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HUBUNGAN KADAR GUKOSA TERHADAP PERUBAHAN KADAR ASAM URAT, UREUM, DAN KREATININ SERUM PENDERITA DIABETES MELITUS TIPE 2 DI MALANG RAYA

SKRIPSI

Untuk Memenuhi Persyaratan

Memperoleh Gelar Sarjana Kedokteran

Oleh

KHAIRUL LIZAM DAI

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PROGRAM STUDI KEDOKTERAN

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RINGKASAN

Dai, Lizam Khairul. Fakultas Kedokteran, Universitas Islam Malang, September 2020. Hubungan Kadar Glukosa Terhadap Perubahan Kadar Asam Urat, Ureum, dan Kreatinin Serum Penderita Diabetes Melitus Tipe 2 di Malang Raya. **Pembimbing 1**: Rahma Triliana. **Pembimbing 2**: Fenti Kusumawardhani Hidayah

Pendahuluan: Diabetes melitus tipe 2 (DMT2) memiliki komplikasi berupa *diabetic nephropathy* (DN) yang ditandai dengan peningkatan kadar asam urat, ureum, dan kreatinin serum. Kendali gluokosa berperan pada progresifitas komplikasi DM termasuk DN. Di Malang raya, DMT2 merupakan penyakit terbanyak keempat. Namun, penelitian tentang hubungan kadar glukosa dengan kadar asam urat, ureum, dan kreatinin serum belum pernah dilakukan di Malang raya sehingga perlu dilakukan penelitian ini.

Metode: Studi *analitic observational* dilakukan secara *cross sectional* dengan responden penderita DMT2 tanpa komplikasi berumur >40 tahun di Malang raya yang dibagi menjadi kelompok glukosa terkendali (GT) dan glukosa tidak terkendali (GTT) berdasarkan hasil pemeriksaan glukosa darah dan HbA1c. Kadar asam urat, ureum, dan kreatinin serum diukur dengan metode spektrofotometri. Data dianalisa menggunakan *independent t-test* dan korelasi *spearman* dengan nilai signifkansi $p<0,05$.

Hasil: Penentuan kelompok GT dan GTT dilakukan melalui berbagai proses dan didapatkan perbedaan signifikan kadar gula darah acak ($p=0,05$), gula darah puasa ($p=0,007$), glukosa serum ($p=0,040$), dan HbA1c ($p=0,000$) antara kelompok GT dan GTT. Pada kelompok GT didapatkan rerata dan standar deviasi asam urat (6,06 ± 1,87), ureum (37 ± 21,38), dan kreatinin (1,25 ± 1,26) sedangkan pada kelompok GTT didapatkan kadar asam urat (5,36 ± 4,54), ureum (25,40 ± 6,70), dan kreatinin (0,78 ± 0,24) dengan perbedaan signfikan semuanya. Terdapat hubungan sedang tidak searah pada kadar HbA1c terhadap kadar asam urat (r=-0,447, $p=0,006$), ureum (r=-0,459, $p=005$), dan kreatinin (r=-0,433, $p=0,008$), sementara hubungan kuat tidak searah didapatkan pada GDP terhadap asam urat (r=-0,706, $p=0,010$) dan kreatinin (r=-0,629, $p=0,028$), dan hubungan sedang tidak searah didapatkan pada GDA terhadap asam urat (r=-0,404, $p=0,010$). Hal ini menunjukan bahwa semakin tinggi kadar glukosa darah maka semakin rendah kadar asam urat, ureum, dan kreatinin darah.

Kesimpulan: Kadar glukosa berhubungan dengan perubahan kadar asam urat, ureum, dan kreatinin serum penderita DMT2 di Malang raya.

Kata Kunci: *Kendali glukosa, asam urat, ureum, kreatinin, nefropati diabetik.*

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SUMMARY

Dai, Lizam Khairul. Medical Faculty, Islamic University of Malang, September 2020. The Relationship of Glucose Levels Changing the Serum of Uric Acid, Ureum, and Creatinine Levels On Patients With Type 2 Diabetes Mellitus in Malang Region. **Supervisor 1**: Rahma Triliana. **Supervisor 2**: Fenti Kusumawardhani Hidayah.

Introduction: Type 2 diabete melitus (T2DM) can lead into diabetic nephropathy (DN) which is characterized by an increasing in serum of uric acid, urea, and creatinine levels. Glucose control plays the role in progression of DM complications including DN. In Malang Region, T2DM is the fourth most common disease. Nevertheless, research about the relationship between glucose levels and the serum of uric acid, urea and creatinine levels has never been has never been done in Malang Region, so this research need to be done.

Methods: An analytic observational study was conducted in a cross-sectional manner with respondents with T2DM without complications aged> 40 years in Malang Region which were divided into controlled glucose (CG) and uncontrolled glucose (UG) groups based on the test results of blood glucose and HbA1c . The serum of uric acid, urea and creatinine levels were measured by spectrophotometric method. Data were analyzed using independent t-test and Spearman correlation with a significance value of p <0,05.

Results: The determination of the CG and UG groups were carried out through various processes and there were significant differences in random blood sugar (p=0,05), fasting blood sugar (p=0,007), serum glucose (p=0,040), and HbA1c (p= 0,000) levels between the CG and UG groups. In the CG group, the mean and standard deviation of uric acid (6,06 ± 1,87), urea (37 ± 21,38), and creatinine (1,25 ± 1,26) were obtained while in the UG group uric acid levels were obtained (5,36 ± 4,54), urea (25,40 ± 6,70), and creatinine (0,78 ± 0,24) were all significant differences. There was a negative significantly relationship between HbA1c levels and uric acid levels (r=-0,447, p=0,006), urea (r=-0,459, p=005), and creatinine (r=-0,433, p=0,008), while strong negative association was found in FBS against uric acid (r=-0,706) and creatinine (r=-0,629, p=0,010), and a moderate negative significantly relationship was found in RBS to uric acid (r=-0,404, p=0,010). This shows that the higher the blood glucose level, the lower of the uric acid, urea, and blood creatinine levels.

Conclusion: Glucose levels had a relationship in changing the serum of uric acid, urea, and s creatinine levels towards patinets with T2DM in Malang Region.

Keywords: Glucose control, uric acid, urea, creatinine, diabetic nephropathy.

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BAB 1
PENDAHULUAN

1.1. Latar Belakang

Diabetes melitus (DM) pertama kali ditemukan di Mesir kuno sekitar 3000 tahun yang lalu (Ahmed, 2002). DM dibagi menjadi tipe 1 dan 2 (Isselbacher *et al*.,2000) dengan DM tipe 2 (DMT2) ditandai oleh hiperglikemia akibat resistensi insulin disertai defisiensi insulin relatif (Abbas and Maitra, 2005). Menurut *American Diabetic Association* (ADA), kriteria DM didasarkan pada kadar hemoglobin terglikasi (HbA1c) ≥6,5% atau kadar gula darah puasa (GDP) ≥126 mg/dL atau kadar gula darah 2 jam setelah makan (GD2PP) ≥200 mg/dL atau gejala klasik hiperglikemi dsiertai kadar gula darah acak (GDA) ≥200 mg/dL (ADA, 2018).

Berdasarkan data *World Health Organization* (WHO), diperkirakan 422 juta orang berusia ≥18 tahun menderita DM yang terbanyak berada di Asia Tenggara (96 juta jiwa) dan wilayah Pasifik barat (131 juta jiwa) (WH0, 2016). Di Indonesia, penduduk usia ≥15 tahun yang mengalami DM di tahun 2018 meningkat 2% jika dibandingkan dengan tahun 2013 sedangkan di Jawa Timur, jumlah penderita DM menduduki peringkat kelima dari total 34 propinsi di Indonesia (RISKESDAS, 2018). Di kota Malang, DMT2 merupakan penyakit terbanyak urutan keempat setelah infeksi saluran pernafasan atas (ISPA), hipertensi primer, dan gastritis (DINKES Kota Malang, 2016). Oleh sebab itu, penyakit DM perlu mendapatkan lebih banyak perhatian.

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Perhatian lebih pada penderita DM ditujukan untuk mencegah komplikasi DM baik akut maupun kronis (Fatimah, 2015). Komplikasi akut maupun kronis DM dapat dicegah dengan pengendalian kadar glukosa darah yang baik (ADVANCE, 2008). Penderita DMT2 yang gagal mengendalikan kadar glukosa darah dapat mengalami kerusakan pembuluh darah/angiopati diabetik, mata/retinopati diabetik, saraf/neuropati diabetik, peningkatan resiko penyakit jantung, dan stroke serta kerusakan ginjal/*diabetic nephropathy* (WHO, 2016). Untuk mengetahui komplikasi DM ke ginjal atau *diabetic nephropathy*, maka evaluasi fungsi ginjal perlu dilakukan dengan cara mengukur kadar kretainin, asam urat, dan ureum serum (Verdiansah, 2016).

Ureum merupakan hasil metabolisme asam amino yang secara normal dibuang melalui saluran pencernaan sebanyak 15% dan melalui ginjal sebanyak 85% (Gounden *et al*.,2020). Laju filtrasi glomerular (LFG) mengontrol jumlah ureum yang masuk ke dalam tubulus proximal dan sekitar 30-50% ureum yang terfiltrasi akan diekresikan melalui urin (Klein *et al*.,2011). Penderita DMT2 dengan kendali glukosa yang buruk akan mengalami kerusakan endotel kapiler glomerulus ginjal sehingga terjadi gangguan filtrasi glomerulus (*diabetic nephropathy*, Brownlee, 2005), dan dikaitkan dengan peningkatan kadar ureum dalam darah (Molitoris, 2007). Namun, peningkatan kadar ureum darah juga dapat terjadi akibat faktor *pre-renal* seperti asupan protein dari makanan, perubahan perfusi ginjal, dan lain-lain atau dari faktor post-renal seperti obstruksi saluran kemih, sehingga kadar ureum darah dianggap kurang spesifik sebagai indikator fungsi ginjal jika dibandingkan dengan kadar kreatinin darah (Murray *et al*., 2014).

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Kreatinin merupakan hasil metabolisme keratin fosfat di otot yang diekseresikan melalu urin sebanyak 100% (Wyss and Kaddurah-Daouk, 2000) sehingga perubahan konsentrasi kadar kreatinin darah lebih menggambarkan perubahan LFG (Griffin *et al*.,2018). Hal ini menyebabkan kadar kreatinin darah lebih spesifik sebagai marker fungsi ginjal jika dibandingkan dengan kadar ureum (Murray *et al*.,2014). *Diabetic nephropathy* (DN) akibat kerusakan glomerulus (Isselbacher *et al*.,2000) juga ditandai oleh peningkatan kadar kreatinin darah (Anjaneyulu and Chopra, 2004) sehingga kreatinin darah dapat menjadi marker DN. Meskipun kadar kreatinin darah merupakan penanda spesifik fungsi ginjal, namun peningkatan kreatinin secara signifikan hanya ditemukan pada penurunan LFG lebih dari 50%, sehingga dianggap kurang sensitif untuk menilai kerusakan ginjal (Murray *et al*.,2014). Maka dari itu, perlu pemeriksan kadar asam urat darah sebagai marker lainnya.

Asam urat merupakan hasil akhir katabolisme purin yang sebanyak 30% diekskresikan melalui usus dan sebanyak 70% dibuang melalui urin (Murray *et al*.,2014). Ginjal mengatur homeostasis kadar asam urat darah melalui filtrasi glomerulus yang kemudian direabsorbsi kembali oleh tubulus (90%) sebelum diekskresikan melalui urin (Bobulescu and Moe, 2012). Penurunan ekskresi asam urat akibat kerusakan ginjal atau DN dapat menyebabkan peningkatan kadar asam urat dalam darah sehingga terjadi hiperurisemi (Ficociello *et al*., 2010). Selain kelainan ginjal, hiperurisemi juga dapat terjadi akibat kelebihan produksi purin seperti pada diet tinggi purin, alkoholisme, obesitas, dan dislipidemi (Syukri, 2007). Untuk itu, penilaian parameter ureum, kreatinin dan asam urat tidak dapat dipisahkan dalam menentukan kelainan ginjal pada pasien dengan DM. Untuk

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mencegah kerusakan ginjal yang ditandai peningkatan asam urat, ureum,dan kreatinin darah diperlukan pengendalian kadar glukosa darah yang baik.

Kendali glukosa yang baik dapat mencegah komplikasi DN karena dapat memperlambat penurunan LFG (MacIsaac *et al*.,2017). Penelitian ini didukung oleh *statement* dari Narang, et al. (2019) yang telah menemukan bahwa kendali glukosa yang buruk meningkatkan insiden mikroalbuminuria pada penderita DM. Albuminuria pada penderita DMT2 merupakan marker yang sensitif dan spesifik ginjal untuk DN (de Zeeuw, 2007). Sedangkan Penderita DMT2 yang menjalani kendali glukosa secara intensif memiliki risiko gagal ginjal yang lebih rendah (Holman *et al*.,2008). Nasution (2013), juga menyatakan bahwa kendali glukosa yang baik akan menurunkan kejadian mikroalbuminuria dan resiko DN pada penderita DMT2. Oleh karena di Malang belum terdapat banyak data dan penelitian terkait kadar asam urat, ureum, dan kreatinin penderita DMT2, maka perlu dilakukanya penelitian terkait peran kendali glukosa terhadap kadar asam urat, ureum, dan kreatinin darah pada penderita diabetes melitus tipe 2 di Malang raya.

1.2. Rumusan Masalah

Adapun permasalahan penelitian yang diangkat pada penelitian ini adalah "apakah hubungan kadar glukosa terhadap perubahan kadar asam urat, ureum, dan kreatinin serum penderita diabetes melitus tipe 2 di Malang raya?"

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1.3. Tujuan Penelitian

Penelitian ini bertujuan untuk mengetahui hubungan kadar glukosa terhadap perubahan kadar asam urat, ureum, dan kreatinin serum penderita diabetes melitus tipe 2 di Malang raya.

1.4. Manfaat Penelitian

1.4.1. Manfaat Praktis

Hasil penelitian diharapkan bermanfaat untuk masyarakat dan tenaga kesehatan dalam memberikan intervensi kesehatan masyarakat dan kedokteran komunitas dalam penanganan komplikasi nefropati diabetikum dengan pengukuran kadar asam urat, ureum, dan kreatinin.

1.4.2. Manfaat Teoritis

Hasil penelitian ini diharapkan dapat menjadi landasan penelitian-penelitian selanjutnya terkait hubungan kadar glukosa terhadap komplikasi nefropati diabetikum dalam skala penelitian yang lebih luas dengan jumlah sampel yang lebih banyak. Selain itu, penelitian ini juga diharapkan dapat memberikan informasi serta menjadi dasar penelitian patomekanisme dan manajemen pasien DM di Malang raya.

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BAB VII
PENUTUP

7.1. Kesimpulan

Berdasarkan hasil penelitian ini maka dapat diambil kesimpulan bahwa terdapat hubungan kadar glukosa terhadap perubahan kadar asam urat, ureum, dan kreatinin serum penderita DMT2 di Malang raya. Kadar asam urat, ureum, dan kreatinin serum berbeda signifikan antar kelompok dengan nilai rata-rata yang lebih tinggi pada kelompok glukosa tekendali dibandingkan kelompok glukosa tidak terkendali. Hal ini didukung dengan hasil uji korelasi yang menujukan hubungan negatif bermakana antara kadar GDA, GDP, dan HbA1c terhadap kadar asam urat, ureum, dan kreatinin serum. Adanya faktor lain seperti usia dan diet protein diduga mempengaruhi hasil penelitian.

7.2. Saran

Berdasarkan hasil pembahasan, maka disarankan:

1. Melakukan penelitian lanjutan dengan jumlah responden total yang lebih banyak dengan komposisi yang sama antara kelompok glukosa terkendali dan kelompok glukosa tidak terkendali.
2. Mengeklusikan responden dengan riwayat hiperurisemia sebelum diketahui menderita DM.
3. Mengurangi variasi pekerjaan dari responden penelitian.
4. Menggunakan kuisioner standar aktivitas fisik dan diet protein yang berbeda.

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5. Menggunakan desain penelitian *cohort* atau *case control* untuk menilai hubungan kendali glukosa dengan kepatuhan minum obat anti diabetes, diet, dan aktivitas fisik.
6. Menghitung nilai laju filtrasi glomerulus pada setiap responden.
7. Mengukur *albumin to creatinine ratio*

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