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Diabetes Update

Vol. 3 | Issue 36| 2022

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.

- The TODAY Study's Results on the Development and Progression of Diabetic Retinopathy in Adolescents and Young Adults with Type 2 Diabetes
- A meta-analysis on closed-loop insulin system in patients with type 1 diabetes
- A study on Vitamin D Deficiency and Mortality in Diabetic Kidney Disease Adults
- A case report of central diabetic insipidus caused by COVID19 infection.

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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The TODAY Study's Results on the Development and Progression of Diabetic Retinopathy in Adolescents and Young Adults with Type 2 Diabetes

Type 2 Diabetes Mellitus (T2DM) is a multifactorial disease characterised by hyperglycemia, which can lead to macrovascular and microvascular problems. Diabetic retinopathy is one of the microvascular problems that might occur. Diabetic retinopathy (DR) is the most common cause of vision problems in individuals who are still working.[1] Diabetic retinopathy (DR), the most prevalent consequence of uncontrolled diabetes mellitus, is still one of the most common causes of legal blindness around the world.[2] The findings imply that in individuals diagnosed with type 2 diabetes at a young age, β-cell decrease is more rapid and failure to reach glycemic objectives with oral medications is more common and occurs sooner than in those identified later in life.[3] In the Treatment Options for Type 2 Diabetes in Adolescents and Youth, this study aimed to report the risk variables linked with DR advancement in youth-onset type 2 diabetes (TODAY).

The TODAY clinical trial enrolled 699 people over the period of 4.5 years, and they were followed for 2.0–6.5 years. Following the completion of the TODAY trial in 2011, 572 people were enrolled in the TODAY2 observational follow-up research. The results of 517 participants' stereoscopic colour fundus images were reported. Fundus photos were gathered from 423 participants during the TODAY2 observational follow-up research. The Early Treatment Diabetic Retinopathy Study (ETDRS) scale was used to score the photographs. At both assessments, a total of 367 patients with gradable fundus pictures in at least one eye were included in studies of DR advancement, which was defined as a rise of three or more steps on the ETDRS scale.

The subjects had a 49% prevalence of any DR, with a mean ± SD age of 25.4± 2.5 years and a diabetes duration of 12.0 ± 1.5 years. With a mean diabetic duration of 4.9 years, 315 (85.8%) people with repeated fundus

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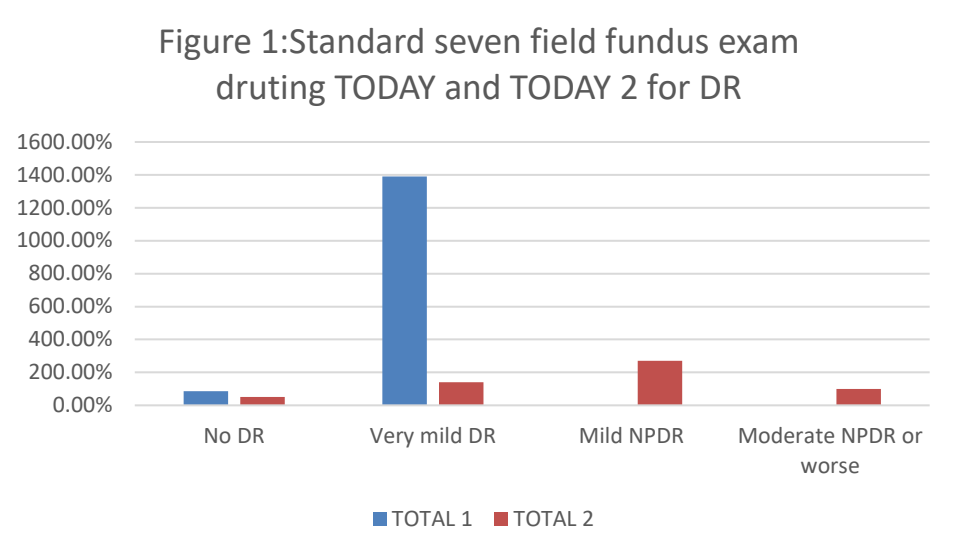
photography had no evidence of DR at the initial test, and 52 (13.9%) participants had very weak nonproliferative (NPDR) (Fig. 1). After seven years, the percentage of individuals who had no retinopathy had dropped to 51%. Five (1.4%) of those who advanced had severe NPDR, ten (2.7%) had early or stable treated proliferative (PDR), and four (1%) had high risk PDR (Fig. 1). Participants who advanced three or more steps had a lower BMI, higher HbA1c, higher blood pressure, increased triglycerides, decreased C-peptide, and a higher frequency of various comorbidities than nonprogressors. HbA1c was found to be the most important factor influencing DR development in multivariate analysis.



Nearly half of the TODAY study participants acquired DR after _10 years of follow-up and an average diabetes duration of 12 years. Patients moved from very moderate NPDR on initial assessment to more advanced stages of DR in the 7 years between retinal exams, with 5% of participants advancing to severe NPDR or PDR while being just 25 years old on average.

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In youth-onset type 2 diabetes, poor glycemic control increases the likelihood of DR progression, including advanced, sight-threatening illness by early adulthood.

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A meta-analysis on closed-loop insulin system in patients with type 1 diabetes

Diabetes is a metabolic condition marked by persistent hyperglycemia caused by abnormalities in insulin secretion, action, or both.[1] Type 1 diabetes (T1D) is characterised by a shortage of insulin as a result of autoimmune processes that kill the pancreas' insulin-producing cells.[2] According to the International Diabetes Federation, 50,600 children aged 0-19 in Africa have type 1 diabetes mellitus (T1DM), with around 18,300 new cases diagnosed each year. Diabetes has been on the rise over the past three decades, with the fastest growth occurring in low and middle-income countries (LMIC).[1] To improve type 1 diabetes therapy in modern countries, insulin analogues and mechanical technology (such as insulin pumps and continuous glucose monitoring (CGM)) are frequently used. In addition, recent advancements have resulted in the development of an artificial

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pancreas: the closed-loop insulin system (CLS). The researchers used a systematic review and meta-analysis to assess the effectiveness and safety of long-term usage of a closed-loop insulin system (CLS) in non-pregnant patients with type 1 diabetes mellitus (T1DM).[3]

MEDLINE, EMBASE, and the Cochrane Library were used to conduct a literature search. All CLS-related randomised controlled clinical trials with a study term of at least 8 weeks were considered eligible. The primary aim of the study was to assess the efficacy and safety of a closed-loop insulin pump in type 1 diabetic patients. Time over goal range (TAR) (>10 mmol/L or >180 mg/dL), time below target range (TBR) (<3.9 mmol/L or <70 mg/dL), and HbA1c (percent) were all secondary outcomes determined at the end of each research. CLS was compared to controls in adults and children with type 1 diabetes using RevMan V.5.3.5 in a meta-analysis.

The control groups included continuous subcutaneous insulin infusion (CSII) with blinded Continuous glucose monitoring (CGM) or unblinded sensor-augmented Pump (SAP) treatment, multiple daily Injections (MDI), and the predictive low-glucose suspend (PLGS) device, while the experimental groups included single-hormone CLS. The duration of the study ranged from eight to twenty-six weeks. In CLS, which was equal to 2 hours and 27 minutes per day, time in target range (TIR) was 10.32% (95% CI 8.70% to 11.95%, $p<0.00001$, $I^2=21\%$) greater than in controls, with a weighted mean (WM) of 56.91% (2 hours and 39 minutes per day) for SAP (fig.1). CLS had a positive effect on HbA1c, with a decrease of 0.30 percent (95 percent CI -0.41 percent to -0.19 percent, $p<0.00001$, $I^2=0$ percent) compared to controls, with a WM of 7.51 percent for the controls (fig. 2). In terms of daily insulin dose, quality of life assessment, and diabetes treatment satisfaction, there were no significant changes between the CLS and the control group.

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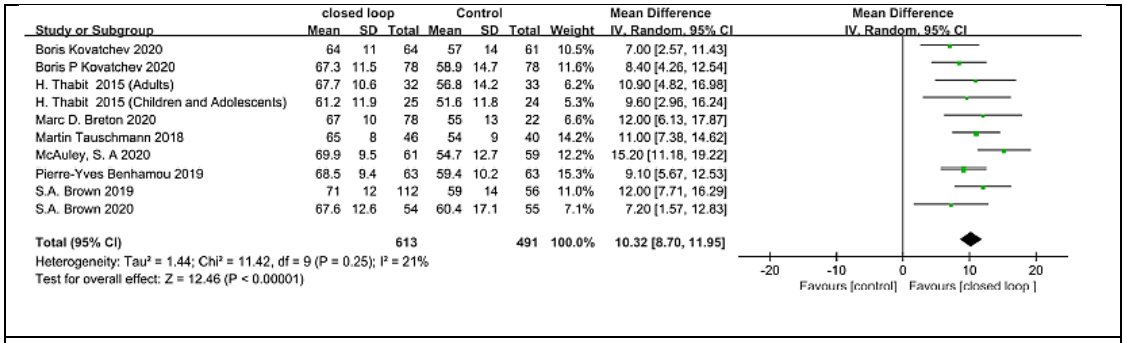

Figure 1: Forest plot for time in target range (70–180 mg/dL). IV, inverse-variance.

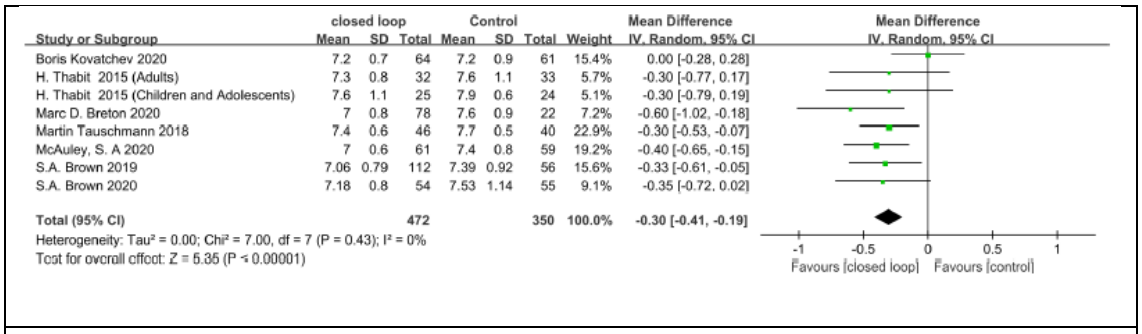

Figure 2: Forest plot for glycated hemoglobin changes (%). IV, inverse-variance.

This systematic review and meta-analysis found that CLS application increased TIR and decreased TBR, TAR, and HbA1c in non-pregnant T1DM patients compared to controls, confirming previous findings that CLS improves glucose control and reduces the risk of hypoglycemia even with longer applications.[3] In a 16-week experiment involving children with type 1 diabetes, Breton MD found that using a closed-loop system kept glucose levels in the target range for a higher percentage of the time than using a sensor-augmented insulin pump.[4]

In non-pregnant T1DM patients, long-term usage of CLS improved glucose management and reduced the occurrence of hypoglycemia and GV when compared to controls (CSII with blinded CGM or unblinded SAP therapy

or MDI or PLGS system). CLS may become more commonly employed in clinical practise in the future for long-term T1DM treatment.

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A study on Vitamin D Deficiency and Mortality in Diabetic Kidney Disease Adults

Diabetes mellitus (DM) is one of the most common chronic diseases in the world, with an increasing incidence and prevalence. Diabetic kidney disease (DKD) is the largest cause of kidney failure and a long-term consequence of diabetes. Although multiple clinical phenotypes and processes related to DKD progression have been identified, microcirculatory abnormalities have been recognised as an early and persistent pathogenic trigger of DKD.1 Vitamin D receptors have been discovered in a wide range of cell types, including pancreatic cells, and active vitamin D is thought to play a role in insulin production and secretion. Low serum 25 hydroxyvitamin D concentrations have been linked to an increased risk of type 2 diabetes in

observational studies. Vitamin D deficiency appears to play a role in the development of diabetic kidney disease, according to new research (DKD). However, there is no compelling evidence of a link between vitamin D and mortality in people with DKD. As a result, the goal of this study was to see if there was a link between blood 25-hydroxyvitamin D (25(OH)D concentrations and mortality in persons with DKD.3

Data from the ongoing National Health and Nutrition Examination Survey (NHANES) from seven survey cycles, with a total of 72,126 participants, were used in this analysis. The study population consisted of 38,913 eligible individuals (all under the age of 20). The DiaSorin radioimmunoassay kit was used to quantify serum 25(OH)D concentrations in NHANES subjects. The National Death Index was used to determine all-cause mortality data. According to the Endocrine Society Clinical Practice Guidelines, participants were divided into quartiles based on their 25(OH)D levels (<25.0, 25.0 to <50, 50.0 to <75, and ≥75 nmol/l). The hazard ratios (HRs) and 95% confidence intervals (CIs) for relationships between 25(OH)D concentrations and survival were calculated using Cox and competing-risks regression. This observational study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) principles and employed three models.

For all-cause mortality, the multivariate-adjusted HRs (95 percent CIs) from the lowest to the highest 25(OH)D group (<25.0, 25.0 to <50, 50.0 to <75, and ≥75 nmol/l) were 1.00 (reference), 0.60 (0.42, 0.86), 0.46 (0.32, 0.67), and 0.52 (0.34, 0.78) (P for trend = 0.003). (Table 1). There was an 18% decreased risk of all-cause death for every one-unit increase in natural log-transformed 25(OH)D level (Table 1).

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Table 1: HR (95% CIs) for all-cause mortality according to serum 25(OH)D concentrations among patients with DKD in NHANES

Model	<25.0	Serum 25(OH)D	concentrations	(nmol/l)	P	Per one-unit increment in natural log-transformed 25(OH)D
Model 1*	1.00	0.60 (0.42, 0.86)	0.46 (0.32, 0.67)	0.52 (0.34, 0.78)	0.003	0.82 (0.73, 0.93)
Model 2) 1	1.00	0.63 (0.42, 0.95)	0.51 (0.34, 0.78)	0.55 (0.34, 0.88)	0.021	0.85 (0.73, 0.97)
Model 3*	1.00	0.45 (0.25, 0.83)	0.37 (0.20, 0.69)	0.33 (0.16, 0.68)	0.010	0.74 (0.59, 0.93)

∗Model 1: adjusted for age, sex, and race. †Model 2: further adjusted (from model 1) for BMI, education levels, and family income-poverty ratio. ‡Model 3: further adjusted (from model 2) for glucose, glycohemoglobin, total cholesterol, HDL, LDL, triglyceride, creatinine, and blood urea nitrogen.

The overall mean 25(OH)D concentration in the serum was 55.9 ± 26.3. Vitamin D deficiency (25ðOHÞD < 50 nmol/l),insufficiency(50 ≤ 25ðOHÞD < 75 nmol/l), and sufficiency (25ðOHÞD ≥ 75 nmol/l) were found in 552 (45.9%), 409 (34.0%), and 241 (20.0%) persons, respectively. After controlling for potential confounding factors, higher vitamin D levels were related with lower all-cause, nonaccidental, and malignant neoplasm-cause mortality in people with DKD. According to Lu Q et al., higher vitamin D levels were associated with a lower risk of all-cause and CVD-related death in individuals with diabetes and prediabetes.[4] The NHANES study with nationally representative samples with DKD and many potential confounding factors were adjusted to discover relative relationships are among the study's strengths.[3]

In total, evidence was established that DKD patients with high vitamin D levels had a decreased all-cause mortality rate. This finding suggested that maintaining appropriate vitamin D levels could help in the primary prevention of mortality in people with DKD.

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A case report of central diabetic insipidus caused by COVID-19 infection.

Insulinomas are rare insulin-secreting pancreatic neuroendocrine tumours (pNETs) with a 4 case per million annual incidences. Because of independent insulin secretion, most insulinomas are sporadic, solitary, and benign, yet they are associated with life-threatening hypoglycemia. Insulinomas are cancerous in about ten percent of cases, and 4 percent to seven percent are linked to multiple endocrine neoplasia syndrome type I. Insulinoma is frequently misdiagnosed due to its deceptive, vague symptoms that resemble other conditions such as mental illness.[1] Due to the increased amount of carbs taken to prevent or counter hypoglycemia, an individual with an insulinoma may present with increased body weight. An adolescent female presented with hypoglycemia due to an insulinoma as part of the multiple endocrine neoplasia type 1 syndrome, according to this study (MEN 1). [2]

Case Presentation:

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In the year 2020, the coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which causes the disease COVID-19 (coronavirus disease 2019), would have infected over 9.5 million individuals around the world. Although COVID-19 is well known for causing severe respiratory disease, it can also cause a variety of extrapulmonary symptoms.1 COVID-19 has the ability to impact multiple organ systems, which is one of its most notable characteristics. One of the problems with COVID-19, like other viral diseases, is the occurrence of both common and rare disease symptoms. Uncommon symptoms are more likely to go undetected for extended periods of time. COVID-19's endocrine presentation range is yet incomplete as an unusual manifestation. The paper describes a rare instance of diabetes insipidus as a probable late-onset response to infection with the severe acute respiratory syndrome coronavirus 2 (SARSCoV-2).2

Excessive thirst, growing polyuria, and polydipsia were all symptoms of a 50-year-old Iranian woman. She was diagnosed with COVID-19 six weeks prior to seeing the endocrinologist, after a reverse transcription-polymerase chain reaction (RT-PCR) test on a nasopharyngeal swab specimen. An initial laboratory test was performed to determine the aetiology of polyuria. Hyperglycemia was ruled out as a possibility. Renal ultrasonography revealed no abnormalities, and renal function tests revealed no abnormalities. Table 1 lists the results of several laboratory tests. Due to non-compliance with the test and a lack of consent, the water deprivation test was not conducted. 10 mcg desmopressin acetate (DDAVP) was given intranasally. (Table 2) The patient was diagnosed with central diabetes insipidus after laboratory tests revealed decreased urine osmolarity and high serum osmolarity. Urinary osmolarity increased after nasal desmopressin was given, and the patient's symptoms improved. Desmopressin medication, on the other hand, was required to stabilise her condition.

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Table 1: Laboratory results of the patients			
Laboratory test	**Result**	**Reference value**	**Unit**
White Blood Cells	6.5	4-11.3	10^3 x mm^3/ul
Red Blood Cells	6.2	4.5-6.4	106 x ml/mm^3
Hemoglobin	14.1	13.8-17	g/dl
Platelets	230	150-450	10^3 x mm^3/ul
FBS	93.1	80-110	mg/dl
Urea	14.3	16-60	mg/dl
Serum creatinine	0.84	0.70-1.42	mg/dl
Serum sodium	144	132-150	meq/l
Serum potassium	4.4	3.5-5	meq/l
TSH	4.11	0.32-5.2	mlU/l
Thyroxin (Total T4)	7.6	4.7-12.5	mg/dl
Prolactin	319	118-555	mlU/l
Cortisol (8 AM)	486.7	171-536	nmol/l

FBS fasting blood sugar, *TSH* thyroid-stimulating hormone,

Table 2: Laboratory results before and after desmopressin administration		
Laboratory test	**Before desmopressin**	**After desmopressin**
Serum sodium	144 meq/l	140 meq/l
Serum potassium	4.4 meq/l	4.2 meq/l
Serum osmolarity	298 mosm/l	289 mosm/l
Urine specific gravity	1.005	1.025
Urine output (24 h)	13,300 ml	2850 ml
Urine osmolarity (24 h)	164 mosm/l	810 mosm/l

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According to early findings, tanycytes and median eminence capillaries, which are part of the extremely permeable blood–brain barrier, contain angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine (TMPRSS), which may allow SARS-CoV-2 viral entry into the hypothalamus. Another theory is that after the acute clinical phase of the disease, SARS-CoV-2 may cause a delayed immune-mediated response that involves the central nervous system.[3] The patient in this investigation had a persistent small vessel infarction in the periventricular area, which could be the source of SARS-CoV-2 access to the hypothalamus. However, due to the constraints of this case study, the underlying process could not be proven. Unknown etiologies cannot be excluded out either.[2]

In cases of new-onset polyuria and polydipsia after COVID19 disease, central diabetes insipidus may be included in the clinical symptoms of the COVID-19. Despite this, no causal link has been shown between the patient's symptoms and the SARS-CoV-2 infection.

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