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Tuberculosis and HIV co-infection in healthcare workers in England and Wales, 1999–2005

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SUMMARY

This study used linked national tuberculosis (TB) and HIV surveillance data to investigate recent trends and factors associated with HIV co-infection (TB-HIV) in healthcare workers (HCWs) with TB in England and Wales. Methods applied were the χ^2 trend test and logistic regression. Overall 14% (231/1627) of HCWs with TB were co-infected with HIV, increasing from 8% in 1999 to 14% in 2005 ($P<0{\cdot}001$). Most (78%) HCWs were non-UK born and 74% of these developed TB $\geqslant$2 years post-entry. Being born in Sub-Saharan Africa was an independent predictor for TB-HIV, especially for female HCWs (odds ratio 66·5, 95% confidence interval 16·3–271·1), who also had a lower median CD4 count than other co-infected women (106/mm^3, interquartile range 40–200, $P<0{\cdot}01$). Voluntary HIV testing of new HCWs should be encouraged as an opportunity for early diagnosis. Post-entry, a high index of clinical suspicion for TB in those most at risk remains important.

Key words: Epidemiology, health policy, HIV/AIDS, screening programme, tuberculosis (TB).

INTRODUCTION

During the late 1990s the National Health Service (NHS) started to actively recruit healthcare workers (HCWs) from overseas [1]. Many of the countries of recruitment have established human immunodeficiency virus (HIV) epidemics and/or a high incidence of tuberculosis (TB) [2]. Persons who are HIV positive have an increased risk of developing TB from initial or reactivating infection with *Mycobacterium tuberculosis* [3, 4].

In 2007 new guidance was issued by the Department of Health on health clearance for TB, hepatitis B, hepatitis C and HIV for new HCWs [5]. This new guidance was developed partly in response to the recruitment of staff from overseas subsequently found to be infected with HIV [6]. National estimates of the numbers of HIV-infected HCWs, however, have not been available.

The primary aim of the 2007 guidance [5] was to reduce the risk of transmission of TB and bloodborne viruses, including HIV, from HCW to patient. HCWs who are HIV positive are not prevented from working in the NHS but are restricted from working in clinical settings that may pose a risk to patients or to their own health.

The guidance recommends that all new or returning HCWs have checks for TB disease and immunity and are offered a HIV test prior to starting work. Additional health clearance confirming HIV-negative serostatus is required for new HCWs (or those moving to a new post) who will perform exposure-prone

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procedures (EPPs). Post-screening, the HCW is under a professional code of conduct (duty of care) to seek advice about testing if they have been exposed to a serious communicable disease [5].

We present the epidemiology of, and recent trends in, TB and HIV co-infection (TB-HIV) and investigate factors associated with HIV co-infection in HCWs with TB in England and Wales for the years 1999–2005. In the light of the study's findings the potential impact of, and implications for the new guidelines are discussed.

METHODS

Enhanced Tuberculosis Surveillance (ETS) collects demographic, clinical and microbiological information, including occupation, on reported TB cases.

The case definition for ETS includes culture-confirmed disease due to *M. tuberculosis* complex and, in the absence of culture confirmation, any patient with a clinical diagnosis and a decision to treat with a full course of anti-TB therapy.

The national reporting of HIV cases by virologists and clinicians, has been described elsewhere [7]. Only patients aged $\geqslant 15$ years are included as HIV diagnosed in children is reported separately.

Ethical approval

The Health Protection Agency has permission to collect and analyse surveillance data.

Data linkage

Cases from the national ETS database for the years 1999–2005 in England and Wales were matched with records in the national HIV database for the years 1979–2006 by in-house software which used a scoring system based on the degree of similarity across personal identifiers [initial(s), soundex [8] of surname, sex and date of birth, ethnic group and country of birth]. After record linkage, patient identifiable information was removed to protect confidentiality.

Using the information recorded by ETS on occupation, cases of TB and TB-HIV co-infection in HCWs were identified.

Analyses

Descriptive analysis of HCWs with TB, including their HIV co-infection status was undertaken. Proportions were calculated for all cases including those with missing clinical or demographic information.

The χ^2 test for trend was used to investigate the change over time in the proportion of HIV co-infected cases in HCWs with TB, as well as in non-HCWs with TB.

To investigate factors associated with HIV co-infection in HCWs with TB, univariable and multivariable logistic regression analyses were used. The main multivariable model looked at potential risk factors for HIV co-infection (age, sex, world region of birth, time since entry into UK), including those variables significant on univariable analysis ($P<0{\cdot}05$). Other factors (healthcare occupation group, region of diagnosis, site of disease, sputum microscopy result, culture confirmation, drug resistance) that were significantly associated with TB-HIV co-infection were then assessed by correcting for demographic factors used in the main model. Interactions between explanatory variables were explored using likelihood ratio tests and considered significant at the $P<0{\cdot}01$ level.

HIV diagnosis

To asses whether late diagnoses of HIV were more or less common in HCWs compared to non-HCWs we compared these two groups in terms of (1) the proportion of co-infected cases with a diagnosis of TB within 90 days of the HIV diagnosis and (2) the median of the reported CD4 counts within 90 days of the HIV diagnosis. Significance was tested using the χ^2 and Wilcoxon rank-sum (Mann–Whitney) tests, respectively.

All analyses were conducted using Stata version 10 (StataCorp, USA).

RESULTS

HCWs with TB

Information on occupation was available for 23 783 (53%) of the 44 738 TB cases (age $\geqslant 15$ years) reported from 1999 to 2005 in England and Wales. Cases with information on occupation were slightly younger [median age 36 years, interquartile range (IQR) 27–55 years] than cases without information on occupation (39 years, IQR 28-60 years) but were otherwise similar in terms of gender, UK status and world region of birth.

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Of the cases with occupation reported 1627 (7%) were HCWs: 386 (24%) were nurses, 301 (19%) doctors, 179 (11%) community care workers, 13 (1%) dentists and 748 were listed as other (10%) or unknown (36%).

The median age of HCWs with TB was 33 years (IQR 29-42 years). The majority of cases were female (64%) and non-UK-born (1271 cases, 78%) with the latter mainly born in Sub-Saharan Africa (48%) and Asia (43%). Those with a European country of birth were mainly UK-born (88%). Of non-UK-born HCWs with a known time since entry 74% were diagnosed with TB more than 2 years after arrival in the UK. About one third (35%) of HCWs with TB were reported from London. Pulmonary disease was diagnosed in 54% of cases of which 45% were sputum positive.

TB/HIV co-infection

Fourteen percent (231/1627) of HCWs with TB were co-infected with HIV compared to 5·3% (2303/43 111) of all other reported cases of TB ($P<0·01$).

Between 1999 and 2005, rates of co-infection in HCWs with TB almost doubled, increasing from 8·1% (11/135) to 14·2% (59/415) with a peak prevalence of 18·9% in 2004 ($P<0·01$) (Table 1). The co-infection rate also increased in non-HCWs from 2·5% (132/5188) to 6·2% (447/7178) with a peak of 6·9% (430/6275) in 2003 ($P<0·01$).

Demographic and clinical characteristics of HCWs with TB are shown by HIV co-infection status in Table 2. The 'unknown' professional category of HCW accounted for the highest proportion of cases (37%) followed by nurses (32%) and community care workers (20%) with doctors/dentists accounting for the smallest proportion (2%). Nearly all co-infected HCWs were non-UK-born (223, 97%) of whom 96% were born in Sub-Saharan Africa.

Predictors of HIV co-infection in HCWs with TB

In the multivariable analysis age, sex, and country of birth were significantly associated with TB-HIV co-infection in HCWs. There was, however, strong evidence that the effect of region of birth was modified by sex (LR test, $P<0·01$) and results of the multivariable analysis stratified by sex are presented in Table 3.

Male and female HCWs with TB who had been born in Sub-Saharan Africa were significantly more likely to be co-infected with HIV than those born in Europe. These odds were significantly larger in women than in men. No female HCWs from Asia were co-infected with HIV and there were no co-infected HCWs (males or females) from 'other' world region of birth. Female HCWs aged $\leqslant$45 years were more likely to be HIV co-infected than older women. A similar but non-significant association with age was found in men. No significant association was observed for co-infection status by region diagnosed, site of disease and culture positivity when adjusting for age and region of birth, stratified by sex.

Table 1. *Healthcare workers with tuberculosis by HIV co-infection status and year, England and Wales, 1999–2005*

Year	HIV +ve	Not HIV +ve	Total	%HIV (95% CI)
1999	11	124	135	8·1 (4·1–14·6)
2000	6	98	104	5·8 (2·1–12·6)
2001	13	132	145	9·0 (4·8–15·3)
2002	33	178	211	15·6 (10·8–22·0)
2003	48	246	294	16·3 (12·0–21·6)
2004	61	262	323	18·9 (14·4–24·3)
2005	59	356	415	14·2 (10·8–18·3)
Total	231	1396	1627	14·2 (12·4–16·2)

CI, Confidence interval.

HIV diagnosis

Of TB-HIV co-infected HCWs 67% (155/231) had a diagnosis of TB within 90 days of the HIV diagnosis compared to 55% (1269/2301) of all other co-infected cases ($P<0·01$). HCWs had a lower, but non-significant, median reported CD4 count compared to non-HCWs [106/mm^3 (IQR 40-210), 139 observations *vs.* 126/mm^3 (IQR 40-271), 1212 observations, respectively; $P=0·17$]. Although this difference was not significant in all cases, female HCWs had a significantly lower median CD4 count compared to all other co-infected women [105/mm^3 (IQR 40-200), 117 observations *vs.* 140/mm^3 (IQR 46-280), 572 observations, respectively; $P<0·01$).

DISCUSSION

In England and Wales, the level of HIV co-infection in HCWs with TB increased significantly from 1999 to 2005. An increase was also observed in non-HCWs, but the overall level of co-infection was more than 2½ times higher in HCWs than in other TB cases. HCWs

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Table 2. *Case characteristics of healthcare workers with tuberculosis by HIV co-infection status, England & Wales, 1999–2005*

Category/level	HIV +ve ($N=231$)	HIV −ve ($N=1396$)	Total ($N=1627$) (%)	Univariable OR* (95% CI)
Age group				
15–44 years	209	1085	1294 (80)	1·0 (ref.)
⩾45 years	22	306	328 (20)	**0·42 (0·27–0·67)**
Unknown	0	5	5 (0)	n.a.
Sex				
Male	38	537	575 (35)	1·0 (ref.)
Female	193	854	1047 (64)	**3·19 (2·22–4·60)**
Unknown	0	5	5 (0)	n.a.
Region diagnosed				
London	96	470	566 (35)	**1·4 (1·05–1·86)**
Outside London	135	926	1061 (65)	1·0
World region of birth				
Europe	6	306	312 (19)	1·0 (ref.)
Asia	5	543	548 (34)	0·47 (0·14–1·56)
Sub-Saharan Africa	213	392	605 (37)	**27·71 (12·14–63·23)**
Other†	0	41	41 (3)	n.a.
Unknown	7	114	121 (7)	**3·13 (1·03–9·52)**
Time since UK entry (non-UK- born only)				
<2 years	52	223	275 (22)	1·0 (ref.)
2–4 years	99	344	443 (35)	1·23 (0·85–1·80)
⩾5 years	52	315	367 (29)	0·71 (0·46–1·08)
Time unknown	20	166	186 (15)	**0·52 (0·3–0·90)**
Healthcare worker category				
Care worker	46	133	179 (11)	1·43 (0·94–2·18)
Doctor/dentist	4	310	314 (19)	**0·06 (0·02–0·15)**
Nurse	75	311	386 (24)	1·0 (ref.)
Other	20	136	156 (10)	0·61 (0·36–1·04)
Unknown	86	506	592 (36)	**0·70 (0·50–0·99)**
Site of disease				
Pulmonary	163	720	883 (54)	1·0 (ref.)
Extrapulmonary	67	669	736 (45)	**0·44 (0·32–0·60)**
Unknown	1	7	8 (1)	0·63 (0·8–5·16)
Sputum microscopy				
Sputum +ve	76	319	395 (45)	1·10 (0·78–1·54)
Not sputum +ve	87	401	488 (55)	1·0 (ref.)
Culture				
Positive	173	903	1076 (66)	**1·63 (1·18–2·24)**
Not positive	58	493	551 (34)	1·0 (ref.)
INH‡				
Resistant	11	57	68 (7)	1·00 (0·51–1·96)
Sensitive	151	785	936 (93)	1·0 (ref.)
MDR‡				
Resistant	4	12	16 (2)	1·75 (0·56–5·50)
Sensitive	158	830	988 (98)	1·0 (ref.)

OR, Odds ratio; CI, confidence interval; INH, isoniazid; MDR, multi-drug resistant; n.a., not applicable (no HIV cases). HIV −ve implies not matched to HIV database, % by column, bold confidence intervals are significant at $P<0·05$ level

* HIV positive compared to HIV −ve cases.

† Other = South and Central America, the Caribbean, North America, Oceania, North Africa and Eastern Mediterranean.

‡ Cases with known susceptibility results. Pulmonary includes cases with or without extrapulmonary disease.

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Table 3. *Multivariable analyses for HIV co-infection in healthcare workers with tuberculosis, stratified by sex, England & Wales, 1999–2005*

Co-infected *vs.* not co-infected (category/level)	Males (574 observations, 38 cases)			Females (1043 observations, 193 cases)		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age group (years)						
15–44	Ref.		0·072	Ref.		0·02
⩾45	0·32	0·09–1·11		0·52	**0·3–0·91**	
World region of birth						
Asia	0·34	0·09–1·30	<0·001	0	n.a.	<0·001
Europe	Ref.			Ref.		
Sub-Saharan Africa	5·22	**1·75–15·57**		66·47	**16·3–271·12**	
Other	0	n.a.		0	n.a.	
Unknown	0·37	0·04–3·39		11·52	**2·26–58·69**	

OR, Odds ratio; CI, confidence interval; n.a., not applicable (no HIV cases); bold confidence intervals are significant at $P<0.05$ level.

born in Sub-Saharan Africa, especially women, had the greatest risk of TB-HIV co-infection. HIV was commonly detected late in co-infected HCWs and often coincided with signs and symptoms of disease.

This is the first study in England and Wales that has been able to provide national estimates of TB-HIV co-infection in HCWs. The use of data linkage is likely to provide an underestimate of the number of TB cases co-infected with HIV because the methodology is reliant on the accuracy and completeness of records from two data sources. This, however, should not affect the observed trends and comparison with other TB cases as any under-ascertainment by data linkage is likely to be similar across years and between groups of TB patients.

Only 53% of cases had information on occupation reported, which may have introduced bias. Baseline demographic data of cases with missing information was, however, similar. Results concerning the specific HCW occupations should be interpreted with caution since a large proportion of these cases were listed as unknown or other.

The level of co-infection was higher in HCWs compared to other TB cases, which might partly be as a result of ascertainment bias between the two groups. For example, HCWs may have been more likely to be tested for HIV if their duties involved EPPs, although the proportion of HCWs that actually perform these duties is small.

The higher risk of co-infection associated with HCWs from Sub-Saharan Africa is a reflection of the much higher incidence of TB and HIV in this region compared to Europe or South Asia [4]. Female HCWs from Sub-Saharan Africa were shown to have a higher risk of co-infection than males, a finding consistent with the higher risk of HIV infection for females in this region [4]. Nurses and community care workers are predominately female, and form the bulk of the personnel recruited to the NHS from overseas [9].

The recent increase in HIV co-infection in HCWs with TB is likely to be due to increased recruitment of workers from overseas countries with established HIV epidemics [9]. For example between 1999 and 2003 the number of nurses from Zimbabwe registered with the UK Nursing and Midwifery Council increased from 52 to 485 [10]. Further evidence comes from the observation in the study data of an increase over time in the proportion of HCWs with TB that were non-UK-born, including Sub-Saharan Africans (results not shown).

The results indicate that the trend in HIV co-infection in HCWs may have peaked before the new guidance was issued. A similar but less pronounced trend in HIV co-infection was observed in TB cases that were not HCWs, a large proportion of which also occur in Sub-Saharan Africans [11]. This observation is further supported by the observed trend in new HIV diagnoses in Black Africans [12]. The decrease seen in 2005 may therefore be due to a drop in recruitment of HCWs from overseas [13] or a general change in migration patterns from Sub-Saharan Africa to the UK. Another contributing factor may also be the declining incidence of HIV in Sub-Saharan Africa [14].

An alternative explanation for the observed increase in HIV co-infection in HCWs with TB could be that an increase in testing for HIV occurred over this

period. TB guidelines at the time recommended the offer of a HIV test to persons with TB at risk for co-infection [15]. However, this recommendation was not commonly put into practice [16]. It was not until 2007 that a policy was issued to improve the offer of HIV testing in wider settings [17]. Furthermore, a recent study, estimating trends in prevalence of HIV infection (diagnosed and undiagnosed), in adults aged 15–44 years in England and Wales, showed that there was no evidence of a decline in the prevalence of undiagnosed infection between 2001 and 2008 [18].

The current guidelines, issued in 2007, are a response to reduce the risks to patients and maintain public confidence in the healthcare workforce [5]. The trends presented here show why the issue of HIV-infected HCWs became a cause for concern in the early 2000s. TB accounts for about 30% of AIDS cases in Africans resident in the UK [19]. Using our estimate, the total number of HIV-infected HCWs with manifestations of AIDS, including non-tuberculous manifestations, is likely to have been close to 700 (3×231) over the study period.

A CD4 count <200 mm^3 is considered 'advanced HIV disease' and is associated with a high risk of death within 3 months of diagnosis [20]. The general consensus is that more people should be tested for HIV to reduce the consequences of late diagnosis [21]. Moreover, HCWs are uniquely placed in a setting which can provide easy access to testing and advice. Most nursing posts in the NHS, however, do not involve EPPs and there is opposition towards mandatory testing for all new HCWs because of ethical and cost-effectiveness considerations [22]. The main aim of the current guidelines is to protect patients but more could be done to emphasize the benefits to HCWs of an early HIV diagnosis. To ensure earlier diagnosis and treatment it is essential that HIV testing is offered and recommended to all new HCWs.

Our results also suggest that most cases of TB in non-UK-born HCWs (regardless of co-infection status) are likely to occur some years after employment screening. Pre-employment screening for TB is targeted towards detecting active disease and immunity (BCG status), and is less effective at detecting latent infection, particularly in HIV-infected individuals who are immunosuppressed [23]. In addition, HCWs who are diagnosed with latent TB are considered for, but do not necessarily receive, prophylaxis.

Interferon gamma release assays (IGRAs) offer the possibility of targeting latent TB more effectively, before progression to disease, and do not cross-react with BCG [24]. IGRA tests are also more sensitive than the tuberculin test for detecting latent TB in individuals with HIV [23]. IGRA testing is becoming more common in the UK and there is a growing consensus to tackle latent TB more aggressively with this tool [25]. Indeed guidelines from the National Institute of Clinical Guidance have very recently been updated and recommend the use of IGRA tests for HCWs from high TB incidence countries, regardless of whether they have had BCG [26]. After entry into the NHS any delay in a HCW self-reporting symptoms of TB will put patients at risk [27]. Therefore post-entry, a high index of clinical suspicion for relevant symptoms will remain important for those HCWs considered most at risk for TB.

HIV co-infection in HCWs with TB in England and Wales rose substantially between 1999 and 2005 and was most strongly associated with being born in Sub-Saharan Africa. The increasing numbers are most likely due to the increased recruitment of workers from overseas countries with established HIV epidemics. The offer of a HIV test to new HCWs should be strongly recommended to reduce the number and consequences of late diagnosis. For TB there is now the opportunity to target latent infection more effectively through the use of IGRA tests, if the latest policy is put into practice. However, vigilance still needs to be maintained after entry into the NHS for those considered most at risk for disease. The results presented here, which predate the guidelines, should provide a baseline for future assessment.

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DECLARATION OF INTEREST

None.

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