

Conclusion The incidence of NTM has continued to rise since the last national survey. This represents an almost ten-fold increase since 1995. The majority of these are pulmonary isolates (in particular MAI). Possible explanations include greater awareness amongst clinicians leading to increased sampling, improvements in laboratory techniques for speciation or laboratory reporting practices. However, such a large increase most likely reflects a genuine rise in NTM infection in the population. Given this change in culture confirmation, it is imperative that a comprehensive clinical database is set up to provide national monitoring of clinically significant infections, and establish the true burden of disease present in EW and NI.

P189 SHOULD SCREENING FOR CHRONIC VIRAL HEPATITIS IN PATIENTS WITH TUBERCULOSIS BE INTRODUCED TO NICE GUIDELINES?

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Background Screening for viral hepatitis is not routinely recommended in patients diagnosed with tuberculosis (TB). However there are significant similarities in the global distribution of TB and hepatitis B (HBV) and C (HCV). It remains unclear whether co-infection with HBV or HCV is a risk factor for hepatotoxicity in patients receiving anti-tuberculous therapy and significant morbidity and mortality is associated with a late diagnosis.

Objectives To determine the prevalence of HBV and HCV infection among new cases of active TB across treatment centres in East London and to assess the adverse drug reactions to anti-tuberculous treatment experienced by this population.

Methods We conducted a retrospective study including all patients diagnosed with active TB during 2013 at two TB clinics in London. Data on demographic characteristics, HBV surface antigen (HBsAg), HCV antibody, human immunodeficiency virus (HIV) and adverse drug reactions were retrospectively analysed.

Results In total, 472 cases of active TB were notified during 2013. The mean age was 37.7 (+/- 15.3) years (range: 5–92). Males accounted for 62.3% of our cohort. 84.7% of patients were born outside of the UK with the majority of patients being born in either Bangladesh (16.5%), India (27.8%) or Pakistan (15.9%). Overall, 304 patients were screened for HBV, 302 for HCV, and 447 for HIV. Of those screened, HBsAg was detected in 3.3%, HCV antibody in 2.0% and HIV in 3.4%. All patients infected with HBV or HCV were foreign born. Hepatotoxicity was defined as an ALT greater than 5 times the upper limit of normal or requiring a change in treatment. There was no significant difference in rates of hepatotoxicity in either in HepBsAg status ($p = 0.371$), HCV status ($p = 0.597$) or HIV status ($p = 0.413$) but numbers of HBV and HCV infection were small.

Conclusions The prevalence of HBV and HCV was significantly higher in our cohort of TB patients than the background UK prevalence, which is 0.4% for HCV, 0.3% for HBV and 0.15% for HIV. Routine screening for HBV and HCV on an opt-out basis would be justified in our setting given the high proportion of foreign-born patients. Further research into the magnitude of HBV/HCV co-infection with active or latent TB, any increased risk in drug-induced hepatotoxicity and the cost-effectiveness of routine screening is needed.

P190 DRUG INDUCED LIVER INJURY IN THE TREATMENT OF TUBERCULOSIS IN A BUSY UK CENTRE

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Introduction We describe the incidence and management of drug induced liver injury (DILI) in active TB at the largest UK centre, using a nurse-led local protocol derived from 1998 BTS guidelines.

Methods All active TB cases were identified from April 2010 to May 2014. Patients were identified with DILI by following criteria: Type 1 DILI (ALT >3x upper limit normal (ULN-55iu/l), Type 2 DILI (ALP >2x ULN(150 iu/l) and Bilirubin >21 iu/l) or Type 3 DILI (Bilirubin >40 iu/l). Patient demographics, TB treatment (ATT), timing, management and outcomes of DILI were described. Baseline characteristics and ATT doses were matched with controls.

Results 105 individuals with DILI were identified out of 1529 patients with active TB (6.9%). 81% were on standard first line therapy (Rifampicin (R), Isoniazid (H), Pyrazinamide (Z) and Ethambutol (E)). 7.8% were on Moxifloxacin (M) instead of E and 1.9% were on RHME. Type 1 DILI was most frequent (81%) with median peak ALT 296 iu/l (IQR 227–505). Median time from treatment start to onset of DILI was 12.5 days (7–30). Symptoms at presentation included nausea/vomiting (54%), abdominal pain (18%) and jaundice (12.4%). 45.7% patients had all medication stopped, 7.6% continued ethambutol with amikacin (A), 26.7% continued all medication, 6.7% stopped Z only, 3.8% substituted Z for a quinolone. Median time from stopping to reintroduction was 10 days (6–17). Of 66 reintroduction patients, regimens included H >R >E(45%), H>R>E>M (31%) and R>E>M (15%). Median time from reintroduction to full treatment restart was 14 days (12–18). 81% of patients were uneventfully reintroduced, 5% suffered a 2nd DILI. 32% patients required hospital admission and 4(3.8%) died.

DILI cases were matched to 200 controls. Cases more likely ($P < 0.05$) to; be HIV positive, have quinolones in initial regimen and lower body weight. Quinolone use gave an adjusted hazard ratio 5.41 (2.96, 9.91).

Conclusion DILI remains the most important toxicity of ATT and usually occurs during the first month. The BTS guideline provides a useful template for the diagnosis and management of DILI which may be largely nurse led and ambulatory. Most patients are successfully reintroduced without pyrazinamide. HIV status, body weight and quinolone use are risk factors.

P191 WITH A LOW INCIDENCE OF DRUG-INDUCED HEPATITIS, SHOULD WE BE OFFERING LATENT TB TREATMENT TO MORE PATIENTS OVER THE AGE OF 35?

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Introduction NICE guidelines recommend patients >35 yrs at risk of tuberculosis (TB) on screening, but without active disease, should not be offered latent TB infection (LTBI) treatment unless a healthcare worker, or HIV positive. This is based on perceived

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Abstract P190 Table 1

	Controls (n = 200)	Cases (n = 105)	P-value†
	n (%)	n (%)	
Characteristics of cases (DILI) and controls			
Sex			0.49
Age (years)			0.34
Ethnic origin			0.46
HIV +ve	4/185 (2.2%)	7/95 (7.4%)	0.03
Quinolone use	26 (13.0%)	48 (45.7%)	<0.001
	median (IQR)	median (IQR), n	
Baseline ALT (IU/L)	19 (14–29), n = 185	24 (17–35), n = 105	0.02
Baseline ALP (IU/L)	86 (71–102), n = 187	96 (75–121), n = 105	0.02
Baseline BILI (µM/L)	8 (5–10), n = 185	8 (6–13), n = 105	0.03
Weight (kg)	61.2 (54.5–69.6), n = 178	55.0 (49.0–65.0), n = 101	0.001
Rifampicin dose per kg (if given)	9.7 (8.6–10.7), n = 178	10.0 (9.0–11.2), n = 100	0.08
Isoniazid dose per kg (if given)	4.9 (4.3–5.5), n = 178	5.5 (4.6–6.1), n = 101	<0.001
Pyrazinamide dose per kg (if given)	25.0 (22.0–27.6), n = 166	26.1 (23.1–29.9), n = 98	0.06
Moxifloxacin dose per kg (if given)	6.2 (5.7–7.0), n = 21	7.2 (6.2–8.1), n = 46	0.04
Odds ratios for exposures among DILI cases compared with controls			
	Cases, controls	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)† †
Log baseline ALT (IU/L)	105, 185	1.44 (1.02, 2.03)	1.35 (0.93, 1.96)
Log baseline ALP (IU/L)	105, 185	2.12 (1.20, 3.76)	1.87 (0.99, 1.02)
Log baseline BILI (µM/L)	105, 185	1.80 (1.12, 2.87)	1.79 (1.09, 2.96)
Weight (kg)	101, 175	0.97 (0.95, 0.99)	0.96 (0.94, 0.98)
Rifampicin dose per kg	100, 175	1.14 (0.97, 1.33)	1.18 (1.00, 1.39)
Isoniazid dose per kg	101, 175	1.57 (1.22, 2.03)	1.77 (1.34, 2.34)
Pyrazinamide dose per kg	98, 163	1.04 (0.98, 1.10)	1.05 (1.00, 1.11)
Moxifloxacin dose per kg	46, 21	1.56 (1.03, 2.37)	1.85 (1.13, 3.04)
Quinolone use (yes/no)	105, 185	5.15 (2.93, 9.06)	5.41 (2.96, 9.91)
HIV	95, 183	3.56 (1.02, 12.5)	3.81 (1.03, 14.0)

† P-values from Chi-squared test (proportions) or Kruskal-Wallis test (medians)
 †† Adjusted for age, sex and baseline ALT, ALP and BILI

risks of drug-induced hepatitis, and reduced diagnostic sensitivity of LTBI in >35's. 3 months Rifampicin/Isoniazid (3RH) is commonly used however in a review of LTBI treatment, only one Hong-Kong based study found 1766/100,000 (n = 170) had symptomatic hepatitis or alanine aminotransferase (ALT) >250 IU (Grade 3 hepatitis).¹

Prompted by improved sensitivity of LTBI case finding with interferon gamma testing, and local case of active TB in a contact >35 yrs, we studied whether those >35 yrs with LTBI, treated with 3RH experienced greater hepatotoxicity than

Method We retrospectively analysed electronic patient records detailing LTBI patient treatments from June 2008–2013 from two hospitals, collecting baseline clinical data and ALT level >2 weeks into treatment.

Results Of 270 eligible patients, 151 had complete results and were included. 98/151 (65%) were 35 yrs (range 35–75), of whom 32 (60%) were male.

Only 3 patients (2 males) developed ALT >250 IU/L (rate of 1,987/100,000), all patients were symptomatic and required

treatment cessation. Ages were 31, 32 and 52 yrs and the single female patient was pregnant starting treatment. None required admission and all liver function returned to normal following cessation.

Discussion This study, although small, provides a similar rate of hepatitis (defined >250 IU/L or symptoms) to the only previous study using the 3RH regimen and shows no age specific differences in ALT results. In light of this, we raise the question; with increasing rates of TB in the UK, a large proportion of which is attributable to latent infection, should we be offering LTBI treatment to more patients >35 yrs? This study suggests the need, and provides important information for, planning a larger study to help answer this question.

REFERENCE

1 Ormerod *et al.* BTS recommendations for assessing risk and for managing Mycobacterium tuberculosis infection and disease in patients due to start anti-TNF-α Thorax 2005;60:800–805

P192 ASIDE FROM AGE, DO OTHER FACTORS INCREASE THE RISK OF HEPATOTOXICITY IN PATIENTS TREATED FOR LATENT TB INFECTION?

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Background Reactivation of latent tuberculosis infection (LTBI) occurs in a number of at-risk groups including: tuberculosis (TB)

Abstract P191 Table 1 Absolute ALT rise and number of patients whose peak ALT rose x2 upper limit of normal (>70 IU/L)

	<35 (n = 98)	>35 (n = 53)	Total (n = 151)
Rise in ALT IU/L (+/-95% CI)	18.1 (10.4)	12.4 (17.8)	16.1 (9.0)
Number of patients with ALT >70 IU/L (%)	10 (10.2)	3 (5.7)	13 (8.6)
Number of patients with ALT >250 IU/L (%)	2 (2.0)	1 (1.8%)	3 (2.0%)