



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.

- Diabetic ketoacidosis drives COVID-19 related hospitalizations in children with type 1 diabetes
- Relationships between Hand Grip Strength, Upper Limb Anthropometric Characteristics and Hand Disability in Middle- Aged and Older Adults with Type-2 Diabetes Mellitus
- Efficacy and Safety of Imeglimin in Patients with Type 2 Diabetes Results from TIMES 1 study

Should you require any specific article or medical information, please feel free to contact us at

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

Diabetic ketoacidosis drives COVID-19 related hospitalizations in children with type 1 diabetes

In people with coronavirus disease 2019 (COVID-19), adults with type 2 diabetes mellitus are at increased risk for severe illness and increased mortality. However, there are fewer reports from populations of people with type 1 diabetes, and very little is known about these risks among children with type 1 diabetes. Severe illness and death from COVID-19 appear to be very rare among people with type 1 diabetes under age 55.



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T1D Exchange coordinated a US type 1 diabetes COVID-19 registry. Forty-six diabetes centers submitted pediatric cases for patients with laboratory confirmed COVID-19. Associations between clinical factors and hospitalization were tested with Fisher's Exact Test. Logistic regression was used to calculate odds ratios for hospitalization. The 33-question survey captures patient demographics, duration of type 1 diabetes, presenting symptoms, diabetes management and device use, comorbidities, relevant behaviors, highest level of care, duration of COVID-19 symptoms, and clinical outcomes in patients with positive SARS-CoV-2 PCR tests. Data presented here were collected between April 9, 2020 and January 15, 2021. The registry remains open.

Data from 266 patients with previously established type 1 diabetes aged <19 years with COVID-19 were reported. Diabetic ketoacidosis (DKA) was the most common adverse outcome (n=44, 72% of hospitalized patients). There were four hospitalizations for severe hypoglycemia, three hospitalizations requiring respiratory support (one of whom was intubated and mechanically ventilated), one case of multisystem inflammatory syndrome in children, and ten patients who were hospitalized for reasons unrelated to COVID-19 or diabetes. Hospitalized patients (n=61) were more likely than nonhospitalized patients (n=205) to have minority race/ethnicity (67% vs 39%, $p<.001$), public insurance (64% vs. 41%, $p<.001$), higher A1c (11% [97 mmol/mol] vs 8.2% [66 mmol/mol], $p<.001$), and lower insulin pump and lower continuous glucose monitoring use (26% vs 54%, $p<.001$; 39% vs 75%, $p<.001$). Age and gender were not associated with risk of hospitalization. Higher A1c was significantly associated with hospitalization,

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with an odds ratio of 1.56 (1.34-1.84) after adjusting for age, gender, insurance, and race/ethnicity

N = 266	Adjusted OR
A1c	1.56 (1.34, 1.84)
Age	0.98 (0.89, 1.08)
Female gender	0.88 (0.44, 1.74)
Public insurance	1.11 (0.48, 2.54)
Minority Race/ethnicity	1.34 (0.61, 2.95)

Hyperglycemia, shortness of breath, nausea, and vomiting were more common among hospitalized children compared to those who were not hospitalized. The frequencies of other symptoms did not differ between these two groups. The most common adverse outcome as DKA, which occurred in 72% of hospitalized patients and 16.5% of all patients. Most recent HbA1c was >9% (>65mmol/mol; median 11%, 97 mmol/mol) in 38 of the 44 patients (86%) with DKA. Four patients were hospitalized with severe hypoglycemia, and three received respiratory support, two of whom received oxygen by nasal cannula and one who underwent intubation with mechanical ventilation. There were no deaths.

Higher A1c remained the only predictor for hospitalization with COVID-19. Diabetic ketoacidosis is the primary concern.

Source: Alonso GT et al. J Diabetes. 2021 Apr 14. doi: 10.1111/1753-0407.13184. Epub ahead of print. PMID: 33855813.

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Relationships between Hand Grip Strength, Upper Limb Anthropometric Characteristics and Hand Disability in Middle-Aged and Older Adults with Type-2 Diabetes Mellitus

Diabetes is a significant health burden. The last few decades have witnessed an exponential increase in the prevalence of Diabetes Mellitus especially Type-2 Diabetes Mellitus (T2DM) due to series of lifestyle changes globally. Risk factors contributing to high preponderance of T2DM include but not limited to increasing prevalence of obesity, poor dietary habit, rapid urbanization, cigarette smoking, aging population and physical inactivity. The last four decades have witnessed an unprecedented increase in the prevalence of Diabetes Mellitus especially Type-2 Diabetes Mellitus (T2DM) due to series of lifestyle changes globally. Risk factors contributing to high preponderance of T2DM include but not limited to increasing prevalence of obesity, poor dietary habit, rapid urbanization, cigarette smoking, aging population and physical inactivity.

People with T2DM demonstrated poor and hand grip strength and moderate to high hand disability.

This cross-sectional study involved 150 patients with T2DM (male: $n = 83$; female: $n = 67$) receiving treatment at a Nigerian tertiary Hospital using purposive sampling method. Socio-demographic and physical characteristics data were recorded. HGS was measured using an electronic hand dynamometer while ULAC including right and left arm girth, forearm girth, wrist circumference, hand length, hand span and palm length were measured using a non-elastic tape measure. HdD was assessed using the upper extremity functional index. Data were analyzed using descriptive and inferential statistics. Alpha level was set at $p < 0.05$. The mean age of participants was 59.10 ± 12.13 years.

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Variable	Hand Disability		p-value
	OR ^a	95% CI	
Age category			
Middle age	1.00 (Ref)		
Older Adult	3.34	1.08-10.27	0.001 ^{**}
Gender			
Female	1.00 (Ref)		
Male	0.58	0.15-2.17	0.462
Marital status			
Single/divorced	1.00 (Ref)		
Married	0.94	0.31-2.82	
Widow/widower	1.52	1.30-1.77	0.121
Occupation			
Unemployed	1.00 (Ref)		
Civil servant	1.13	0.95-1.34	
Artisan/ Farmer	0.84	0.27-2.49	
Retiree	2.17	1.12-4.14	0.206
Time since diagnosis of T2DM (year)			
< 5	1.00 (Ref)		
> 5	2.83	2.58-3.12	0.032 [*]

^{*}p < 0.05; ^{**}p < 0.001; OR^a: Adjusted Odd Ratio; CI: Confidence Interval.

Logistic regression analysis of associations between hand disability, age group, socio-demographic characteristics and time since diagnosis among participants with poor hand grip strength (n = 82).

There were significant correlations between dominant, non-dominant HGS and selected ULAC ($p < 0.05$). Older adult; OR = 3.34, (95%CI = 1.08-10.27; $p = 0.001$) and above 5 years diagnosis of T2DM; OR = 2.83, (95%CI = 2.58-3.12; $p = 0.032$) showed significant associations with HdD.

People with T2DM demonstrated poor and hand grip strength and moderate to high hand disability. Furthermore, selected upper limb anthropometric characteristics were significantly correlated with handgrip strength. However, older adults and greater than 5 years since diagnosis of T2DM were possible risk factors associated with hand disability. Consequently,

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people with T2DM are possibly at greater risk of physical disability than their age-matched healthy counterparts.

Source: Awotidebe TO et al. Int J Diabetes Clin Res 8:135. doi.org/10.23937/2377-3634/1410135

Efficacy and Safety of Imeglimin in Patients with Type 2 Diabetes Results from TIMES 1 study

Type 2 diabetes is a widespread disease, affecting 500 million people worldwide. It is characterized by pancreatic islet b-cell dysfunction and peripheral insulin resistance leading to hyperglycemia. In addition to long-term lifestyle modifications, pharmacologic management is usually required to maintain effective glycemic control. Unmet medical needs are still a reality in type 2 diabetes, and new therapeutic agents with durable efficacy and improved pharmaceutical profiles are still needed.

Imeglimin is a first-in-class, novel, oral antidiabetic investigational agent to treat type 2 diabetes. Its mode of action is distinct from all other antihyperglycemic classes; imeglimin's underlying mechanism involves targeting of mitochondrial bioenergetics and improving mitochondrial function. Imeglimin modulates mitochondrial respiratory chain complex activities while decreasing reactive oxygen species production. Imeglimin has been shown to amplify glucose-stimulated insulin secretion by improving b-cell glucose responsiveness in patients with type 2 diabetes and to improve insulin sensitivity. The aim of this study was to investigate

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the efficacy and safety of imeglimin, the first in a new class of oral antidiabetic agent, in Japanese patients with type 2 diabetes.

This was a double-blind, randomized, parallel-group, placebo-controlled phase 3 trial in 30 sites in Japan. Eligible participants were individuals aged >20 years with type 2 diabetes treated with diet and exercise, stable for 12 weeks prior to screening, and whose HbA1c was 7.0–10.0% (53–86 mmol/mol). Patients were randomly assigned (1:1) to either oral imeglimin (1,000 mg twice daily) or matched placebo for 24 weeks. Investigators, participants, and the sponsor of the study remained blinded throughout the trial. The primary end point was the change in mean HbA1c from baseline to week 24, and the key secondary end point was the percentage of responders (according to two definitions) at week 24.

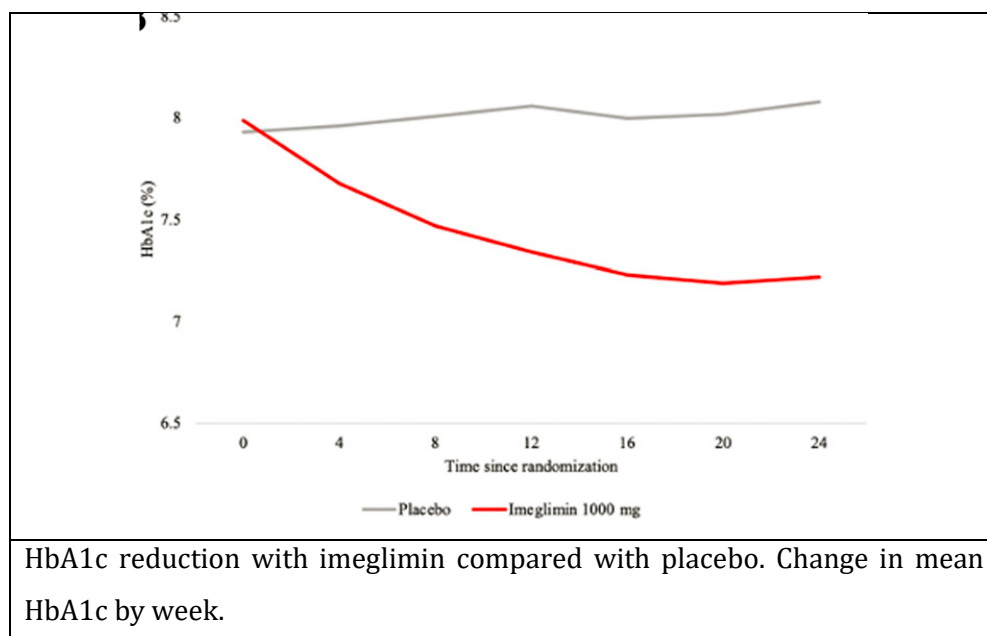
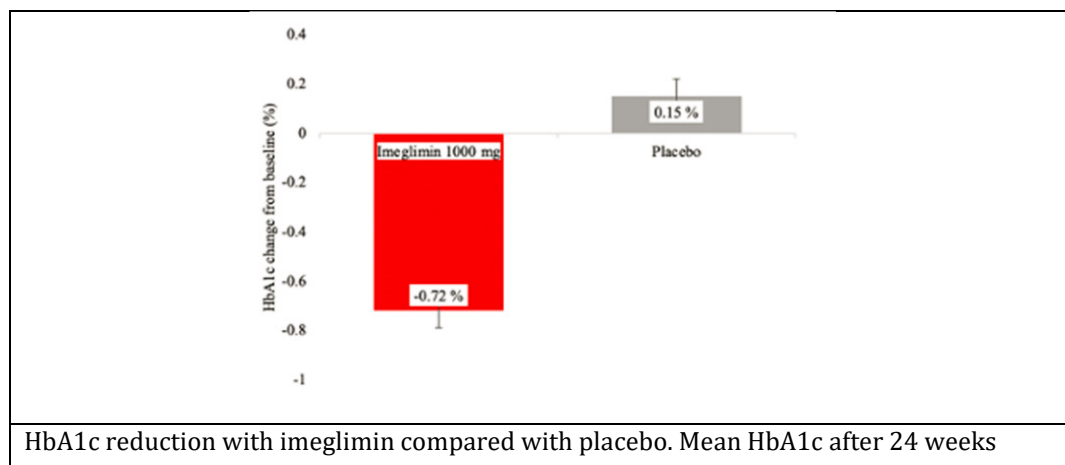
A total of 106 and 107 patients were randomly assigned to treatment with imeglimin and placebo, respectively. Compared with placebo, the adjusted mean difference in change from baseline HbA1c at week 24 was 20.87% (95% CI 21.04 to 20.69 [29.5 mmol/mol; 95% CI 211.4 to 27.5]; $P < 0.0001$). Forty-seven (44.3%) patients reported 1 adverse event in the imeglimin group versus 48 adverse events (44.9%) in the placebo group.

At week 24, HbA1c had significantly decreased by 0.72% (95% CI 20.86 to 20.58 [7.9 mmol/mol, 95% CI 29.4 to 26.3]) with imeglimin versus a nonsignificant increase of 0.15% (95% CI 0.01 to 0.29 [1.6 mmol/mol, 95% CI 0.1 to 3.2]) with placebo (estimated treatment difference vs. placebo: 20.87%, 95% CI 21.04 to 20.69 [29.5 mmol/mol, 95% CI 211.4 to 27.5]; $P, 0.0001$) (Fig.).

Imeglamin significantly improved HbA1c in Japanese patients with type 2 diabetes.

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At week 24, HbA1c ,7% (53 mmol/ mol) was achieved by significantly more patients in the imeglimin group (n=38 of 106 patients; 35.8%) compared

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with the placebo group (n =8 of 106 patients [7.5%]; P , 0.0001). At week 24, a relative decrease of >7% from baseline HbA1c was achieved by significantly more patients in the imeglimin group (n=61 of 106 patients; 57.5%) compared with the placebo group (n = 12 of 106 patients [11.3%]; P= 0.0001).

Imeglimin significantly improved HbA1c in Japanese patients with type 2 diabetes compared with placebo and had a similar safety profile to placebo. Imeglimin represents a potential new treatment option for this population.

Source: Dubourg J et al. Diabetes Care 2021 Apr; 44(4): 952-959.
<https://doi.org/10.2337/dc20-0763>



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