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Letter to the Editor

HIV-Tuberculosis co-infection: A growing public health issue and the need for guidelines development

Tuberculosis (TB) is the main cause of death amongst human immunodeficiency virus (HIV)-infected individuals worldwide, while 14 million people are estimated to be dually infected [1]. In Europe only, the estimated number of deaths from TB in HIV infected patients exceeded 5100 in 2016. What is more, in EU/EEA countries coinfection was most prevalent amongst males and those between ages 25–44 years [2]. A recent study has shown that migration has played a major role in the increasing numbers of co-infected individuals in Europe, as migrants coming from a low-income background were shown to be more susceptible to co-infection compared to national population. The purpose of this article is to highlight the need for a concrete framework of action towards this growing public health issue.

In this frame, we need to acknowledge its endogenous limitations. To begin with, TB diagnosis is challenging, as no evidence-based tool is able to offer a definite diagnosis in all circumstances and at the same time, presentation of the disease is widely variable in HIV-infected individuals [3]. WHO suggests screening the newly diagnosed HIV patients for TB before the start of antiretroviral treatment as well as during regular follow ups. Moreover, questions should not only be directed at the presence of chronic cough but rather current cough, fever, night sweats or weight loss [4]. A recent European study indicated that up to 22% of HIV-TB patients suffer from EPTB. Solovic et al. have attributed misdiagnosis to the variability of screening methods and symptoms, the referral of patients to non-specialized doctors and the exclusion of EPTB from differential diagnosis as an uncommon disease [4]. Different diagnostic methods include: cultures, the tuberculin skin test, interferon gamma release assays (IGRA), sputum smear microscopy, imaging, and nucleic acid amplification testing (NAAT). The former, while very accurate and the current golden standard, has major disadvantages as it is not cost-effective and requires 4 weeks to produce results. The Bactec 320, an automated machine used for cultures as well as drug susceptibility testing (DST), has received excellent reviews and limits the time needed for results. The tuberculin skin test on the other hand is limited in that it cannot provide information as to whether the patient has latent or active TB infection. IGRA tests, such as the QuantiFERON® TB Gold test and the T-SPOT® TB test that have been FDA approved, offer advantages in that results can be obtained within 24 h and do not produce false positive results in case of a previous BCG vaccination. IGRA however, can only diagnose latent TB [5].

Furthermore, sputum smear microscopy either fluorescent light, or more recently, LED microscopy, are the most commonly used diagnostic methods in countries with high rates of TB infection and provide fast results but lack sensitivity. Lastly, radiographic findings largely depend on the patient's level of immunodeficiency as extra pulmonary involvement is more common in advanced stages [9]. NAAT is reliable and more specific but not sensitive enough. A promising tool, the GeneXpert-MTB/RIF for the rapid diagnosis of TB as well as rifampicin resistance amongst HIV-infected individuals with clinical suspicion of TB offers extremely good sensitivity and specificity and has been endorsed by the WHO, but more scientific evidence and evaluation studies are needed [6].

TB screening plays a pivotal role in HIV care and infection control. In a study done by Corbett E. L. and MacPherson P., the optimal screening strategies for different priority patient groups as well as appropriate algorithms that will maximize prevention are discussed [7]. TB – HIV co-infection management requires novel vaccination strategies. BCG is currently the only available vaccine for all age groups. However, there are not enough studies to manifest the actual protective value of the vaccine in HIV-infected individuals and thus currently its administration in immunocompromised individuals is contraindicated by the WHO. Factors such as strain variation, dose, patient age, nutritional status, genetic factors, environmental infections, and geographic location would definitely play a role in the development of an ideally appropriate vaccine for such patients [8].

Management of the co-infection is difficult, as it necessitates multiple medications which in turn mean: subsequent drug interactions and a high tablet number that definitely has an impact on patient adherence. The WHO guidelines for management of HIV-infected TB patients recommend a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) in addition to one non-nucleoside reverse transcriptase inhibitor (NNRTI) for first line therapy [9]. However, due to significant drug-to-drug interactions there is high variability in the treatment protocols followed by different countries. Concerning the existing TB drugs, it is well established that boosted PIs and nelfinavir administration requires switching from rifampicin to rifamputin whereas efavirenz is not compatible with either of them. Moreover, the interaction between ARTs and new TB drugs such as bedaquilin needs to be further studied [10].

Nation-based guidelines have been developed for Africa whereas the guidelines for the EU and the USA have been designed on a continental model [11,12]. Several factors have played a role in this distribution ranging from the epidemiology of the coinfection and application of screening programs to the availability of pharmaceutical agents.

In the future, the country and the continental model of management guidelines may be evaluated. However, outcomes may differ due to other variants such as the access of population to health services, the variability of viral subtypes (HIV) and bacterial strains (TB) or the trends in pharmaceutical market. The increasing incidence of HIV - TB coinfection in the EU and the USA ought to alert health professionals and institutions [12].

Although prevention and informative campaigns have been established, more effective methods of communication should be explored. Addressing the HIV-TB issue in the “healthcare - policymakers/stakeholders - society” context requires engagement of the civil society and

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political will to tackle the problem (enforcing screening by law, making screening or prophylactic treatment accessible to patients without insurance etc). A more precise account of resistant TB ought to be formulated in the next years - The appearance of physicians specialized in HIV - TB management and its implications from academia to clinical practise.

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