HIV / HCV
&
TUBERCULOSE

PREFEITURA DA CIDADE DO
RIO DE JANEIRO

SECRETARIA MUNICIPAL DE SAÚDE

Secretaria Municipal de Saúde do Rio de Janeiro
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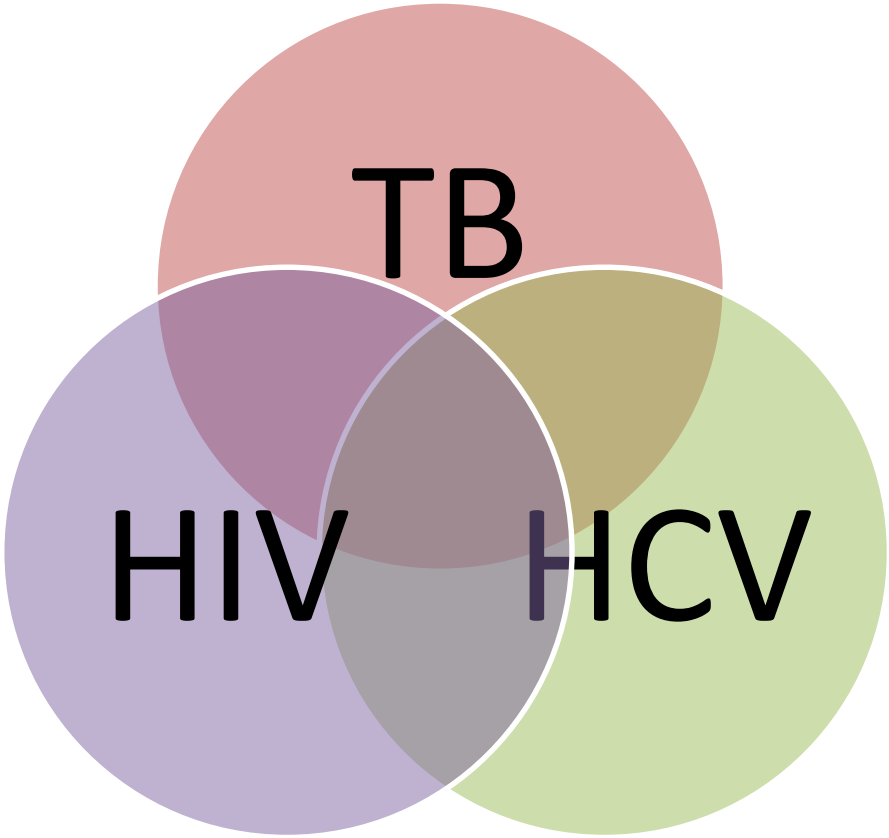
Superintendência de Atenção Primária
Coordenação de Doenças Crônicas Transmissíveis
Gerência Técnica das Doenças Pulmonares Prevalentes

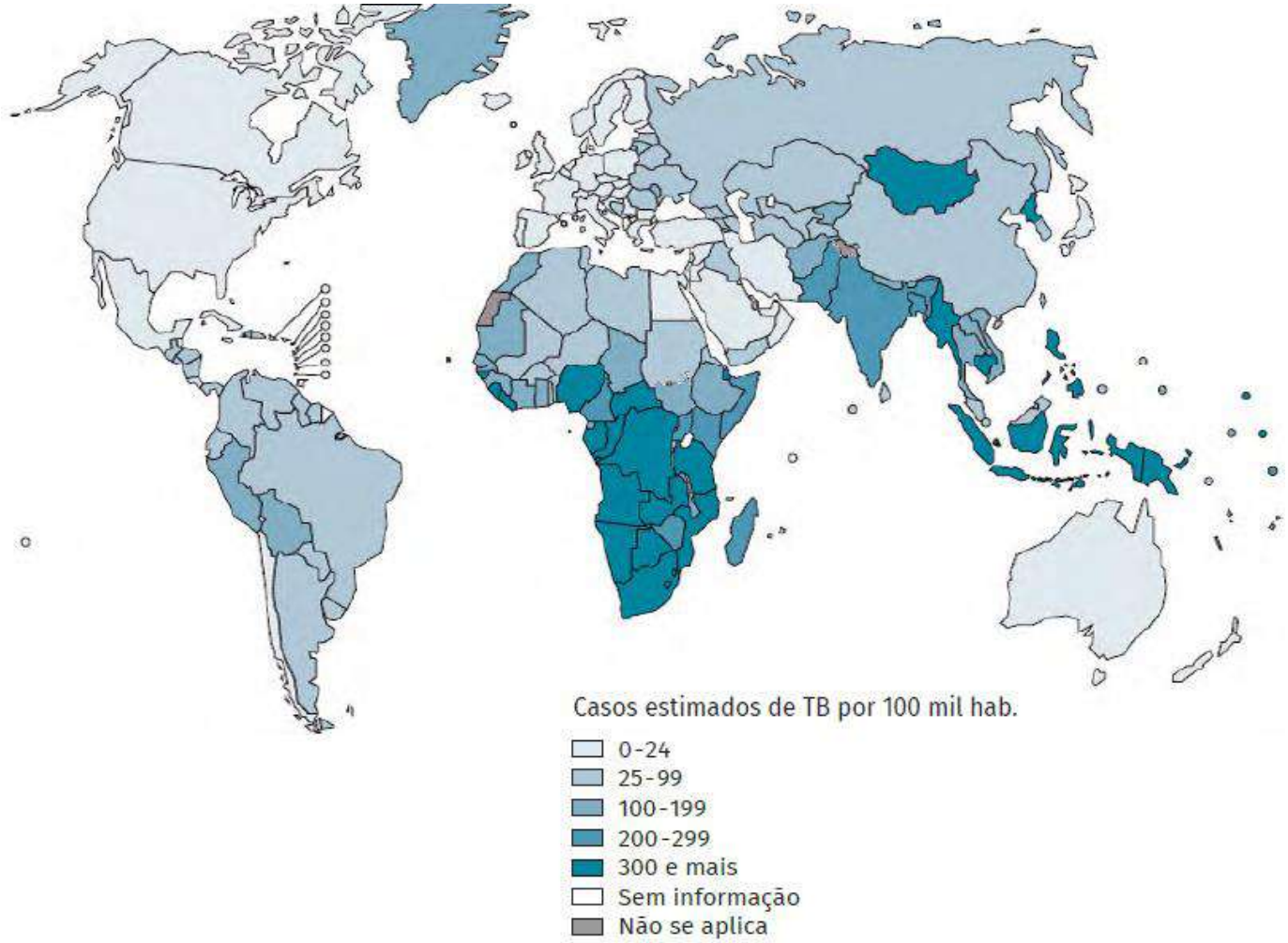
v. 28/05/2017


TB
HIV
HCV

Frequência da coinfecção

- Alta prevalência
- Compartilham formas de transmissão
- Mais frequentes em populações semelhantes
- Potencializam a transmissão

Estimativa do coeficiente de incidência de tuberculose no mundo em 2015



Fonte: Organização Mundial da Saúde (2016).

Carga da Tuberculose

Segundo a OMS em 2016

10,4 milhões de pessoas
adoeceram com tuberculose em 2015.

1,1 milhão de pessoas
vivendo com HIV desenvolveram tuberculose.

1,8 milhão de homens, mulheres e crianças
morreram de tuberculose em 2015, incluindo 400 mil pessoas vivendo com HIV.

Em 2014, 480 mil pessoas
desenvolveram tuberculose multidrogarresistente, com 190 mil mortes associadas.

Carga da Tuberculose no Brasil

Segundo o MS em 2016

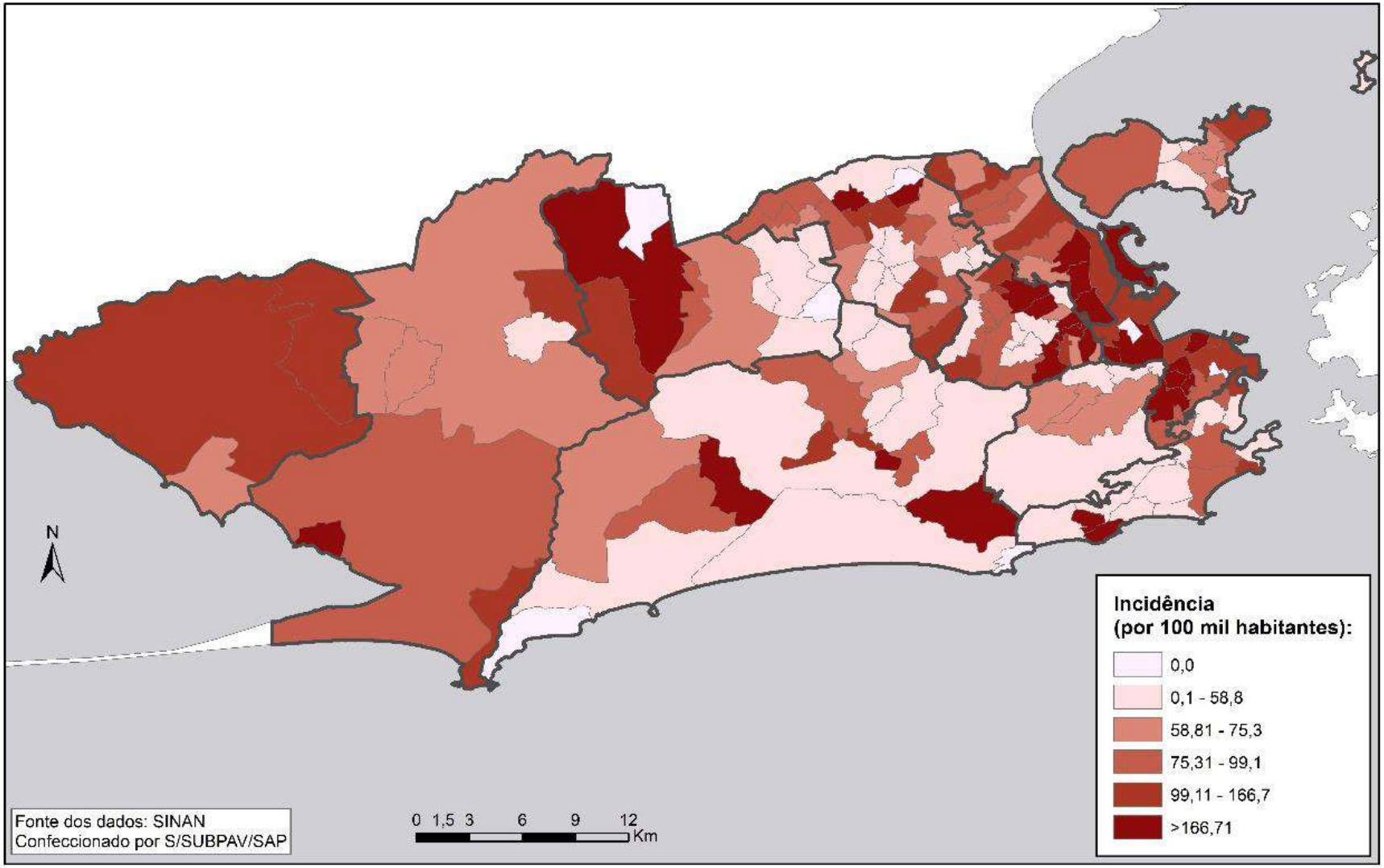
69 mil pessoas
adoeceram com tuberculose.

6,8 mil pessoas
vivendo com HIV
desenvolveram tuberculose.

4,5 mil homens, mulheres e crianças
morreram de tuberculose.

1.077 pessoas
desenvolveram tuberculose
multidrogarresistente.

Incidência de tuberculose por bairro de residência - 2016
Residentes do Município do Rio de Janeiro



Impacto da coinfecção

- Mortalidade aumentada
- Maior frequência de efeitos adversos
- Redução da adesão ao tratamento
- Agravamento da imunossupressão

Antituberculosis Drug–induced Hepatotoxicity

The Role of Hepatitis C Virus and the Human Immunodeficiency Virus

JAIME R. UNGO, DENIS JONES, DAVID ASHKIN, ELENA S. HOLLENDER, DAVID BERNSTEIN, ANTHONY P. ALBANESE, and ARTHUR E. PITCHENIK

The University of Miami School of Medicine, Division of Pulmonary Diseases and Critical Care Medicine, Division of Gastroenterology, Department of Internal Medicine, Miami; A. G. Holley State Hospital, Lantana; Addiction Treatment Program Mount Sinai Medical Center, Miami Beach; V. A. Medical Center, Miami; The Florida Bureau of Tuberculosis Control and Prevention, Tallahasse, Florida; The Division of Gastroenterology, Winthrop University Hospital, Mineola, New York

RELATIVE RISKS FOR DEVELOPING DRUG-INDUCED HEPATITIS

	Patients		DIH				
Viral Serologies	(*n*)	(%)	(*n*)	(%)	Relative Risk	95% Confidence Limits*	p Value†
HCV (−) HIV (−)	55	43	3	5	1	—	—
HCV (+) HIV (−)	29	23	7	24	5	1.305–23.311	0.028
HIV (+) HCV (−)	33	26	7	21	4	1.114–19.541	0.036
HIV (+) HCV (+)	11	9	5	45	14.44	2.740–76.135	0.002

* Significant when confidence interval does not include 1.

† Fisher's exact test. Significant when compared with patients without risk factors.

- Um study indicated that 45% of HIV/TB/HCV patients developed DIH, compared with 21% of HIV/TB patients and 24% of TB/HCV patients.
- **Antituberculosis Drug–induced Hepatotoxicity**
- **The Role of Hepatitis C Virus and the Human Immunodeficiency Virus**
- **JAIME R. UNGO, DENIS JONES, DAVID ASHKIN, ELENA S. HOLLENDER, DAVID BERNSTEIN,**
- **ANTHONY P. ALBANESE, and ARTHUR E. PITCHENIKAM J RESPIR CRIT CARE MED 1998;157:1871–1876.**

Prevalence of hepatitis C virus and human immunodeficiency virus in a group of patients newly diagnosed with active tuberculosis in Porto Alegre, Southern Brazil

Cintia Costi[1], Tarciana Grandi[1], Maria Laura Halon[1], Márcia Susana Nunes Silva[2], Cláudia Maria Dornelles da Silva[1], Tatiana Schäffer Gregianini[3], Lia Gonçalves Possuelo[4], Carla Adriane Jarczewski[5], Christian Niel[6]/+, Maria Lucia Rosa Rossetti[1,2]

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BACKGROUND Porto Alegre is the Brazilian state capital with second highest incidence of tuberculosis (TB) and the highest proportion of people infected with human immunodeficiency virus (HIV) among patients with TB. Hepatitis C virus (HCV) infection increases the risk of anti-TB drug-induced hepatotoxicity, which may result in discontinuation of the therapy.

OBJECTIVES The aim of this study was (i) to estimate prevalence of HCV and HIV in a group of patients newly diagnosed with active TB in a public reference hospital in Porto Alegre and (ii) to compare demographic, behavioural, and clinical characteristics of patients in relation to their HCV infection status.

FINDINGS Anti-HCV antibody, HCV RNA, and anti-HIV antibodies were detected in 27 [20%; 95% confidence interval (CI), 13-26%], 17 (12%; 95% CI, 7-18%), and 34 (25%; 95% CI, 17-32%) patients, respectively. HCV isolates belonged to genotypes 1 ($n = 12$) and 3 ($n = 4$). Some characteristics were significantly more frequent in patients infected with HCV. Among them, non-white individuals, alcoholics, users of illicit drugs, imprisoned individuals, and those with history of previous TB episode were more commonly infected with HCV ($p < 0.05$).

MAIN CONCLUSIONS HCV screening, including detection of anti-HCV antibody and HCV RNA, will be important to improving the management of co-infected patients, given their increased risk of developing TB treatment-related hepatotoxicity.

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Prevalence, drug-induced hepatotoxicity, and mortality among patients multi-infected with HIV, tuberculosis, and hepatitis virus

Pingzheng Mo [a], Qi Zhu [b], Caroline Teter [c], Rongrong Yang [a], Liping Deng [a], Yajun Yan [a], Jun Chen [b], Jie Zeng [b], Xi-en Gui [a,*]

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SUMMARY

Objectives: To investigate the prevalence, incidence of abnormal liver function tests (LFTs), and mortality during anti-TB treatment in patients multi-infected with HIV, tuberculosis (TB), and hepatitis virus (hepatitis B virus (HBV) and hepatitis C virus (HCV)).

Methods: Three hundred and sixty-one HIV-positive TB patients were enrolled and divided into an HIV/TB group, HIV/TB/HBV group, and HIV/TB/HCV group; 1013 HIV-negative TB patients were selected randomly as controls.

Results: One hundred and seventeen (32.4%) HIV-positive TB patients were infected with HBV and/or HCV, compared with 90 (8.9%) HIV-negative TB patients ($p = 0.000$). HIV-positive TB patients had a higher incidence of anti-TB drug-induced hepatotoxicity than HIV-negative TB patients (4.2% vs. 1.0%, odds ratio (OR) 4.348, 95% confidence interval (CI) 1.935–9.769, $p = 0.000$). The incidence of abnormal LFTs in the HIV/TB/HBV group and HIV/TB/HCV group were significantly higher than in the HIV/TB group (40.7% vs. 11.1%, OR 5.525, 95% CI 2.325–13.131, $p = 0.000$; 20.0% vs. 11.1%, OR 2.009, 95% CI 1.057–3.820, $p = 0.031$). A total of 68.4% of patients with HBV-DNA $>1.0 \times 10^5$ copies/ml and 42.9% of patients with HCV-RNA $>1.0 \times 10^5$ copies/ml had abnormal LFTs. Twenty-three (19.7%) patients multi-infected with HIV, TB, and hepatitis virus died during anti-TB treatment.

Conclusions: HIV, HBV, and HCV are risk factors for the development of abnormal LFTs and mortality during anti-TB treatment. TB patients co-infected with HIV and hepatitis virus need close follow-up.

World Journal of Gastroenterology

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Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v21.i29.8920

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ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Prospective Study

Viral hepatitis prevalence in patients with active and latent tuberculosis

Hesam Ahmadi Nooredinvand, David W Connell, Mahmoud Asgheddi, Mohammed Abdullah, Marie O'Donoghue, Louise Campbell, Melissa I Wickremasinghe, Ajit Lalvani, Onn Min Kon, Shahid A Khan

METHODS: Four hundred and twenty nine patients with newly diagnosed TB - either active disease or latent infection - who were due to commence anti-TB therapy between September 2008 and May 2011 were included. These patients were prospectively tested for serological markers of HBV, HCV and human immunodeficiency virus (HIV) infections - hepatitis B core antigen (HBcAg), hepatitis B surface antigen (HBsAg), hepatitis B e antigen, IgG and IgM antibody to HBcAg (anti-HBc), HCV IgG antibody and HIV antibody using a combination of enzyme-linked immunosorbent assay, Western blot assay and polymerase chain reaction techniques. Patients were reviewed at least monthly during the TB treatment initiation phase. Liver function tests were measured prior to commencement of anti-TB therapy and 2-4 wk later. Liver function tests were also performed at any time the patient had significant nausea, vomiting, rash, or felt non-specifically unwell. Fisher's exact test was used to measure significance in comparisons of proportions between groups. A *P* value of less than 0.05 was considered statistically significant.

CONCLUSION: Viral hepatitis screening should be considered in TB patients. DILI risk was not increased in patients with HBV/HCV.

Original Article

Chronic hepatitis B infection and risk of antituberculosis drug-induced liver injury: Systematic review and meta-analysis

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Abstract

Background: Antituberculosis drug-induced liver injury (ATDILI) is a major safety concern for the treatment of tuberculosis (TB). The impact of chronic hepatitis B infection (CHBI) on the risk of ATDILI is still controversial. In this study, we aimed to assess systematically the influence of CHBI on the susceptibility to ATDILI.
Methods: We reviewed all English-language medical literature with the medical subject search headings *hepatitis B* and *antitubercular agents* from the major medical databases. Thereafter, a systematic review and meta-analysis was performed on those publications that qualified.
Results: A total of 938 citations were retrieved on the initial major database search, from which 15 studies were determined to be eligible for analysis. While undergoing anti-TB treatment, 575 cases with drug-induced liver injury (DILI) and 4128 controls without DILI were enrolled into this analysis. The pooled odds ratio of all studies for the CHBI to ATDILI was 2.18 (95% confidence interval, 1.41−3.37). Among the studies with a strict definition of DILI (alanine aminotransferase > 5 × upper limit of normal value) and combination anti-TB regimen, the impact of CHBI on ATDILI was significant only in the prospective studies (odds ratio, 3.41; 95% confidence interval, 1.77−6.59), but not in the case−control studies. However, in the studies with a strict definition of DILI and isoniazid only treatment, the association between CHBI and ATDILI was not statistically significant.
Conclusion: This meta-analysis suggests that CHBI may increase the risk of ATDILI in the standard combination therapy for active TB. Close follow-up and regular liver test monitoring are mandatory to treat TB in chronic hepatitis B carriers.

Keywords: drug-induced liver injury; hepatitis B; meta-analysis; tuberculosis

Medicine

OBSERVATIONAL STUDY

OPEN

Hepatitis C Virus Infection Is Associated With an Increased Risk of Active Tuberculosis Disease

A Nationwide Population-Based Study

Ping-Hsun Wu, MD, Yi-Ting Lin, MD, Kun-Pin Hsieh, PhD, Hung-Yi Chuang, PhD, and Chau-Chyun Sheu, MD

Abstract: Tuberculosis (TB) and hepatitis C virus (HCV) infection contribute to major disease mortality and morbidity worldwide. However, the causal link between HCV infection and TB risk remains unclear. We conducted a population-based cohort study to elucidate the association between HCV infection and TB disease by analyzing Taiwan National Health Insurance Database. We enrolled 5454 persons with HCV infection and 54,274 age- and sex-matched non-HCV-infected persons between January 1998 and December 2007. Time-dependent Cox proportional hazards regression analysis was used to measure the association between HCV infection and active TB disease. Incidence rate of active TB disease was higher among HCV infection than in control (134.1 vs 89.1 per 100,000 person-years; incidence rate ratio 1.51; $P = 0.014$). HCV infection was significantly associated with active TB disease in multivariate Cox regression (adjusted hazard ratio [HR] 3.20; 95% confidence interval [CI], 1.85–5.53; $P < 0.001$) and competing death risk event analysis (adjusted HR 2.11; 95% CI, 1.39–3.20; $P < 0.001$). Multivariate stratified analysis further revealed that HCV infection was a risk of active TB disease in most strata. This nationwide cohort study suggests that HCV infection is associated with a higher risk of developing active TB disease.

(*Medicine* 94(33):e1328)

Abbreviations: CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, HBV = hepatitis B virus, HCV = hepatitis C virus, HIV = human immunodeficiency virus, ICD-9 = International Classification of Diseases, 9th Revision, IRR = incidence rate ratio, LHID = Longitudinal Health Insurance Database, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, TB = tuberculosis.

INTRODUCTION

Tuberculosis (TB), an infectious disease caused by *Mycobacterium tuberculosis*, is the most prevalent infectious disease and the major leading cause of death worldwide, especially in developing countries. According to the Global Tuberculosis Report by World Health Organization, there were an estimated 8.6 million incident cases of TB and approximately 1.3 million people died of TB in 2012.[1] It is endemic in southeastern Asia, as well as Taiwan. An epidemiological study declared the incidence of active TB disease in Taiwan was 74 per 100,000 person-years.[2]

TB is considered as an immunodeficiency-related infection. Our recent work demonstrated that liver cirrhosis was associated with increased risk of active TB disease.[3] Liver cirrhosis, and subsequent complications of both hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are major health problems in Taiwan.[4] However, a comprehensive evaluation from HCV patients without cirrhosis remains unavailable. HCV infection is one of the contributing factors for developing TB infection is our hypothesis. Previous observation study showed that HCV infection and TB share the same high risks population, especially in homeless people,[5] prisoners,[6] and human immunodeficiency virus (HIV) patients.[7] Furthermore, one case-control study using the US Veterans data demonstrated that HCV infection is ass ated with TB disease.[8] However, results from this hospital-ba case-control study cannot be extended to the general populat In order to fill this knowledge gap, this nationwide cohort st analyzed healthcare data to clarify the association between H and active TB disease using large-scale data from the Tai National Health Insurance (NHI).

CONCLUSION

The present study provides epidemiological evidence that HCV infection is associated with a higher risk of active TB disease. Prolonged fever or chronic respiratory symptoms in HCV-infected patients should raise the suspicion of active TB disease. The deterioration of cellular immune response by HCV infection may explain the association between HCV infection and active TB disease, but further studies are needed to understand the underlying mechanisms.

Necessidade de criação de diretrizes

- Diagnóstico mais precoce
- Esquemas de tratamento
- Monitoramento mais próximo

Manual de Recomendações para controle da tuberculose

Quadro 14 - Conduta frente a hepatopatias

Com doença hepática prévia: - hepatite viral aguda - hepatopatia crônica: viral, autoimune e criptogência - hepatopatia alcoólica: esteatose hepática, hepatite alcoólica	Sem cirrose	TGO/TGP > 3 x LSN	2 SRE / 7RE 2 SHE / 10 HE 3 SEO / 9 EO
		TGO/TGP < 3 x LSN	Esquema Básico
	Com cirrose	3 SEO / 9 EO	
Sem doença hepática prévia (hepatotoxicidade após o início do tratamento)	TGO/TGP 5 x LSN (ou 3 x LSN com sintomas)	Reintrodução RE → H → Z	Reintrodução do Esquema Básico ou substituto
	Icterícia		
	Persistência de TGO/TGP 5 x LSN por quatro semanas ou casos graves de TB		3 SEO / 9 EO

Obs.: limite superior da normalidade – LSN.

Tratamento da HCV/HIV/Tuberculose
Associações que devem ser evitadas

SOFOSBUVIR	SIMEPREVIR	DACLATASVIR
rifampicina	rifampicina	rifampicina
rifabutina	rifabutina	rifabutina
rifapentina	rifapentina	rifapentina
tipranavir/ritonavir		atazanavir/ritonavir
	efavirenz	efavirenz
	nevirapina	nevirapina
	etravirina	etravirina
	tenofovir	tenofovir
	IPs	

Protocolo Clínico e Diretrizes Terapêuticas para Hepatite C e Coinfecções/ Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de DST, Aids e Hepatites Virais. – Brasília : Ministério da Saúde, 2015.

Planilha de acompanhamento dos casos de tuberculose no município do Rio de Janeiro

	Inicio do tratamento	Mês de tratamento completado					Consulta final
		1º	2º	3º	4º	5º	
Microbiologia							
Escarro: TRM	X						
Escarro:BAAR (retratamento)	X						
Escarro: BAAR		X	X	X	X	X	X
Escarro: cultura e TSA[1]	X						
Imagem							
Rx de tórax ou outro exame que se faça necessário[2]	X		X				X
Avaliação clínica							
Peso[3]	X	X	X	X	X	X	X
Sintomas	X	X	X	X	X	X	X
Adesão[4]: avaliar perfil e checar adesão	X	X	X	X	X	X	X
Laboratório							
Teste rápido HIV	X						
Teste rápido hepatites virais	X						
Hemograma	X						
Glicemia	X						
Transaminases	X						

Fonte:Linha de cuidado da tuberculose

Gerência Técnica de Doenças Pulmonares Prevalentes

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