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Diabetes Update

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "DIABETES UPDATE" which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Serum Uric Acid Levels Are Associated with Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus Patients, Particularly for Tibial Nerve Motor Conduction Velocity.
- Haemoglobin A1c stability in elderly diabetic patients and its relationship to mortality and complications
- Increased A1C and weight loss in response to lifestyle intervention.
- A case report of a young-onset type 2 diabetic Chinese girl with familial renal glycosuria brought on by a new SLC5A2 mutation.

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

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Serum Uric Acid Levels Are Associated with Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus Patients, Particularly for Tibial Nerve Motor Conduction Velocity.

After tumours and cardiovascular illnesses, diabetes mellitus is the third most prevalent disease with a steadily rising prevalence. Diabetes mellitus is a metabolic disorder with numerous aetiologies that is characterised by chronic hyperglycemia. Diabetic peripheral neuropathy (DPN), a common consequence with symptoms including pain, numbness, weakness, and altered sensation in the limbs, is a result of inadequate glycemic management and the progression of diabetes.[1] Natural antioxidants like uric acid are important in the body's ability to fight oxidative damage.[2] The purpose of this study was to identify the function of serum uric acid (SUA) in type 2 diabetes mellitus (T2DM) patients' DPN.

A total of 106 T2DM patients were enlisted and split into the DPN group and the control group. Clinical data were gathered, with a focus on the conduction velocities of the motor and sensory nerve fibres. Comparisons were made between T2DM patients with and without DPN. To investigate the relationship between SUA and DPN, regression and correlation analyses were carried out.

49 patients without DPN demonstrated higher SUA levels and lower HbA1c in comparison to 57 individuals with DPN. In addition, with or without accounting for HbA1c, SUA levels are inversely correlated with the motor conduction velocity of the tibial nerve. Additionally, multiple linear regression analysis suggests that lower SUA levels might have an impact on the tibial nerve's motor conduction speed. By using binary logistic regression analysis, the study further showed that decreasing SUA level is a risk factor for DPN in patients with T2DM.

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Similar to this, a prior investigation revealed reduced SUA in T2DM patients with mild cognitive impairment compared to those without cognition decline3, which is a form of CNS dysfunction[3]. The conduction velocity of the nerve was examined in order to confirm the presence of DPN. There is no doubt that patients lacking DPN had quicker motor and sensory conduction fibre velocities of the ulnar, radial, median, tibial, and common peroneal nerves, as well as a higher rate of conduction for these nerves.

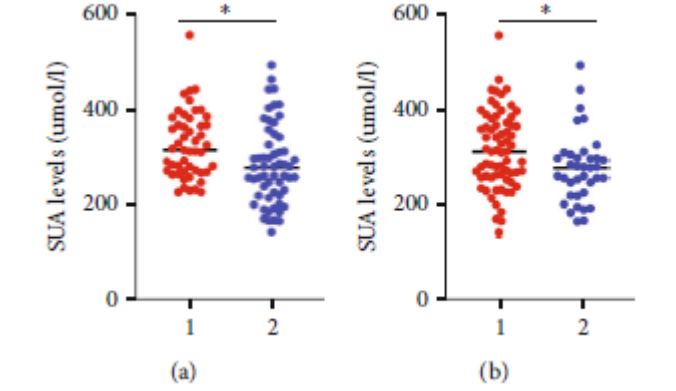

Figure 1: SUA levels in different patients with T2DM.

Due to the lower SUA levels in DPN patients, Pearson's correlation was used to find a link between SUA and the higher nerve conduction velocity. The study discovered that the conduction rates of the tibial nerve motor fibres, median nerve sensory fibres, and sural nerve sensory fibres were all favourably correlated with SUA levels.

Lower SUA is a risk factor for DPN in people with T2DM, it can be concluded. Additionally, decreasing SUA may have an impact on peripheral neuropathy damage, particularly for the tibial nerve's motor conduction velocity.

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Haemoglobin A1c stability in elderly diabetic patients and its relationship to mortality and complications

Diabetes complications and chronic hyperglycemia have a complicated link. The amount of haemoglobin A1c (A1c) and its variation over time may have clinical repercussions, according to a number of lines of evidence. With type 2 diabetes, lowering A1c to 7.0% lowers the risk of microvascular complications but has little effect on CVD or mortality, and there is a non-linear relationship between average A1c and death. Independent of A1c levels, increased A1c variability is linked to a higher risk of CVD and mortality.1 With regard to having A1c values that are primarily within, above, or below their patient specific goal ranges, this study sought to assess the risks of death as well as macrovascular and microvascular problems among older persons with diabetes.

Veterans with diabetes who underwent at least four A1c tests over a baseline period of three years were the subject of a retrospective observational cohort study that was conducted from 2004 to 2016. Based on the proportion of

time that baseline A1c readings were within patients' individual goal ranges, we created four unique categories: 60% time in range (TIR), 60% time below range (TBR), 60% time above range (TAR), and a mixed group with all times 60%. The study evaluated the relationships between these categories and problems related to the macrovascular and microvascular systems.

The researchers studied 397 634 patients (mean age 76.9 years, SD 5.7) with an average of 5.5 years of follow-up. Mortality was higher in the 60% TBR, 60% TAR, and mixed groups compared to the 60% A1c TIR, with HRs of 1.12 (95% CI 1.11 to 1.14), 1.10 (95% CI 1.08 to 1.12), and 1.06 (95% CI 1.04 to 1.07), respectively. Estimates of macrovascular complications were 1.04 (95% CI 1.01 to 1.06) and 1.06 (95% CI 1.03 to 1.09), respectively, with 60% TBR and 60% TAR(Table 1). Microvascular problems were more common with 60% TAR and less common with 60% TBR (HR 1.11, 95% CI 1.08 to 1.14) respectively. Results with higher TIR thresholds, shorter follow-up, and competing mortality risk were comparable.

Table 1: Adjusted HR (95% CI) predicting mortality and diabetes complications by ≥80% A1c time above or below range categories

	Time below range ≥80%*	**Time above range ≥80%***	**Mixed group***
Mortality (n=397 634)	1.20 (1.17 to 1.22)	1.18 (1.15 to 1.21)	1.18 (1.15 to 1.21)
Macrovascular complications (n=89 625)	1.08 (1.05 to 1.11)	1.10 (1.06 to 1.13)	1.04 (1.01 to 1.16)
Cardiovascular (n=122 135)	1.08 (1.05 to 1.11)	1.10 (1.05 to 1.13)	1.02 (1.00 to 1.15)
Cerebrovascular (n=277 234)	1.06 (1.03 to 1.09)	1.14 (1.10 to 1.18)	1.06 (1.03 to 1.08)
Peripheral vascular (n=228 583)	1.07 (1.04 to 1.10)	1.20 (1.16 to 1.25)	1.08 (1.05 to 1.11)
Microvascular complications (n=74 016)	1.00 (0.97 to 1.03)	1.14 (1.10 to 1.18)	1.02 (1.00 to 1.05)
Retinopathy (n=235 580)	0.93 (0.90 to 0.96)	1.29 (1.24 to 1.34)	1.03 (1.01 to 1.06)
Neuropathy (n=222 274)	0.97 (0.95 to 0.99)	1.16 (1.13 to 1.20)	1.05 (1.03 to 1.07)

Nephropathy (n=168 616)	1.03 (1.00 to 1.05)	1.13 (1.10 to 1.17)	1.03 (1.01 to 1.06)

According to the study, older persons with diabetes who maintain their A1c levels within specific goal ranges throughout time had a lower risk of mortality and macrovascular problems. A higher A1c TBR had a lower risk of certain microvascular sequelae and an increased risk of death. All unfavourable outcomes were connected with higher odds of increased A1c TAR. After accounting for a number of factors and running further analyses with higher A1c TIR thresholds, a shorter outcome period, and mortality as a competing risk, the results were consistent and the HRs were tiny but significant. These results imply that chronically out-of-range A1c levels are linked with unique dangers, while A1c stability over time within patient-specific ranges offers a little decreased risk of poor outcomes.[2]

A1c stability within certain ranges is linked to a reduced risk of mortality and complications from diabetes in older persons with the disease. This is consistent with earlier research showing that higher A1c fluctuation raises the risk of mortality and complications from diabetes. The findings of this study expand on this construct by employing patient-specific A1c ranges and also highlight the distinct hazards entailed by A1c levels that gradually depart from these ranges in various directions.

In older persons with diabetes, increased time above and below personal A1c target ranges is related with death and macrovascular problems. Patients with lesser risk of negative outcomes may be identified by having higher A1c TIR.

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Increased A1C and weight loss in response to lifestyle intervention.

In actual clinical practise, the impact of intensive lifestyle intervention (ILI) on A1C is erratic and commonly overestimated.It is understated how intensive lifestyle interventions (ILI) affect people with diabetes' A1C levels. Improvement in A1C is thought to depend on how much weight is lost.2 Here, the study assessed the quantity of weight reduction and the size of A1C drop in people with diabetes who received ILI during a 13-year period in actual clinical practise.

The Weight Achievement and Intensive Treatment (Why WAIT) programme, a 12-week multidisciplinary ILI programme created for real-world clinical practise, included 590 patients with diabetes in total. Based on baseline A1C, the researchers divided the subjects into three groups: A1C 9% in group A, and 8 to 8% in group B

All groups experienced a drop in body weight following the 12-week intervention, and pairwise analyses of A1C reductions revealed that group A had an A1C reduction that was 1.3% greater than group B's and 2% greater than group C's ($p = 0.0001$), while group B had an A1C reduction that was 0.7% greater than group C's ($p = 0.0001$).

Table 1: Association of change in systolic BP and change in total cholesterol, and baseline A1C.

	Unadjusted model	**Adjusted model**

	β (95% CI)	p value	β (95% CI)	p value
Change in systolic BP after 12 weeks of ILI	-1.46(-3.23 to 0.32	0.11	-2.30 (-4.25 to -0.34	0.02
Change in Total cholesterol after 12 weeks of ILI	-4.68 (-7.99 to -1.36	0.006	-2.64 (-6.25 to 0.98	0.15

Based on baseline A1C, researchers separated the study cohort of 222 patients with T2D and obesity into three groups: group 1 had an A1C below 6.8%, group 2 had an A1C above 6.81% but below 7.7%, and group 3 had an A1C above 7.8%. The study findings showed that multidisciplinary ILI for 12-weeks in real-world clinical practice decreased body weight by an average of 7.9%, and decreased A1C by up to 2.5%. Having a large cohort to evaluate the impact of baseline A1C on their glycemic response to the ILI.[2] The first study was a post-hoc analysis, in which researchers divided the study cohort of 222 participants with T2D and obesity into three groups based on baseline A1C; group 1 with A1C ≤ 6.8%, group 2 with A1C > 6.81% and <7.7%, and group 3 with A1C ≥ 7.8%. The study found that group 3 achieved the greatest improvement after 12-weeks of lifestyle intervention

ILI may lower A1C by up to 2.5% in persons with diabetes, according to the study's findings. A1C reduction was more pronounced in patients with higher baseline A1Cs at similar weight loss rates. This may help clinicians set reasonable expectations for how the A1C will alter in response to ILI.

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A case report of a young-onset type 2 diabetic Chinese girl with familial renal glycosuria brought on by a new SLC5A2 mutation.

A uncommon hereditary condition of proximal tubular glucose transport known as familial renal glycosuria (FRG) causes increased urine glucose excretion even when blood glucose levels are within the normal range. It has been determined that this condition is caused by mutations in the SLC5A2 gene, which codes for the sodium-glucose cotransporter 2 (SGLT2).1

There are no reports linking FRG to type 2 diabetes with juvenile onset.2 In this work, the clinical features of a Chinese girl with juvenile-onset type 2 diabetes and FRG were described. FRG may have been caused by a new mutation in the SLC5A2 gene (NM_003041.4:c.1129 + 2 T > C).

All participants' genomic DNA was extracted from peripheral blood using the QIAamp DNA extraction kit (manufactured by the German QIAGEN firm). The proband's genomic DNA sample underwent DNase fragmentation and polymerase chain reaction amplification. On a NovaSeq 6000 sequencer (Illumina, USA), the target region of the entire exome was collected, purified, and sequenced to produce mean sequence coverage of more than 90, with more than 98% of the target bases having at least 20 coverage. GATK (v4.0.6.0) was used to get the variant calling, and ANNOVAR (v20211019) was used to get the variant annotation.

A 20-year-old Chinese woman named the proband after her repeated episodes of glycosuria and ketonuria caused by diabetes that lasted for six years and began at age 14 with polyuria, polydipsia, and weight loss. She was referred to the diabetes unit for treatment. Endocrine exams were properly carried out following admission to our facility. 10.6% (range [RR] 4.1%–6.0%) was the serum haemoglobin A1c value. The findings of the mixed meal tolerance test revealed fasting plasma glucose (FPG) levels of 187.92 mg/dL (RR 61.2-109.8 mg/dL), 2-hour postprandial glucose (PG)

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levels of 222.12 mg/dL, and fasting C-peptide levels of 20.9 ug/L (RR 9.9-39.64 ug/L) and 31.8 ug/L, respectively.

Through whole exome sequencing, 20 genes linked to neonatal diabetes mellitus and 14 genes linked to MODY were analysed. But no mutation was discovered. Finally, type 2 diabetes with a young onset was identified in her.

Large dose insulin (57 IU/d) plus metformin alone were unable to successfully keep hyperglycemia under control. Although her blood sugar level was nAdditionally, because the UTI was recurrent, the therapy was not as effective as it had been in the past.Ketonuria (ranging from + to +++) and glycosuria continued to be present even after the normal range.

Her parents' serum creatinine and protein excretion levels were both within normal ranges, and none of them had any renal diseases. In SLC5A2, 14 coding exons and their surrounding intronic regions were examined (Figure 1). The proband was found to have an SLC5A2 T-to-C transition at complementary deoxyribonucleic acid (cDNA) (Genome Reference Consortium human genome build 37/human genome 19 16:31499813).

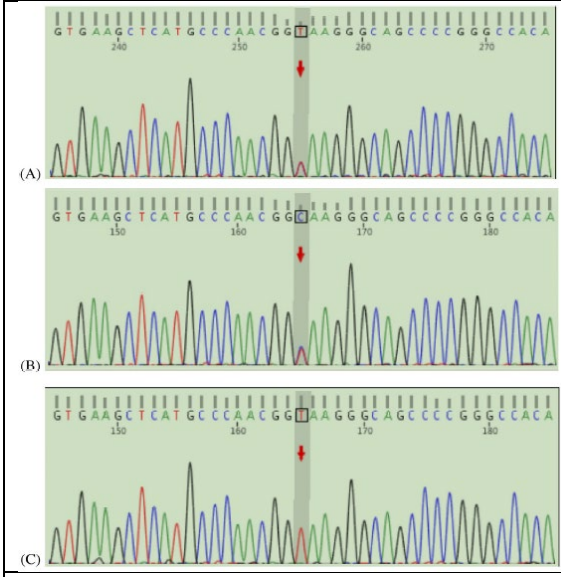

Figure 1: Mutation analysis of the solute carrier family affected with familial renal glycosuria. The positions of

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the mutations are indicated by the red arrows.

MODY is a unique kind of diabetes mellitus that accounts for a small but significant portion of diabetic patients (1%–5%).3 and 1%–6% of paediatric cases.6 The diagnosis of MODY was also ruled out in this patient since none of the 14 genes linked to the disorder have mutations in them.

Similar to MODY, youth-onset type 2 diabetes has a clinical appearance, but the individuals are typically obese or overweight. Other forms of diabetes mellitus were ruled out, and the patient's type 2 diabetes was confirmed as having started when they were young.

The proband received large doses of insulin and metformin treatment; nonetheless, even when blood glucose levels were almost in the normal range, glycosuria and ketonuria could not be controlled. A potential concomitant FRG diagnosis was then predicted.

Diabetes mellitus has a variety of aetiologies, and diabetic patients frequently exhibit a wide range of symptoms. When determining specific gene mutations in patients or members of their families, genetic studies, including next-generation sequencing, are very helpful in ensuring the best possible treatment and follow-up.

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