

ABSTRAK

Pendahuluan. Sarcopenia merupakan salah satu gangguan struktur *textus muscularis striatus non cardiacus* pada pasien diabetes melitus yang menyebabkan gangguan mobilitas dan kerentanan kecelakaan. Beberapa publikasi telah melaporkan kelainan pada otot tikus model diabetes yaitu *myofibra* yang lebih kecil, infiltrasi sel inflamasi, fibrosis, dan lesi nekrotik secara terpisah, dan belum dilaporkan terjadi dalam waktu bersamaan pada satu model tikus diabetes. Karakteristik yang dilaporkan tersebut dapat dipengaruhi oleh klotho. Klotho adalah protein anti penuaan dan anti inflamasi yang juga diekspresikan pada otot skelet dan dilaporkan menurun ekspresinya pada ginjal tikus model diabetes. Belum ada data ekspresi *Klotho* pada otot skelet tikus model diabetes.

Tujuan. Mempelajari gambaran histopatologis dan ekspresi mRNA *Klotho* pada *musculus gastrocnemius* tikus putih jantan *Sprague Dawley* model diabetes setelah induksi streptozotocin nicotinamide (STZ-NA).

Metode. Duabelas tikus putih jantan *Sprague Dawley* dibagi menjadi 2 kelompok, kelompok kontrol dan kelompok diabetes yang diinjeksi STZ (65 mg/kgBB) dan NA (100 mg/kgBB) dosis tunggal. Penentuan diabetes jika kadar gula darah tikus di atas 200 mg/dL setelah 1 minggu. Hewan dikorbankan setelah 10 minggu. *Musculus gastrocnemius* dikumpulkan, ditimbang, dan disimpan di dalam RNA later di suhu 80 °C untuk isolasi RNA, dan di dalam paraformaldehyde 4% untuk blok parafin. Pengukuran ekspresi relatif mRNA *Klotho* dilakukan dengan qRT-PCR, menggunakan *GAPDH* sebagai *housekeeping gene* dan dianalisis menggunakan perhitungan $2^{-(\Delta\Delta Ct)}$. Hasil irisan blok paraffin setebal 5 µm diwarnai dengan HE, Verhoeff, dan PAS dan diamati menggunakan mikroskop cahaya. Parameter yang dinilai yaitu ukuran *myofibra*, letak *nucleus*, infiltrasi sel imun, fibrosis, *splitting* dan deposit glikogen.

Hasil. Terdapat perubahan gambaran histologis pada otot skelet tikus diabetes berupa ukuran *myofibra* yang bervariasi, letak *nucleus* berada di tengah *myofibra*, inflamasi sel imun, nekrosis, fibrosis, *splitting* dan penurunan deposit. Ekspresi mRNA *Klotho* pada tikus diabetes dan tikus non diabetes tidak didapatkan perbedaan signifikan.

Kesimpulan. Terdapat perubahan gambaran histologis berupa degenerasi dan inflamasi tanpa adanya penurunan ekspresi mRNA *Klotho* pada *textus muscularis striatus non cardiacus* tikus model diabetes.

Kata kunci: diabetes, inflamasi, *myofibra*, streptozotocin, *Klotho*

ABSTRACT

Background. *Sarcopenia is one of the disorders affecting the structure of textus muscularis straitus non cardiacus in diabetes mellitus patients, leading to mobility impairment and susceptibility to accidents. Several publications have reported abnormalities in the muscles of diabetic mouse models, such as smaller myofibers, infiltration of inflammatory cells, fibrosis, and necrotic lesions, but separate and these have not been reported to occur simultaneously in one diabetic mouse model. These reported characteristics may be influenced by Klotho. Klotho is an anti-aging and anti-inflammatory protein that is also expressed in skeletal muscles and has been reported to decrease its expression in the kidneys of diabetic mouse models. However, there is no data on the expression of Klotho in the skeletal muscles of diabetic mouse models.*

Objectives. *The aim of study to assess the histopathological structure and mRNA expression of Klotho in the musculus gastrocnemius of male Sprague Dawley white rats as a diabetes model after streptozotocin nicotinamide (STZ-NA) induction.*

Methods. *Twelve male Sprague Dawley white rats were divided into 2 groups, a control group, and a diabetes group induced by a single injection of STZ (65 mg/kg body weight) and NA (100 mg/kg body weight). Diabetes was determined if the rat's blood glucose level was above 200 mg/dL after 1 week. The animals were sacrificed after 10 weeks. The gastrocnemius muscle was collected, weighed, and stored in RNA later at 80 °C for RNA isolation, and in 4% paraformaldehyde for paraffin block. The measurement of relative mRNA expression of Klotho was performed using qRT-PCR, with GAPDH as the housekeeping gene, and analyzed using the 2⁻($\Delta\Delta C_t$) method. The paraffin blocks were sectioned at a thickness of 5 μ m and stained with HE, Verhoeff, and PAS for observation under a light microscope. The parameters assessed were myofiber size, nucleus position, immune cell infiltration, fibrosis, splitting, and glycogen deposition.*

Results. *There were histological changes in the skeletal muscle of diabetic rats, including variation in myofiber sizes, internal nuclei, infiltration of inflammatory cells, necrosis, fibrosis, and splitting. However, there was no significant difference in Klotho mRNA expression between diabetic and non-diabetic rats.*

Conclusion. *There were histological changes, such as degeneration and inflammation, without any decrease in Klotho mRNA expression in the textus muscularis straitus non cardiacus of the diabetic rat model.*

Keywords: *diabetic, inflammation, myofibra, streptozotocin, Klotho*