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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.

- **Impact of Visceral Fat Area and BMI on Arterial Stiffness among T2DM Patient's Cardiovascular Health Metrics**
- **Effects of key metabolites on the relationship between childhood obesity and insulin resistance**
- **Determination of clinical features and trends in drug use among type 2 diabetes mellitus patients**
- **Diabetic Striatopathy in a Patient with Poor Glycaemic Control and Abnormal Movements: A Case Report**

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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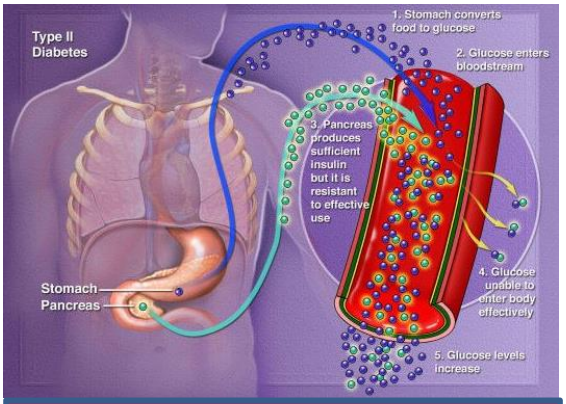
Impact of Visceral Fat Area and BMI on Arterial Stiffness among T2DM Patient's Cardiovascular Health Metrics

INTRODUCTION



TYPE 2 DIABETES

In individuals with type-2 diabetes, when it comes to assessing obesity using anthropometric measures within the seven ideal cardiovascular health metrics (ICVHMs), VFA (visceral adipose tissue) appears to be a more effective predictor of cardiovascular risk than BMI.

Cardiovascular disease (CVD) is a leading cause of disability and premature death globally, but CVD-related mortality has decreased in recent decades. People with type-2 diabetes mellitus (T2DM) are at twice the risk of CVD compared to those without diabetes, experiencing it earlier and more severely.[1] The American Heart Association (AHA) first proposed ideal cardiovascular health metrics (ICVHMs) in 2010. ICVHMs included seven items: ideal levels of untreated blood pressure (BP), fasting blood glucose (FBG), and total cholesterol (TC), as well as four behavioral metrics (non-smoking, ideal body mass index [BMI], physical activity at goal levels, and a recommended dietary pattern). Accumulating epidemiological data revealed that lower ICVHMs were linked to decreased CVD and all-cause mortality risks.[2] As the percentage of obese persons worldwide rises gradually, obesity-related morbidities are becoming a major issue in human civilization. Visceral fat is more strongly linked to cardiovascular risk than subcutaneous fat, it is well known that cardiovascular risk varies based on where body fat is located in our bodies.[3] The present study assessed the link between visceral fat area (VFA) as an obesity measure and arterial stiffness in seven ideal cardiovascular health metrics (ICVHMs).

METHODS

This was a multicenter study that used an observational, cross-sectional approach. It included 37,486 adult patients aged 18 or older diagnosed with T2DM. Out of these, 29,048 eligible

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participants were included in the final analysis, focusing on individuals aged 40 and above. These patients completed comprehensive questionnaires and underwent anthropometric measurements, lab tests, and diabetes complications screening at the beginning of the study. Data on demographics, lifestyle, family and medical history were collected through standardized questionnaires. Dietary habits were assessed by asking about daily fruit and vegetable intake. Physical activity was evaluated based on self-reported intensity, frequency, and duration. Smoking status, including duration, intensity, and time since quitting, were self-reported. Blood pressure was measured after a 5-minute rest using an automated sphygmomanometer. Glycated hemoglobin (HbA1c) and lipid profiles were analyzed at local medical centers. Arterial stiffness was assessed using brachial-ankle pulse wave velocity (BaPWV), with values of ≥1400 cm/s indicating increased stiffness. Multivariate regression models were employed to compare the effects of BMI and VFA on arterial stiffness.

RESULTS

The study included 29,048 participants, with 75.7% having arterial stiffness (baPWV over 1400 cm/s). Those with higher baPWV were generally older, had longer diabetes duration, more women, lower education, less physical activity, higher BMI, worse metabolic control, and fewer ideal cardiovascular health metrics (ICVHMs). They were also more likely to have a history of hypertension and hyperlipidemia. Participants with higher baPWV had greater visceral fat area (VFA), subcutaneous adipose tissue (SAT), larger waist circumferences, and waist-to-hip ratios. The ORs for baPWV ≥1400 cm/s were 1.08 for lower BMI and 0.85 for lower VFA after controlling for sex, age, duration of diabetes, history of stroke, coronary heart disease (CHD), and other ICVHM components. Low waist-to-hip ratio participants also

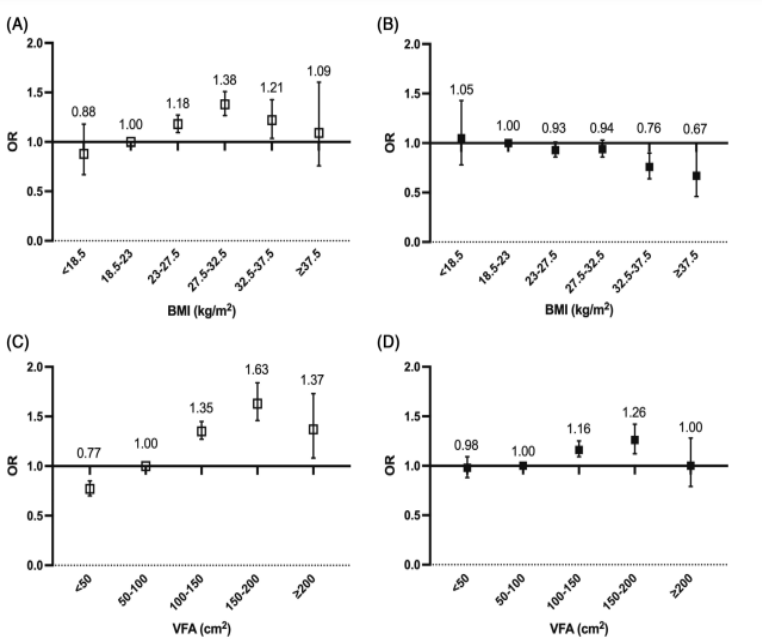

Figure 1. Odds ratio for arterial stiffness according to BMI categories (A, B) and VFA categories (C, D). Odds ratios are shown as numbers above each box, while the vertical lines show 95% confidence intervals. Odds ratios are shown in white boxes when they have been adjusted for age, sex, the length of diabetes, and stroke and CHD history. Black boxes represent odds ratios which have been corrected for age, sex, duration of diabetes, history of stroke and CHD and other ideal cardiovascular health measures. BMI- Body mass index, CHD- Coronary heart disease, OR- odds ratio, VFA- visceral fat area.

exhibited lower odds ratios for arterial stiffness. In categorical analysis, after adjusting for age, sex, duration of diabetes, history of stroke and CHD, and BMI levels between 18.5-23 kg/m^2 and 27.5-32.5 kg/m^2, participants in the higher category of BMI (27.5-32.5 kg/m^2) had a 38% higher risk of arterial stiffness. However, persons with the greatest BMI (>37.5 kg/m^2) displayed the lowest OR of arterial stiffness after additional correction for other ICVHM components. Conversely, the risk increased with a rising VFA. Prior to and following additional correction, persons with a VFA between 150 and 200 cm^2 were at the greatest risk of arterial stiffness (Figure 1). Subgroup analysis by sex and age revealed similar trends, with some variations. A higher number of ICVHMs decreased the risk of arterial stiffness, especially in participants with BMI ≥23 kg/m^2. In patients under the age of 60, the incremental risk for arterial stiffness was larger and associated with less ICVHMs.

DISCUSSION

This study found that higher VFA increased the risk of arterial stiffness, while lower BMI did not independently protect against lower baPWV. Additionally, combining VFA with other ICVHM components exhibited improved correlation. Similar results were seen across different ages and genders. Moreover, participants with VFA >100 cm^2 and more than three ICVHMs had a lower risk of arterial stiffness compared to those with normal VFA levels.[1] BaPWV had a notable positive correlation with BMI on its own, but this correlation decreased significantly when accounting for age, gender, and other cardiovascular risk factors.[4] Kammerlander et al. found that VFA had a stronger association with incident cardiometabolic risk factors and CVD events in women compared to BMI. However, this same outcome was not observed in men.[5]

CONCLUSION

In summary, there was a strong link between VFA and increased baPWV. Combining VFA with other ideal cardiovascular health metrics proved effective in predicting arterial stiffness. VFA appears to be a more accurate measure of body fatness than BMI when assessing cardiovascular health in T2DM patients. These findings suggest that using visceral adiposity may be advantageous for evaluating obesity in T2DM patients, rather than relying solely on BMI and ICVHMs.

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Effects of key metabolites on the relationship between childhood obesity and insulin resistance

INTRODUCTION

Obese children have common key metabolites associated with Insulin Resistance(IR), and by combining these key metabolites with BMI-SDS, it is possible to predict the likelihood of IR.

One of the biggest public health issues in the world today is childhood obesity. According to the World Health Organisation (WHO), the number of obese children worldwide has increased more than 10-fold in the past 40 years.[1] Childhood obesity frequently includes insulin resistance, which is thought to be a key factor in the association between adiposity and the risk of type 2 diabetes and cardiovascular disease. Another essential element of the metabolic syndrome is insulin resistance, which is becoming more common in paediatric patients, especially obese kids and teenagers. Increased levels of free fatty acids as well as several hormones and cytokines generated by adipose tissue are among the variables linked to the pathophysiology of obesity-related insulin resistance.[2] Metabolic abnormalities are also directly associated with insulin resistance, dyslipidaemia, changes in glucose metabolism, and type 2 diabetes mellitus. In this study, the prevalence of IR in children with normal weight and obesity were evaluated and checked for alterations in important metabolites linked to both conditions. This study identified promising biomarkers for the development, diagnosis, and assessment of childhood obesity and insulin resistance, and it is also extremely important for preventing IR in obese children .[1]

METHODS

A total of 259 participants, comprising 88 normal-weight children and 171 obese/overweight children aged 6 to 14 years were recruited. Various physical measurements, including height, weight and waist circumference (WC) were carried out. BMI was calculated and then the participants were categorized into normal weight and overweight/obese groups. After a 12-hour fasting period, 3ml of venous blood was drawn from each participant in the morning to

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measure fasting blood glucose (FBG) using the hexokinase method and fasting blood insulin (FBI) using radioimmunoassay. Additionally, insulin resistance was assayed through the homeostasis model. Acylcarnitine analysis was conducted using liquid chromatography-tandem mass spectrometry. The study employed multiple linear regression and correlation analysis to investigate the relationship between obesity, insulin resistance and metabolites. Differential metabolites were ranked for importance using random forest (RF) and relative operating characteristic curves were used for prediction purposes.

RESULTS

Obese children had higher BMI, waist circumference(WC), waist-to-height ratio, and hip circumference compared to the control group. No difference was observed in impaired fasting blood sugar, but insulin resistance (IR) differed. Metabolomics analysis was reliable with stable retention times, detecting 195 metabolites, of which 111 had a detection rates above 30%. 30 metabolites significantly differed between normal weight and obese groups. Childhood obesity negatively correlated with amino acids like glutamine (β = -1.675), citrulline (β = -0.415) and arginine (β = -1.210), while fatty acid metabolites increased. 12 metabolites had significant correlations with IR. Metabolites linked to both childhood obesity and IR were categorized into amino acid and fatty acid metabolites. RF models were used to assess the impact and importance of these metabolites on IR, shown in figure 1A for amino acids and figure 1C for fatty acids. Combining BMI-SDS with top 3 amino acid (glutamine, tyrosine, alanine) predicted IR at 80.0% accuracy (figure 1B). For fatty acid metabolites, combining BMI-SDS with

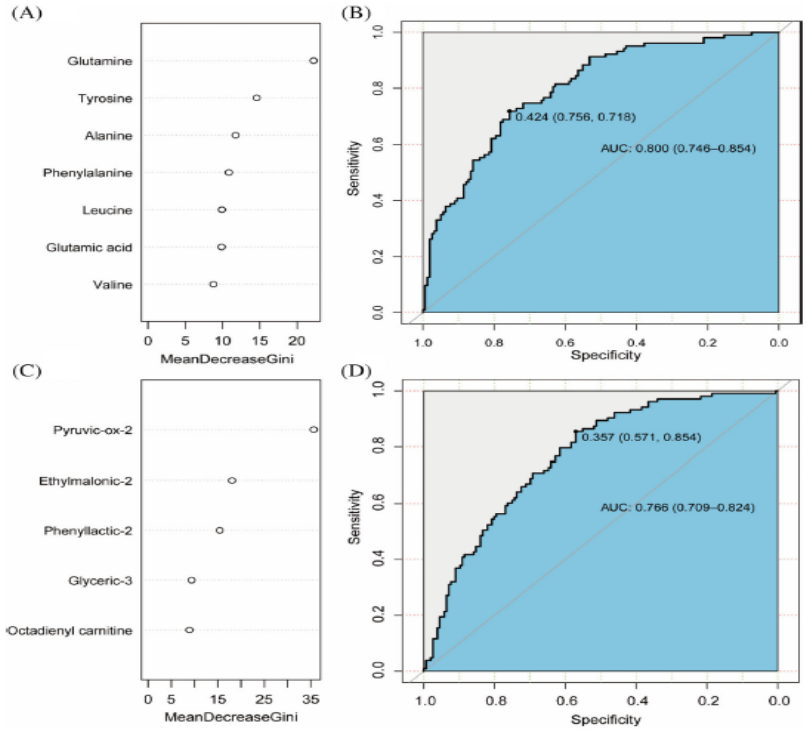

Figure 1. Ranking of various metabolites importance and accuracy in predicting IR. (A). Ranking of amino acid metabolites by significance using a random forest model. (B) the combined accuracy of BMI-SDS and the top three amino acid metabolites in predicting IR in children was 80.0%. (C). Ranking of fatty acid metabolites according to significance using a random forest model. (D) the combined accuracy of BMI-SDS and the top 3 fatty acid metabolites in predicting IR in children was 76.6%

pyruvic-ox-2, ethylmalonic-2, phenyllactic-2 had a AUC of 76.6% (figure 1D). Finally, combining BMI-SDS with the top three amino acids and top three fatty acids reached an 80.4% accuracy in predicting IR in children.

DISCUSSION

In current study, obese children had a significantly increased risk of insulin resistance. The findings suggest that the key metabolites are associated with IR in obese children. A combination of 3 amino acid metabolites (glutamine, tyrosine, alanine) and three fatty acid metabolites (pyruvic-ox-2, ethylmalonic-2, phenyllactic-2) proved effective in predicting IR.[1] Rupérez FJ study investigated potential associations between the observed metabolites and other clinical measurements as the HOMA index, total triglycerides, leptin, and adiponectin. Leptin and alanine together demonstrated a high IR discriminating value in the ROC analysis for both the entire cohort and, when taken into account individually, for boys and girls. It has been noted that obese children and adolescents commonly exhibit insulin resistance.[3]

CONCLUSION

Obese children faced a significantly increased risk of insulin resistance (IR). Multiple linear regression models and correlation analysis was used to examine the connections between specific metabolites and both obesity and IR. The findings suggest that these key metabolites are correlated with IR among obese children. Furthermore, a combination of 3 amino acid metabolites (glutamine, tyrosine, alanine) and three fatty acid metabolites (pyruvic-ox-2, ethylmalonic-2, phenyllactic-2) proved effective in predicting IR. Thus, this study offers valuable insights for predicting IR in children.

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Determination of clinical features and trends in drug use among type 2 diabetes mellitus patients

INTRODUCTION

People with Early-Onset Type 2 Diabetes (EOT2D) had worse metabolic control and were more likely to develop microvascular complications. When deciding on a course of treatment for EOT2D, it can be important to take into account utilizing a combination of novel hypoglycaemic drugs.

Diabetes has grown to be a major public health issue on a global scale in recent years. The majority of instances of diabetes (more than 90%) are caused by type 2 diabetes mellitus (T2DM).[1] Although type 2 diabetes is an aging-related condition, adult early-onset type has become more common worldwide. Early-onset diabetes is associated with an increased risk of acquiring cardiovascular and microvascular complications as compared to late-onset diabetes. Early-onset diabetes patients in Western and Asian nations have higher BMI, HbA1c, and low-density lipoprotein cholesterol (LDL-C) levels and more extensive family histories of the disease, according to studies conducted in hospital settings.[2] Less patients in the EOT2D group got organ-protective medications than in the late-onset type 2 diabetes (LOT2D) group, despite the fact that the first-line therapy for EOT2D, metformin, provides sustainable glycemic control in only half of the children and adolescents with T2DM.[1] So, this study aimed to assess the clinical characteristics and medication usage patterns between patients with EOT2D and LOT2D.

METHODS

A retrospective study was conducted among 1590 patients with T2DM. The data was gathered by retrospectively reviewing clinical information from patients, which encompassed various details like age, gender, age at diabetes onset, diabetes duration, family diabetes history, laboratory test results, and the specific drug regimens employed for diabetes management. Age at the onset of diabetes was determined by deducting the patient's age from the disease duration. Hospitalized adult patients with Type 2 Diabetes Mellitus (T2DM) were divided into two groups: Early-Onset T2DM (EOT2D) if diagnosed before turning 40, or Late-Onset T2DM (LOT2D) if diagnosed at or after the age of 40. The study included nine categories of drugs for lowering glucose levels, which encompassed metformin, sulfonylureas, α-glucosidase inhibitors (AGIs), thiazolidinedione's (TZDs), dipeptidyl peptidase-4 inhibitors (DPP-4i's), glinides, glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium-glucose cotransporter-2 inhibitors (SGLT2i's), and insulin. The measurements encompassed HbA1c, serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C),

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low-density lipoprotein cholesterol (LDL-C), and glucose levels. Statistical analysis was performed using IBM SPSS Statistics.

RESULTS

Out of the total patients, 609 (38.3%) had Early-Onset Type 2 Diabetes (EOT2D), with an average age of diagnosis at 32.2 years, while 981 patients had Late-Onset Type 2 Diabetes (LOT2D) with an average age of diagnosis at 49.6 years. EOT2D patients tended to be younger, had diabetes for a longer duration (13.4 years vs. 12.1 years), were more likely to have a family history of diabetes (75.0% vs. 63.1%), and had a higher body mass index (BMI) compared to LOT2D patients. Family history was identified as a risk factor for EOT2D. EOT2D patients had worse glycemic control, as indicated by higher average HbA1c levels and a lower proportion with HbA1c <7%. They also had lower levels of high-density lipoprotein cholesterol (HDL-C), higher triglyceride (TG) levels, and higher total cholesterol (TC) concentrations (Table 1). EOT2D patients were more likely to be obese and fewer had a BMI <24 kg/m^2. BMI decreased with the age of T2DM diagnosis, with the youngest group having the highest average BMI (28.03 kg/m^2) and the oldest group having a lower average BMI (25.09 kg/m^2). Additionally, EOT2D patients had higher rates of diabetic nephropathy and diabetic retinopathy, which remained significant even after adjusting for age, sex, and disease duration. Hypertension was more prevalent in LOT2D patients. Treatment choices also varied, with EOT2D patients more likely to use metformin, TZDs, SGLT2is, GLP-1RAs, and insulin, while LOT2D patients were more inclined to use AGIs, sulfonylureas, and glinides.

Table 1- Lipid profile, BMI, and glycemic management in individuals with LOT2D and EOT2D.

Clinical index	EOT2D (n = 609) Mean/number (SD or %)	LOT2D (n = 981) Mean/number (SD or %)
HbA1c, %	8.9 (2.0)	8.7 (2.0)
TC, mmol/L	4.8 (1.4)	4.5 (1.2)
LDL-C, mmol/L	2.7 (1.0)	2.6 (0.9)
HDL-C, mmol/L	1.1 (0.3)	1.1 (0.3)
HbA1c <7%	89 (14.6%)	204 (20.8%)
LDL-C <2.6 mmol/L	292 (47.9%)	498 (50.8%)
BMI, kg/m^2	26.8 (4.7)	25.7 (3.7)
Overweight	242 (39.7%)	430 (43.8%)
Obesity	209 (34.3%)	233 (23.8%)
BMI <24 kg/m^2	158 (25.9%)	318 (32.4%)

DISCUSSION

In present study, the EOT2D was observed at average age of 32.2 years. EOT2D patients tended to be younger, were more likely to have a family history of diabetes, and had a higher body mass index (BMI). EOT2D patients had higher rates of diabetic nephropathy and diabetic retinopathy.[1] According to the seminal SEARCH Study1, 13.7% of all young persons with

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diabetes has early-onset T2DM, and this number is increasing year by 4.8%.[3] People with young-onset and early-onset type 2 diabetes have higher excess risks of mortality and macrovascular and microvascular complications compared to those with late-onset diabetes.[4]

CONCLUSION

Patients diagnosed with Early-Onset Type 2 Diabetes (EOT2D) had poorer control over their metabolism and a higher likelihood of experiencing microvascular complications. It might be necessary to think about using a combination of new hypoglycemic medications when choosing treatment for EOT2D. This research underscores the significance of screening for diabetes in younger individuals with elevated risk factors and the yearly examination of diabetes-related complications in EOT2D. Further investigations should extend the observation period to study the impacts of diverse therapies in the future.

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Diabetic Striatopathy in a Patient with Poor Glycaemic Control and Abnormal Movements: A Case Report

INTRODUCTION

Diabetic striatopathy(DS) is a rare hyperkinetic movement disorder that results from either nonketotic or hyperketotic high blood sugar levels.[1] It is linked to basal ganglia involvement and characterized by contralateral, continuous, non-rhythmic, dancing-like motions with a

Combining the patient's clinical symptoms with the distinctive features observed in brain MRI can be an effective diagnostic approach for Diabetic striatopathy.

flailing component on one side of the body. Around 1 in 100,000 patients are thought to be affected. This condition has previously been described in elderly individuals who also had concomitant seizures and were hyperglycemic but not ketotic, with full or partial remission of hemiballismus-hemichorea (HBHC) after glycaemic management and serum osmolality.[2] Here, a case of 72-year-old man with T2DM, ischemic heart disease and dyslipidemia experiencing involuntary upper limb movements for 3 weeks with subtle mouth and tongue movements was presented.

CASE PRESENTATION

A 72-year-old man with type-2 diabetes, ischemic heart disease, and dyslipidemia experienced involuntary movements in his arms and mouth for 3 weeks, with left side being more affected. Despite the worsening symptoms, his speech, swallowing and gait remained normal. He was on multiple medication, but his poor compliance was noted over the past month. He had minimal exposure to toxins, drank alcohol socially and occasionally smoked. On examination, his vital signs were stable and his heart, lungs and abdomen were normal upon examination. The neurological exam revealed high-amplitude, sudden and violent movements in his arms, primarily on the left side, along with subtle tongue and lip movements. His glycated hemoglobin (HbA1C) level was 8.5% on admission. Brain scans showed abnormalities in the basal ganglia with CT scans showing hyper-densities and MRI scans revealing varying signal intensities in different sequences (Figure 1). These findings indicated a condition called striatopathy, likely related to his diabetes. He was started on treatment with subcutaneous insulin. Within 12 hours of achieving glycemic control, there was a significant improvement in his clinical condition. Further investigations were conducted to rule out other potential diagnosis, but no evidence of infection or diabetic ketoacidosis was found. He was transitioned to twice-a-day premixed insulin and by the third day, all involuntary movements had resolved. During follow-up as an outpatient, his neurological findings remained normal with well-controlled blood sugar levels in fasting and postprandial states.

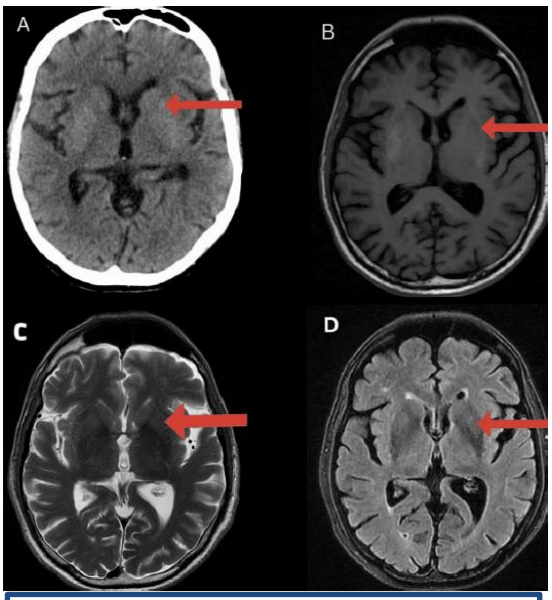

Figure 3 (A)Brain CT scan without contrast (B) MRI with T1 sequence (C) MRI with T2 sequence (D) MRI with FLAIR sequence. Arrows highlight alterations in the opposite side striatum, potentially linked to diabetic striatopathy.

FLAIR: fluid-attenuated inversion recovery

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DISCUSSION

The current study showed DS is marked by hemiballismus-hemichorea (HBHC). The patient experienced involuntary movements in his arms and mouth for 3 weeks, with left side being more affected. Brain scans showed abnormalities in the basal ganglia with CT scans showing hyperdensities and MRI scans revealing varying signal intensities in different sequences. He was started on treatment with subcutaneous insulin. Within 12 hours of achieving glycaemic control, there was a significant improvement in his clinical condition.[1] Similar study by Xu Y et al. showed that hemichorrea, contralateral striatal T1WI hyperintensity, and CT hyperdensity are characteristics of DS.[3] On a head MRI, the left lentiform nucleus had a high T1-weighted signal intensity. With proper blood glucose management and low-dose haloperidol, HBHC greatly improved.[2]

CONCLUSION

DS is a rare movement disorder connected to uncontrolled diabetes and marked by hemiballismus-hemichorea (HBHC). It's unusual for it to affect both sides, making this case unique. Diagnosing DS is challenging due to many possible HBHC causes. Using clinical symptoms and brain MRI can help diagnose DS effectively. Future research should try to organize a standard DS diagnosis protocol.

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