Editorial
Epidemiology
Diabetes Metab J 2013;37:249-251
http://dx.doi.org/10.4093/dmj.2013.37.4.249
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

Diabetes Mellitus and Tuberculosis

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India experiences a rapidly increasing prevalence of both diabetes mellitus [1] and tuberculosis [2]. Jali et al. [3] showed that nearly half of the patients infected with tuberculosis had either diabetes or were at prediabetic status, which corresponded to previous report in India [4]. Furthermore, among patients with tuberculosis, 16% to 20% were of newly diagnosed cases of diabetes [3,5], which is a strikingly high prevalence of diabetes considering that of general population in India [1].

The association between diabetes and tuberculosis has been well documented in other epidemiologic studies. In Korea, a 3-year longitudinal study showed that the risk ratio of tuberculosis in diabetic patients compared to non-diabetic controls was 3.47 (95% confidential interval, 2.98 to 4.03) [6]. A recent meta-analysis showed that diabetes increased the risk of tuberculosis infection regardless of background tuberculosis incidence or geographic region: people with diabetes have an approximately 3-fold risk of developing active tuberculosis [7].

Although the direct mechanism has not yet been clearly identified, reduced immunity in diabetic patients might play a major role in increase the risk of tuberculosis in them: people with diabetes had reduced chemotaxis and oxidative killing potential than those of nondiabetic control [8]. Studies in animal models showed that diabetic mice infected with Mycobacterium tuberculosis have higher bacterial load [9,10] and reduced T cell response against M. tuberculosis antigen [10] compared to euglycemic mice. Hyperglycemia is associated with a lower production of interferon-γ (IFN-γ) and interleukin-12 [10], and the level of IFN-γ is negatively correlated with levels of glycated hemoglobin (HbA1c) [11].

The levels of hyperglycemia are correlated with the severity of tuberculosis infection quantitatively: the level of IFN-γ is negatively correlated with the levels of HbA1c [11], and poorly controlled diabetes augments the severity of infections [12]. Diabetic patients had more symptoms associated with tuberculosis infection than normal control on presentation [13]. Furthermore, diabetes is associated with poor prognosis of tuberculosis infection: early microscopic negative conversion rate in diabetic patients was lower than that in normal control [13]. Treatment failure rate of 6-month's medication in diabetic patients was also significantly higher than that in normal control [13]. Considering the effect of diabetes on tuberculosis, optimal glycemic control might improve the prognosis of tuberculosis, although there has been few randomized clinical trial to elucidate the effect of glycemic control for tuberculosis.

Whereas a high incidence of tuberculosis has been reported in diabetic patients, it is not clear whether tuberculosis increases the risk of diabetes. In general, infections, including tuberculosis, often worsen hyperglycemia [12]. Tuberculosis infection can stimulate free fatty acid synthesis and secretion [14], which mediates insulin resistance by elevating proinflammatory cytokines, specifically tumor necrosis factor-α [15]. Some studies suggest that tuberculosis can cause diabetes, even in those not previously known to have diabetes [16,17]. However, it is unclear whether diabetes mellitus persists in these patients or whether diabetes is more prevalent with tuberculosis than with other infectious diseases.

Considering the association of tuberculosis and diabetes, screening for tuberculosis in those with diabetes should be considered, especially in the region with high tuberculosis incidence. A systematic review of literature demonstrated that screening of diabetic patients yielded active tuberculosis with rates ranging from 1.7% to 36% [18]. Jali et al. [3] showed that

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among 4,118 patients with diabetes, 111 subjects (2.7%) had tuberculosis, which was a somewhat low rate considering the high prevalence of tuberculosis in India. They used respiratory symptoms as a screening tool for tuberculosis [3]. Although basic diagnostic approaches such as tuberculosis symptom screening are always applicable, the diagnostic yield is very limited [19]. Considering that India has high prevalence of tuberculosis and that the risk of tuberculosis is higher in patients with diabetes compared to general population, more extensive diagnostic methods such as X-ray screening for the entire group might be applied for patients with diabetes in India.

The burden of tuberculosis in Korea is also high along with India and China: in 2011, 44,684 new cases were reported in South Korea [2], and the proportion of multidrug resistant tuberculosis is increasing in Asian countries [2]. Furthermore, the prevalence of diabetes has reached 10% in the Korean population [20]. Considering the high burden of tuberculosis and diabetes in Korea, screening strategy for tuberculosis in the patients with diabetes reflecting the prevalence of tuberculosis in Korea and studies to elucidate the optimal management of hyperglycemia during active tuberculosis are warranted.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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