPREVALENCE OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION AMONG TUBERCULOSIS PATIENTS IN THE NYLON DISTRICT HOSPITAL TUBERCULOSIS TREATMENT CENTRE

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ABSTRACT

Background: Tuberculosis (TB) incidence in Cameroon is high with 32% of adult TB patients, all forms, co-infected with HIV. The Nylon District Hospital in Douala runs a centre for the diagnosis and treatment of TB since 2001 and a pioneer Human Immunodeficiency Virus (HIV)/Acquired Immune deficiency Syndrome (AIDS) management programme at district level since 2000.

Objective: To determine the prevalence of HIV infection in TB patients from 2003 to 2006 and to analyse the pattern of TB/HIV co-infection rate over time.

Design: A retrospective study.

Setting: Nylon District Hospital, Douala, Cameroon.

Results: The prevalence of HIV infection in TB patients was 51.6%. This was greater for patients living out of the Nylon Health District ($P=0.001$). Smear positive pulmonary tuberculosis (SPPT) was the most frequent (65%) form of TB diagnosed but extra-pulmonary tuberculosis (EPT) and smear negative pulmonary tuberculosis (SNPT) were more frequently associated with HIV co-infection (80% and 68.6% respectively). While men and women presented equally with TB, women (61.4%) were significantly ($P<0.0001$) more TB/HIV co-infected than men (42%). The co-infection rate was highest among individuals aged 25-44 years (61.4%) and least among the 0-24 years age group (22.5%). The increase in TB/HIV co-infection rate is monotonic over time with a stronger trend among females aged 25-44 years ($P=0.037$) and above 45 years ($P=0.001$).

Conclusion: The NDH selectively attracted HIV positive patients to adhere to their HIV programme. The creation of HIV / AIDS treatment units in institutions providing TB diagnosis and treatment services will reduce the movement of TB/HIV co-infected patients across provinces and health districts as well as enhancing TB/HIV co-infection diagnosis and notification.

INTRODUCTION

HIV is most potent single risk factor for the development of tuberculosis (TB) and is known to be responsible for the resurgence of TB worldwide. Countries with a high prevalence of HIV also have a high incidence of TB hence confirming the happy marriage between TB and HIV. In Africa, the proportion of TB patients infected with HIV ranges from 0.5% in Algeria to 70% in Botswana (1). The World Health Organisation (WHO) African region has the highest TB burden consistent with the high

prevalence of the HIV pandemic in the continent especially in sub-Saharan Africa. In the year 2000, 31% of all new TB cases in adults aged 15-49 years in Africa were attributable to HIV (2).

The impact of HIV on TB is enormous. HIV causes a reduction in cellular immunity which is indispensable for the host response to TB infection. Due to this immune suppression, HIV increases the risk of direct progression of primary disease to full blown TB as well as increasing the risk of reactivating the latent tubercle bacilli (3). HIV negative persons with latent TB have a lifetime risk of about 10% of

developing active TB (4) whereas in HIV positive persons, the risk of 10% is reduced from a lifetime to a year or two risks. Therefore HIV causes a general increase in the reservoir of infectious TB cases in the general population augmenting the potential risk of contamination within a community with high HIV prevalence even among non HIV patients.

On the other hand, TB is the leading cause of morbidity and mortality in HIV/AIDS patients especially in Africa(6). TB enhances HIV replication and hence the natural progression of HIV infection(7). As such the immune response to infection by HIV patients suffering from active TB is further reduced making way for other opportunistic infections to develop hence increasing the likelihood of death.

With an HIV prevalence of 5.5% in 2004 (female to male ratio of 1.7), Cameroon is among African countries with a high HIV burden(8). The incidence and mortality of all forms of TB increased from 65 and 19/100,000 population in 1990 to 174 and 23/100,000 population in 2005 respectively (1). The proportion of TB patients aged 15-49 years among People Living With HIV/AIDS (PLWH/A) in Cameroon also increased from 26% in 2000 (2) to 32% in 2005 (1).

The centre for the treatment and diagnosis of TB at Nylon District Hospital started in April 2001 just five months before the beginning of the Medecins Sans Frontieres/Switzerland (MSF-CH) Douala Project at the same hospital, which aims to provide a comprehensive health care to PLWH/ A by treating opportunistic infections and providing psychosocial support in partnership with the public sector. In April 2003, the Douala project was expanded to PREvention et Traitement Integre du VIH (PRETIVI Project) with the addition of anti-retroviral therapy (ARV) to the already existing package of services. Some other advantages associated with being registered in the PRETIVI project were: free medical and psychosocial consultations, 100% subvention of hospitalisation fee and blood transfusion cost. Healthcare cost for destitutes, ARV drugs, drugs for the treatment of opportunistic infections and paraclinical examinations were subsidised with respect to the patient's capacity to pay. The harmonisation and collaboration between the TB and HIV programmes in terms of patient care actually began in 2004.

Elsewhere, the management of HIV patients in Cameroon was only in tertiary or university teaching hospitals. The PRETIVI project at the Nylon District Hospital was thus a pioneer programme at district level in Cameroon.

Cameroon being a high burden HIV country, studies on the estimation of the HIV prevalence are lagging behind as the most recent dates back to 2004 (8). Bearing in mind the interaction between HIV and TB, the national TB/HIV co-infection rate of 32% in 2005 (1) for all forms of TB in adults is likely to be an under estimation as opposed to the co-infection

rates observed in other high HIV burden countries in Africa. Some cities like Douala, Yaounde, Ngaoundere and Limbe are known to be hot spots in terms of TB/HIV co-infection in Cameroon with rates greater than the reported national rates (Noeske J, personal communication).

The aim of this study was to determine the prevalence of HIV infection in TB patients treated at the Nylon District Hospital from 2003 to 2006, analyse the pattern of TB/HIV co-infection rate over time and determine what proportion of TB/HIV co-infected patients were registered in both TB and HIV programmes. This will provide an orientation in integrating TB and HIV treatment centres within the same health institutions making reporting and notification more efficient.

MATERIALS AND METHODS

Setting: Created in 1992 by support from the Switzerland government, the Nylon health district is one of the six and most populated health districts of the city of Douala. It is an urban slum located in the south eastern part of the city with an estimated population of 400,000 inhabitants distributed over 700 hectares of land. The basis of its creation was to set up a system of community participation in health care which could later be implemented in other health districts nation wide.

It is in this light that the Nylon District Hospital which serves as a first line referral unit in the district was among the first in the province to host the National Tuberculosis Programme (NTP) after its reorganisation in 2001. The PRETIVI project was the first of its kind to provide comprehensive care to PLWH/ A at district level to the over six million inhabitants of three neighbouring provinces (Littoral, South West and West provinces). The integration of both TB and HIV programmes gave the hospital a good reputation and attracted a lot of patients.

Case detection is passive. Patients who present at the hospital with a dry or productive cough for at least three weeks are referred to do a sputum test (three early morning sputum smear in three days). The coughing can be accompanied by other respiratory symptoms like haemoptysis, chest pain and dyspnoea or general symptoms like weight loss, fever and night sweats. Once the clinical suspicion is made, a confirmatory diagnosis and treatment follows the national guidelines (9). Patients with at least two of the three sputum smears positive for acid fast bacilli are declared Smear Positive Pulmonary Tuberculosis (SPPT). Smear Negative Pulmonary Tuberculosis (SNPT) is diagnosed in patients presenting with persistent signs and symptoms of TB, two series of a negative sputum test at ten days interval and with/ without a suspicious chest X-ray film after receiving non specific antibiotic therapy for ten days. Diagnosis

of extra-pulmonary tuberculosis (EPT: TB in any other location apart from the lungs) is mainly clinical and based on the physician's expertise in identifying the signs and symptoms and/or specific para-clinical examinations with respect to the location of the infection. Patients who had never been diagnosed with TB and have never taken TB medications are considered new cases.

Patients are referred for voluntary counselling and testing to the psychosocial department comprising of counsellors, social workers and a psychologist. The test kits were provided by MSF-CH and cost US \$2 per test. Rapid antibody testing techniques were used in the following pairs with respect to the availability: Dermine® HIV-1/2 test (ABBOT Diagnostic Division, Hoofddorp, Netherlands) and Immunocomb II Bispot HIV-1/2 (Orgenetics Ltd, Israel) or Dermine® HIV-1/2 test (ABBOT Diagnostic Division, Hoofddorp, Netherlands) and Camstix HIV-1/2 (Camdiagnostix, Yaounde, Cameroon). A person was considered HIV positive if both tests were positive. If the first test (Dermine®) was negative, the patient was assumed negative and a second test was omitted. Undetermined results were sent to the Centre Pasteur laboratory in Yaounde for a confirmatory test and the results made known to the patients when available. The results were given to the patients from the 48th hour after post-counselling by workers in the psychosocial department. HIV positive patients are automatically proposed to join the PRETIVI Project during post-counselling. A PRETIVI file is opened for patients with a positive response and he/she referred for medical consultation.

Study population and design: It was a retrospective study in which all TB patients registered in the Nylon District Hospital centre for the diagnosis and treatment of TB from 2003 to 2006 were included. The TB register was reviewed for information regarding socio-demographic factors (age, sex and place of residence) and clinical factors (type of TB, HIV status and treatment history).

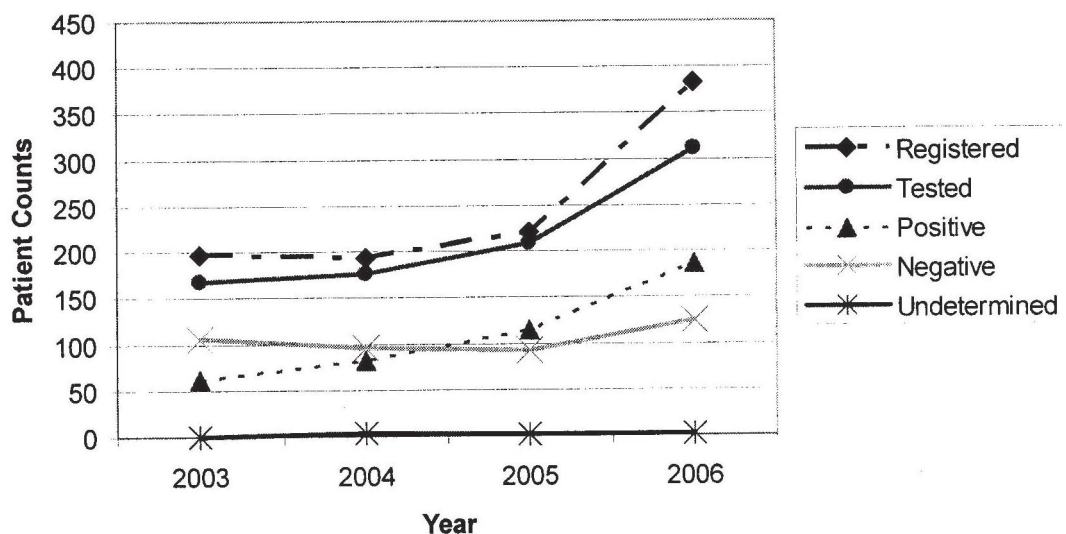
Data analysis: Data was entered and analysed using SPSS 14.0 for Windows and Microsoft Office Excel 2003. After entering of data into SPSS, cleaning up was ensured by running frequency tables and correcting for any errors and missing values using patient treatment cards. Linear regression was used to compare trends in TB/HIV co-infection rate using Excel after creating dummy variables. The value of R^2 per model was reported. The Chi-square tests (with Yates correction when relevant) was used to compare groups of categorical variables and the independent sample t-test to compare mean ages. A 95% confidence interval was calculated and values of $P < 0.05$ were considered significant.

RESULTS

There were 998 registered TB cases from 2003 to 2006. One hundred and thirty three patients were excluded from the analysis: 128 who did not take the HIV test and five whose HIV results were inconclusive. Four patients with combined SPPT and EPT were analysed as SPPT cases. The analysis of 865 patients, is presented.

Figure 1

Prevalence of HIV infection and HIV testing in Nylon District Hospital



Characteristics of the patients: Of the 865 patients, 438 (50.6%) were males. The age ranged from 2 to 75 years. The mean age at diagnosis for TB in males [35.2 ± 11.4] was significantly greater ($P < 0.0001$, 95% CI of the difference = 1.672 to 4.521) than that of the females [32.1 ± 9.9]. Individuals aged 25-44 years constituted the majority 546(63.1%) of patients followed by the 0-24 years age group 182 (21%) while the 45+ years age group was the least affected with 137 (15.8%) cases. Most of the patients 752 (86.9%) were newly diagnosed TB cases. Nylon residents represented only 412(47.6%) of the study population. The most frequent form of TB diagnosed was SPPT 562(65%) cases, followed by EPT 185 (21.4%) cases and lastly SNPT 118 (13.6%) of cases.

TB/HIV co-infection: The prevalence of HIV infection among TB patients (all ages and all forms combined)

was 51.6% (446 HIV positive cases out of 865 patients). The age range of HIV positive patients was 2 to 63 years. The mean age of HIV positive patients [35.4 ± 8.9] with TB was significantly greater ($P < 0.0001$, 95% CI of the difference = 2.231 to 5.069) than that of HIV negative patients with TB [31.7 ± 12.2]. The TB/HIV co-infection rate in adults aged 15-49 years was 52.3% (406 HIV positive tests out of 776 tested adults).

There is an association between HIV status and gender, TB type, age group and health district of residence (Table 1). The prevalence of HIV infection was significantly ($P < 0.0001$) higher among female TB patients (61.4%) and significantly higher ($P = 0.001$) among TB patients not resident in Nylon Health District (57%). The prevalence was lowest among the youths aged 0-24 years (22.5%). EPT (80%) and SNPT (68.6%) were almost always associated with HIV infection.

Table 1

Characteristics of patients by HIV status

Variable and Category		HIV Positive cases	(%)	Total number of patients per category (T)	P-value
Gender					
	Males	184	42	438	
	Females	262	61.4	427	<0.0001
Health District of Residence					
	Nylon Health District	188	45.6	412	
	Non Nylon Health District	258	57	453	0.001
Treatment history					
	New cases	390	51.9	752	
	Old cases	56	49.6	113	0.722
Age group (years)					
	0-24	41	22.5	182	
	25-44	335	61.4	546	
	45+	70	51.1	137	<0.0001
TB Type					
	SPPT	217	38.6	562	
	SNPT	81	68.6	118	
	EPT	148	80	185	<0.0001

P-values from chi square with continuity correction. No. = Number of HIV positive cases per category.

Trends in prevalence of HIV infection among TB patients: Generally there is an upward trend in the prevalence of HIV infection in TB patients over time. The prevalence of HIV infection is increasing similarly over time in both sexes, in patients newly diagnosed with TB as well as those with a history of TB and among patients resident in and out of the Nylon Health District as illustrated by the slopes and P-values in Table 2. Among the males, the slope increases similarly over time with increases in the age of patients. Meanwhile,

the slope of females aged 25-44 years [8.19% per year] is significantly greater ($P = 0.037$) than that of the 0-24 years [-1.98% per year] reference category. Likewise, the slope of females aged 45 years and above [20.45% per year] is significantly greater ($P = 0.001$) than that of the 0-24 years [-1.98% per year] reference category. The highest increase in TB/HIV co-infection rate over time is among EPT cases but the slope is not different from that of the SNPT reference category.

Table 2

Trends in TB/HIV co-infection rate by study variables

Variable and category		Slope [percent per year]	R ²	P(slope)
Gender				
	Males(Ref.)	5.48		*
	Females	9.27	97.4	0.103
Health District of Residence				
	Non Nylon Health District(Ref.)	11.73		*
	Nylon Health District	4.73	90	0.114
Treatment History				
	Old cases(Ref.)	3.79		*
	New cases	8.4	93.7	0.053
Age group/Males (years)				
	0-24 (Ref.)	1.72		*
	25-44	5.68		0.483
	45+	6.57	89.4	0.396
Age group/Females (years)				
	0-24 (Ref.)	-1.98		*
	25-44	8.19		0.037
	45+	20.45	96.1	0.001
TB Type				
	SNPT(Ref.)	-5.000		*
	SPPT	4.82		0.192
	EPT	6.64	84.9	0.132

R² = Percentage variation in TB/HIV co-infection rate that can be explained over time per model. P (Slope) = P-value for the difference of the slope with respect to the reference category obtained from linear regression. Ref. = Reference category.

Registration in both TB and HIV programmes: Of the 466 HIV positive patients with TB, 299(67%) were followed up in both TB and HIV programmes (77.9% if the 62 TB/HIV co-infected patients in 2003 are

excluded). In 2003, co-infected patients followed up in both programmes were not registered in the TB register because of lack of coordination between both programmes.

DISCUSSION

This study shows that 51.6% of the TB patients treated in the Nylon District Hospital from 2003 to 2006 were also infected with HIV. There was a monotonic increase in the TB/HIV co-infection rate from 2003 to 2006 with significantly upward trends only among females aged 25-44 years and 45 years and above age group. Two-thirds of the TB/HIV co-infected patients were followed up in both TB and PRETIVI programmes.

The rate of acceptance of HIV testing with post counselling in our study was unusually high (87.2%: 870 tests done out of 998 registered patients). Caution should be taken not to compare this with other studies not providing the necessary services and a conducive environment for voluntary testing and counselling (VTC) having HIV testing acceptance rate fluctuating around 50%. The Nylon District Hospital has a psychosocial service department with seven permanent staff (all MSF-CH: a psychologist, two social workers and four counsellors) and a number of part-time workers from associations of PLWH/A offering VCT among other services. All patients referred for HIV testing are received for a general health talk before individual counselling. All TB patients were systematically sent for HIV testing as at 2004. The Thyolo Health District in Malawi with a similar setup also has a very high HIV post-testing of 87% (10). Therefore under organised conditions a district hospital is capable of providing maximal HIV testing acceptability levels.

SPPT was the most frequent form of TB in our study population. Similar findings of a higher frequency of infectious TB cases in an era of HIV were reported by studies in Sudan (11) and Italy (12). Most patients were newly diagnosed with TB and young adults aged 25-44 years constitute a greater majority of the patients. The proportion of men and women with TB are similar but women are having TB at a younger age. This gender difference regarding the age at diagnosis of TB may be due to the social roles of women in the society.

In Douala and other parts of Cameroon, women are known to be the ones to care for their sick spouse, children and other family members. According to the 2004 demographic health survey of Cameroon, 67.2% of women in Cameroon live in a union (legally married or not) and 30% of married women are in a polygamous regime. In Cameroon, the median age at first marriage for women and men aged 25-49 years are 17.6 and 24.9 years respectively [Median age at first marriage in Douala for women aged 25-49 years and males aged 30-49 years are 20.6 and 27.5 years respectively]. The legal age for marriage is 15 years for women and 18 years for men in Cameroon (8). In this capacity, women are exposed to the risk of

contracting infectious diseases like TB at a younger age from spouses and other family members. Strikingly, the TB/HIV co-infection rate in our study population was very high and continues to increase. The TB/HIV co-infection rate of all forms of TB and all ages in our study of 51.6% was greater than the national co-infection rate of 32% in 2005 yet lower than rates of over 60% observed in countries with higher HIV burden like South Africa, Swaziland, Zimbabwe, Lesotho and Botswana (2). HIV infection modifies the association between gender, age group and TB. The higher TB/HIV co-infection rate in females and adults aged 25-44 years reflect the high prevalence of HIV in these populations in Cameroon. The seroprevalence of HIV in males and females in the city of Douala are 3.6% and 5.5% respectively while in Cameroon as a whole it is reported to be 8.8% among females aged 25-44 years and 6.8% among men of the same age group but lower in the other age groups (8). Same findings but with lower rates were reported by Chum *et al* (13) in Tanzania, Kiwuwa *et al* in Uganda (14) and Kuaban *et al* (15) in the Chest medicine tertiary hospital in Yaounde-Cameroon. This was not the case in Jamaica where Akpaka *et al* (16) found that TB/HIV co-infection was more prevalent in males than females. This difference is probably due to the fact that in Africa, transmission of HIV infection is mainly heterosexual and women are more vulnerable whereas in Europe and the Americas, intravenous drug use and homosexual routes of transmission are the most common.

TB/HIV co-infection was higher in patients with EPT and SNPT consistent with other studies in Africa (13, 17) affirming the strong relationship between HIV infection and the development of EPT or SNPT. Nylon residents represent only 47.6% of the registered TB patients and the TB/HIV co-infection rate was significantly greater among the non Nylon residents. Of the 453 non Nylon residents, 431 (95.2%) lived in the other five health districts of the city of Douala (26.5% in Deido Health District, 22.5% in Cite de Palmiers Health District, 21.2% in Logbaba Health District, 20.8% in New-Bell Health District and 4.2% in Bonassama Health District) and 22 (4.8%) from other provinces. Bonassama Health District is the furthest of the five health districts from Nylon Health District. Therefore the very high TB/HIV co-infection rate in the Nylon District Hospital TB treatment centre is due to a selection bias from the pool of mostly HIV positive patients coming from all over the city and from neighbouring provinces. They were attracted to the centre because of the need to benefit from an integrated TB and HIV care at a negligible cost. Nonetheless, the TB/HIV co-infection rate for Nylon residents (45.6%) and non Nylon residents (57%) are greater than the national rates over the same period.

The upward trend in TB/HIV co-infection rate in both males and females over a short period of time (four years 2003 to 2006) is an indication that the HIV pandemic in the general population of Cameroon is far from being contained. Noeske and colleagues did a systematic review of reported HIV seroprevalence rates in the general adult population and in adults aged above 14 years with SPPT in Cameroon and found that the TB/HIV co-infection rate increased from 2.9% in 1989 to 29% in 2000 (18). Using their annual average increase co-infection rate of 2.3%, we would expect a TB/HIV co-infection rate of about 39.7% among patients with SPPT after 16 years (1989 to 2005 (5) which is similar to our finding of 38.6% as opposed to the 2005 national rate of 11% in the same group of patients (1) hence supporting our hypothesis of a possible under notification in TB/HIV co-infection rate. Djouffo (19) while studying the TB/HIV co-infection rate of the first trimester in the twenty six TB diagnosis and treatment centres in the Littoral province in Cameroon in 2007, found a TB/HIV co-infection rate of 44.2% (423 positive out of 957 tested TB patients) all forms and all ages, similar to our finding. Up to 774(44.7%) out of the 1731 registered patients did not do their HIV test or did the test but was not registered in the TB register. He also reported that 14 out of the 26 TB treatment centres had an HIV testing rate of less than 50%. Though HIV testing was free in 11 of the TB treatment centres, it cost US \$2 to US \$6 in ten TB treatment centers (19). The non proposal of HIV testing, low notification of HIV test results and high cost of HIV testing are possible factors likely to explain the low reported rate of TB/HIV co-infection in the Littoral province in particular and Cameroon at large.

The upward trend seen only in females aged 25-44 years and 45 years and above age groups predicts a likelihood of female dominance in TB infection in the short term. Surprisingly, despite a national HIV prevalence of 8.3% in female youths aged 15-24 years in 2004, the TB/HIV co-infection rate among females of this age group is decreasing probably indicating a decrease in the HIV prevalence in this age group.

Strengths and limitations: The NDH is well known through its contribution to the creation of 65 HIV/AIDS treatment units nationwide by the government. In this study, we have used just a portion of the considerable data found in the hospital to elucidate the important role district hospitals can play in the diagnosis and follow up of TB patients infected with HIV/AIDS if they are provided with the necessary human and material resources.

This study is the first of its kind since the opening of the NDH tuberculosis treatment centre in 2001. No such detailed evaluation has ever been done. Nonetheless we can identify the following limitations:

- (i) Evaluating TB trends in the Nylon District Hospital treatment centre alone is not representative enough to recommend the creation of an HIV treatment unit in every TB treatment centre around the country despite the severe impact of HIV on TB elucidated by our study. More evaluations of the same type need to be done in other TB treatment centres. More so, the study period is short to clearly elucidate different time trend series.
- (ii) Over the years there is likely to be an increase in the ability of physicians to clinically suspect and diagnose TB especially SNPT and EPT and of laboratory technicians to perform sputum smear tests. The national tuberculosis programme diagnostic criteria remained the same for all of the three forms of TB during the study period therefore any overestimation in diagnosis will be non differential. Though doing the same analysis only among SPPT patients would be more convincing, the contribution of SNPT and EPT in the TB/HIV co-infection burden in the Nylon Health District can not be ignored reason why we included these patients in our study population.
- (iii) Of the 128 TB patients who did not do an HIV test, 79(61.7%) were males. This may introduce a non response bias in the acceptability of HIV testing and gender. Individuals aged 25-44 years constituted the majority of this population (43.8%) similar to those who accepted to do the HIV test.

In conclusion, tuberculosis is a public health problem in the NHD and will remain so for quite sometime so far as the necessary measures are not taken to improve on the prevention of the HIV pandemic which is fueling TB incidence. The burden in the number of TB cases at the Nylon District Hospital is not only due to the increasing number of TB/HIV co-infected patients from other districts but also from within the Nylon Health District. One out of every two TB patients treated in the hospital from 2003 to 2006 also had HIV. The working population aged 25-44 years is the most affected but a clear upward trend over time is seen only among females of this age group hence a risk of female dominance in TB in the short term.

We therefore recommend that, the same evaluation should be carried out in other TB treatment centres around the country to provide a basis for the creation of HIV/AIDS treatment units in hospitals acting as TB diagnosis and treatment centres. Meanwhile, all TB treatment centres should be provided with the necessary resources to do HIV testing and reinforce notification of results.

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