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THE ASSOCIATION BETWEEN SERUM AND TEAR PLASMINOGEN ACTIVATOR INHIBITOR-1 AND TISSUE PLASMINOGEN ACTIVATOR IN PATIENTS WITH DIABETIC RETINOPATHY

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ABSTRACT:

Background :

Diabetic retinopathy (DR) is a serious complication of longstanding type 2 diabetes mellitus (T2DM), which is the forerunner in causing blindness and visual disability in the world. The aim of this study was to investigate the relationship between the activity of tissue plasminogen activator (tPA) and plasminogen activator inhibitor-1 (PAI-1) in tears and serum of patients with DR and those without DR.

Method:

T2DM patients with DR (n=26) were enrolled in this study and compared to those without DR (n= 29). Blood and tear samples were obtained from both groups. The level of PAI-1 and tPA were measured in both the serum and tears. Anthropometric measurements, HbA1c, renal and lipid profile were also obtained.

Results:

Patients with DR had significantly longer disease duration and higher systolic blood pressure compared to those without DR. Serum PAI-1 level was significantly higher in patients with DR compared to those without DR, 32.72 (IQR 32.52) vs 21.37 (IQR 14.93) ng/mL, respectively ($p<0.05$). However, tear PAI-1 were comparable in both groups. Serum and tear tPA levels in both groups were also comparable ($p>0.05$). Among patients with DR, there were no significant correlations between tear and serum of both biomarkers. Patients without DR showed a moderate positive correlation between serum and tear tPA levels with a coefficient of 0.363, albeit no statistical significance. Patients with DR demonstrated a significant positive correlation between levels of tears PAI-1 and BMI ($r=0.555$, $p=0.026$). In the group without

DR, there was a statistically significant positive correlation between serum level of PAI-1 with urine albumin creatinine ratio (UACR) (r=0.501, p=0.013).

Conclusion:

This present study demonstrated significantly greater serum PAI-1 levels in patients with DR compared to those without DR. No significant correlations between tears and serum PAI-1 and tPA were observed. The tear PAI-1 levels positively correlated with BMI among patients with DR, whilst serum PAI-1 level positively correlated with UACR among patients without DR. Thus, the roles of tear biomarkers remain relevant for further investigations.

Keywords: Type 2 diabetes mellitus, diabetic retinopathy, Tissue plasminogen activator (tPA), Plasminogen activator inhibitor-1 (PAI-1),

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is an emerging global epidemic and a major concern for public health. It is associated with many debilitating macro- and micro-vascular complications. According to the International Diabetes Federation (IDF) 9th Edition in 2019, 463 million people have diabetes worldwide, out of which 163 million were in the Western Pacific Region. A modest estimation indicates that this figure will increase to 212 million by 2045 (1). In Malaysia, the National Health Morbidity Surveys (NHMS) has reported a steady rise in the prevalence of T2DM from 8.3% in 1996, to 13.4% in 2015, and to 18.3% according to the last survey in 2019, which could be translated to almost 2 million adults ≥ 18 years old (2).

Diabetic retinopathy (DR) is a serious complication of longstanding and poorly controlled T2DM that could range from mild disease to severe proliferative retinopathy, the forerunner in causing blindness and visual disability (3). According to the estimation of International Association on the Prevention of Blindness (IAPB) in 2015, 145 million people exhibited some characteristic of DR and IAPB also stated that vision threatening DR affected 45 million people. In 2020, Vision Loss Expert Group estimated that 1 million people around the world were blind due to DR, and over three million had moderate-severe vision impairment (4). *Yau et al* reported person with diabetes involving any retinopathy had a prevalence of 34.6% while proliferative (vision threatening) retinopathy was 7% (5). Large prospective studies have revealed a high prevalence rates of DR. The Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) showed a prevalence of 50.1% (n=2990) (6), the diabetes control and complications trial (DCCT) showed a prevalence of 54.2% in insulin-dependent diabetes mellitus (IDDM) patients (n=1613) (7), and the United Kingdom Prospective Diabetes Study (UKPDS) showed the same at 35-39% (n=2964) in patients with non-insulin dependent diabetes mellitus (NIDDM) (8). Local data from the Diabetic Eye Registry in 2007 showed a