MICRO LABS LIMITED

Diabetes Update

Vol. 1 | Issue 14 | 2020

Dear Doctor,

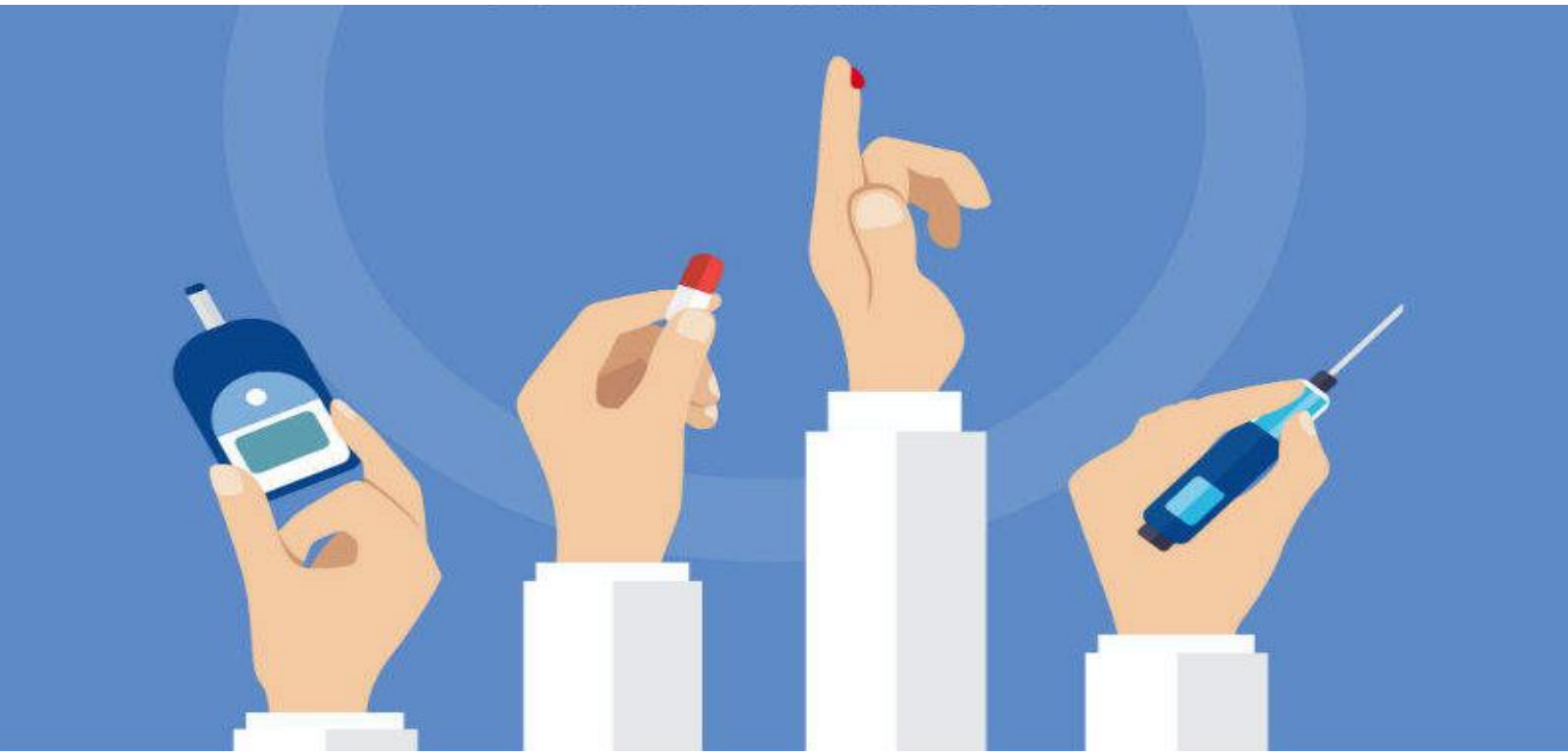
Greetings from Micro Labs Limited. We are happy to bring you **"DIABETES UPDATE"** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Association of Circulating Adhesion Molecules and HbA1c, Hypertension, Nephropathy, Retinopathy: TODAY Study
- Dyslipidemia in Children with Poorly Controlled Type 1 DM: A Cross Sectional Indian Study
- Maternal factors associated with hyperglycemia in pregnancy and perinatal outcomes

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



Association of Circulating Adhesion Molecules and HbA1c, Hypertension, Nephropathy, and Retinopathy: TODAY Study

Binding of mononuclear cells to vascular endothelium is an early step in the atherosclerotic process and is initiated by cellular adhesion molecules and chemokines, which play a key role in endothelial dysfunction and resultant plaque formation. Cellular adhesion molecules function in interactions between cells and extracellular membrane proteins to attract immune cells to the site of inflammation.

The Treatment Options for type 2 Diabetes in Adolescent and Youth (TODAY) study, a randomized clinical trial of three treatments for type 2 diabetes (T2DM) in youth, demonstrated treatment failure (defined as sustained HbA1c ≥8%, or inability to wean insulin after 3 months after acute metabolic decomposition) in over half of the participants. Given that binding of mononuclear cells to vascular endothelium, initiated by cellular adhesion molecules and chemokines, is an early step in vascular injury, Tryggestad et al. sought to evaluate 1) changes in cellular adhesion molecule levels during the trial, 2) effect of diabetes treatment, and 3) association of markers with HbA1c, hypertension, hypercholesterolemia, nephropathy, and retinopathy.

Participants (n=515) that had baseline assessment of adhesion molecules (MCP-1, VCAM, ICAM, and E-Selectin) and at least one other assessment, measured at month 12, 24, or 36, were included.

There were 515 TODAY participants with a baseline

measurement and at least one other annual assessment of adhesion molecule levels, measured at month 12, 24, or 36. The majority of participants (57%) had measurements at all four time points, 33% at three time points, and 9% at two time points. At baseline, participants averaged 13.9 ± 2.0 years of age, 33% black non-Hispanic, 43% Hispanic, 20% white non-Hispanic, with a median duration of diabetes of 5 months (Q1,Q3: 4,10), and average BMI 34.4 ± 7.5 kg/m^2. There were no differences in any of the anthropometric or biochemical measurements at TODAY baseline between the original cohort of 699 participants and the sub-cohort of 515 participants with ≥2 adhesion molecule measurements.

Over 1-3 years, significant increases in MCP-1 and decreases in VCAM (both $p<0.0001$) concentrations were found; however, no significant interactions were identified with treatment group for any molecule. For every 1% increase in HbA1c, ICAM increased by 1.8%, VCAM by 1.5%, and E-selectin by 6.8% (all $p<0.0001$). E-selectin increased by 3.7% and 4.2% for every 10 mm Hg increase in systolic and diastolic blood pressure, respectively (both $p<0.0001$). ICAM was 10.2% higher and E-selectin 15.5% higher in participants with microalbuminuria (both $p<0.01$). There was no significant association of adhesion molecule levels with retinopathy.

Longitudinal Association of Adhesion Molecules with Glycemic Control and Comorbidities, Adjusted for Age, Sex, and Concurrent BMI

	Adhesion Molecules			
	ICAM (pg/mL)	VCAM (pg/mL)	E-selectin (pg/mL)	MCP-1 (pg/mL)
HbA1c (per 1 %)				
% change	1.8	1.5	6.8	0.8
p-value	<0.0001	<0.0001	<0.0001	0.1222
Systolic Blood Pressure (per 10 mm Hg)				
% change	0.7	0.1	3.7	-0.6
p-value	0.3028	0.9099	<0.0001	0.5348
Diastolic Blood Pressure (per 10 mm Hg)				
% change	1.4	0.1	4.2	-0.3
p-value	0.0771	0.9366	<0.0001	0.7992
Hypertension (yes vs. no)				
% difference in means	1.3	1.1	3.3	2.3
p-value	0.5767	0.5795	0.1796	0.4265
LDL Dyslipidemia (yes vs. no)				
% difference in means	-2.7	-1.7	-0.1	-4.1
p-value	0.4400	0.5623	0.9840	0.3463
Microalbuminuria (yes vs. no)				
% difference in means	10.2	-1.3	15.5	4.1
p-value	0.0014	0.5966	<0.0001	0.2645
Hyperfiltration (yes vs. no)				
% difference in means	2.3	-0.7	-1.2	-2.3
p-value	0.3828	0.7533	0.6200	0.4386
Very Mild NPDR (yes vs. no)				
% difference in means	12.5	-3.3	5.7	2.6
p-value	0.2584	0.4157	0.3089	0.6562

Concentrations of cellular adhesion molecules rise with increasing HbA1c in youth with T2DM, and are associated with blood pressure and microalbuminuria, markers of vascular injury.

In conclusion, the study demonstrated that in youth with T2DM, circulating adhesion molecules levels change over time with an increase in MCP-1 and decrease in VCAM. E-selectin, ICAM, and VCAM were related to glycemic control and E-selectin was related to blood pressure. Further studies will be needed to determine if the circulating adhesion molecules could be used to predict risk for micro- and macrovascular disease in youth onset T2DM.

Source: Tryggestad JB et al. Pediatr Diabet. 2020 June [online ahead of print] https://publons.com/publon/10.1111/pedi.13062.

Dyslipidemia in Children with Poorly Controlled Type 1 DM: A Cross Sectional Indian Study

According to International Diabetes Federation report in 2019, among children and adolescents with type 1 diabetes, India has the highest prevalence (95.6 cases per 1000 children) and also the largest number of new cases (15.9 cases per 1000 children). Children with type 1 diabetes having dyslipidemia are at increased risk of developing premature atherosclerosis and cardiovascular disease. There is a wide variation in the occurrence of dyslipidemia and limited data available on dyslipidemia in Indian underprivileged children with type 1 diabetes, we conducted a study to estimate prevalence and predictors of dyslipidemia in Indian children and youth with poorly controlled type 1 diabetes.

The present study aims to determine the prevalence of dyslipidemia and its predictors in poorly controlled Indian children with type 1 diabetes. The cross-sectional study included 235 children and youth (3-18 years) with type 1 diabetes having disease duration of at least 1 year. Demographic data and laboratory findings were obtained from patients' records

Of the 235 children studied, 114 (48.5%) were boys and 121 (51.5%) were girls. The mean age of the children in the study group was 12.5 ± 3.9 years and the average duration of diabetes was 5.2 ± 3.3 years. The minimum and maximum age of the participants involved in the study was 3 years and 18.9 years respectively. The age wise distribution of children was as follows: 63 (26.8%) children

were under the age of 10 years and 172 (73.2%) children were above 10 years. 123 (52.4%) children had disease duration of less than 5 years and the remaining 112 (47.6%) children had disease duration greater than 5 years. The childrens' mean HbA1C was 10.7 ± 1.9% (93 ± 21 mmol/mol). 170 (72%) children were on basal bolus regimen and remaining 65 (28%) children were on split mix or modified split mix regimen (split mix regimen plus one short acting insulin at lunch).

The mean total insulin requirement in our cohort was 1.1 ± 0.3 units/kilogram/day. Seventy two (30.6%) children were prepubertal and the remaining 163 (69.4%) were in puberty or had completed their puberty; 78 (33.2%) children were in puberty and 85 (36.2%) children were post-pubertal. The number of obese and overweight children in our study was 7 (3%) and 27 (11.5%) respectively. The mean TSH of the study group was 1.46 ± 1.48 µIU/mL, with 229 children having TSH below 5 µIU/mL and 6 children having TSH between 5-10 µIU/mL.

High prevalence of dyslipidemia in children with type 1 diabetes including children under age of 10 years which emphasize the need for early screening and regular monitoring of lipid profile in these children

Association between dyslipidemia and clinical/laboratory findings

	Dyslipidemia (n=111)	No Dyslipidemia (n=124)	P value
Age (years)	12.9 ± 3.9	12.2 ± 3.9	NS
Disease duration (years)	5.2 ± 3.5	5.2 ± 3.3	NS
Height Z score*	-0.9 ± 1.1	-0.6 ± 1.1	0.019
Weight Z score	-0.7 ± 1.0	-0.6 ± 1.0	NS
BMI Z score	-0.3 ± 0.9	-0.5 ± 0.9	NS
Systolic BP percentile*	65.3 ± 26.4	57.9 ± 26.9	0.039
Diastolic BP percentile	77.5 ± 18.9	73.5 ± 19.8	NS
HbA1C (%)*	11.0 ± 2.1	10.4 ± 1.7	0.015
TSH (mIU/L)	1.66 ± 1.68	1.28 ± 1.25	0.049
Total Cholesterol (mmol/L)*	4.6 ± 1.0	3.6 ± 0.6	0.000
Triglycerides (mmol/L)*	0.9 ± 0.6	0.8 ± 0.4	0.000
LDL cholesterol (mmol/L)*	2.8 ± 0.9	1.8 ± 0.6	0.000

HDL cholesterol (mmol/L)*	1.2 ± 0.3	1.3 ± 0.2	0.012
Insulin (units/kg/day)	1.1 ± 0.3	1.1 ± 0.3	NS
Physical activity (mins)	62.9 ± 41.1	66.6 ± 49.4	NS
Fat (%)	19.3 ± 10.2	17.1 ± 9.4	NS
Fat Free Mass (%)	80.7 ± 10.2	82.9 ± 9.4	NS

The prevalence of dyslipidemia in the study was 47.2% with abnormal LDL cholesterol being the most common lipid abnormality. Poor glycemic control and higher TSH values were important predictors of likelihood of dyslipidemia and hypertriglyceridemia. Despite a low percentage of overweight and obese children in our study, body fat percentage was a significant predictor of likelihood of high total cholesterol and abnormal HDL. Interestingly, 28 children under the age of 10 years were found to have dyslipidemia which constitutes 11.9% of the total study group

Source: Shah N et al. Wiley Online Ped Diabet. June 2020. https://doi.org/10.1111/pedi.13063

Maternal factors associated with hyperglycemia in pregnancy and perinatal outcomes

Diabetes in pregnancy (DIP) and gestational diabetes mellitus (GDM), both of which are characterized by glucose intolerance first diagnosed in pregnancy, constitute a unique condition now named hyperglycemia in pregnancy (HIP). DIP is hyperglycemia diagnosed in early pregnancy using WHO diagnostic criteria for nonpregnant women; GDM is diagnosed in the second and third trimesters of pregnancy using IADPSG criteria based on the risk of adverse perinatal

results. GDM is the most common metabolic disorder that occurs during pregnancy, and it is associated with adverse short- and long-term effects on both the mother and offspring and an increased risk for future type 2 diabetes mellitus (T2DM), metabolic syndrome (MS) and cardiovascular disease (CVD).

While sufficient evidence supporting universal screening is not available, it is justifiable to look for specific risk factors for gestational diabetes mellitus (GDM) or hyperglycemia in pregnancy (HIP). The objective of this study is to identify independent risk factors for HIP and its adverse perinatal outcomes.

The study included 569 singleton pregnant women who were split into three groups by glucose status: GDM (n = 207), mild gestational hyperglycemia (MGH; n = 133), and control (n = 229). Women who used corticosteroids or had a history of DM were excluded. HIP comprised both GDM and MGH, diagnosed by a 100 g- or 75 g-oral glucose tolerance test (OGTT) and a glucose profile at 24–28 weeks. Maternal characteristics were tested for their ability to predict HIP and its outcomes. Bivariate analysis (RR; 95% CI) was used to identify potential associations. Logistic regression (RRadj; 95% CI) was used to confirm the independent risk factors for HIP and its perinatal outcomes ($p < 0.05$).

Age ≥ 25 years [1.83, 1.12–2.99], prepregnancy BMI ≥ 25 kg/m2 [2.88, 1.89–4.39], family history of DM [2.12, 1.42–3.17] and multiparity [2.07, 1.27–3.37] were independent risk factors for HIP. Family history of DM [169, 1.16–2.16] and hypertension [2.00, 1.36–2.98] were independent risk factors for C-section. HbA1c ≥ 6.0% at

birth was an independent risk factor for LGA [1.99, 1.05–3.80], macrosomia [2.43, 1.27–4.63], and birthweight Z-score > 2.0 [4.17, 1.57–11.10].

MGH presents adverse pregnancy outcomes similar to those observed in the GDM group but distinct from those observed in the control (no diabetes) group. In our cohort, age ≥ 25 years, prepregnancy BMI ≥ 25 kg/m2, family history of DM, and multiparity were independent risk factors for HIP, supporting the use of selective screening for this condition.

Results of the logistic regression analysis—adjusted risk (RRadj) and 95% confidence intervals (CIs) of maternal and pregnancy characteristics (exposure) for HIP and perinatal outcomes (response)

Exposure	Outcome	RR_{adj}	95% CI
Age ≥ 25 years	HIP	1.83	1.12–2.99
Prepregnancy BMI ≥ 25 kg/m^2		2.88	1.89–4.39
Family history of DM (1st degree)		2.12	1.42–3.17
Multiparity (≥ 2)		2.07	1.27–3.37
Family history of DM (1st degree)	C-section	1.69	1.16–2.16
Hypertension		2.00	1.36–298
Prepregnancy BMI ≥ 25 kg/m^2	1st C-section	0.45	0.27–0.57
HbA1c > 6.0%	LGA	1.99	1.05–3.80
	Macrosomia	2.43	1.27–4.63
	BW/GA Z-score > 2.0	4.17	1.57–11.10

Prepregnancy BMI ≥ 25 kg/m2, family history of DM, and multiparity were independent risk factors for HIP.

The results indicated that the intensity of maternal hyperglycemia affects pregnancy outcomes. MGH presents adverse pregnancy outcomes similar to those observed in the GDM group but distinct from the control (no

diabetes) group. In our cohort, age ≥ 25 years, prepregnancy BMI ≥ 25 kg/m2, family history of DM, and multiparity were independent risk factors for HIP, supporting the selective screening for this condition. The study results should be validated in populations with the same characteristics in Brazil or other low- or middle-income countries. Such results would provide evidence to determine the best approach for HIP diagnosis.

Source: Nicolosi et al. Diabetol Metab Syndr 2020. 12:49. https://doi.org/10.1186/s13098-020-00556-w