



Diabetes Update

Vol. 3 | Issue 37 | 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.

- A higher neutrophil count in diabetic persons raises the risk of developing chronic kidney disease
- Early clinical outcome and stent restenosis following carotid artery stenting: Effect of diabetes mellitus
- A Study on Relationship between subclinical atherosclerosis and the blood creatinine to cystatin C ratio in people with type 2 diabetes
- A Case Study on Autoimmune Hypoglycaemia

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Looking forward to your valuable feedback

Diabetes Update

Vol. 3 | Issue 37 | 2022

A higher neutrophil count in diabetic patients raises the risk of developing chronic kidney disease

Thirty to forty percent of people with diabetes mellitus are affected by diabetic kidney disease (DKD), which is the most frequent cause of chronic renal disease. A decline in kidney function and worsening albuminuria are features of DKD development, which is linked to an increase in cardiovascular and all-cause mortality.¹ White blood cell (WBC) count, neutrophil count, and neutrophil-to-lymphocyte ratio (NLR) routine inflammatory blood cell measures have been looked at for a relationship with and potential to predict diabetes and CKD. The purpose of this study was to look into any possible relationships between peripheral inflammatory blood cell parameters and the occurrence and development of chronic kidney disease (CKD) in individuals with diabetes.²

A total of 3582 diabetic patients were screened, and 3252 of them agreed to participate in the study. In all, 1192 diabetic individuals (291 with CKD and 901 NCKD) participated in the cross-sectional study. To assess the relationship between peripheral inflammatory blood cells and CKD, logistic regression and Cox proportional hazards models were applied.

Even after 1:1 case-control matching for age, gender, history of high blood pressure, and duration of diabetes, neutrophil count fared best as an independent risk factor for CKD in the cross-sectional analysis (odds ratio 2.556 [95 percent confidence range 1.111, 5.879]). A substantial linear correlation between the incidence of CKD and a continuous neutrophil count greater than 3.6 10⁹/L was found via spline regression.

Diabetes Update

Vol. 3 | Issue 37 | 2022

After fully controlling for relevant confounders, the findings of the Cox regression analysis revealed that only neutrophil count was independently linked with CKD progression (the highest group vs. the lowest group, hazard ratio 2.293 [95 percent confidence range 1.260, 4.171]). With increasing neutrophil count, the cumulative incidence of CKD development in diabetic patients gradually rose (53 (7.7%) subjects in the lowest group, 60 (8.2%) in the middle group, and 78 (12.2%) in the highest group) (Table 1 and Figure 1).

Table 1: Adjusted hazard ratios of incidence of estimated glomerular filtration rate decrease >30% in relation to tertile of neutrophil count among subjects with diabetes

	Incident case	Crude HR (95% CI)	p	Model 1	p	Model 2	p
Neutrophils							
Lowest group	53 (7.7%)	1.00 (reference)		1.00 (reference)		1.00 (reference)	
Middle group	60 (8.2%)	1.038 (0.717-1.502)	0.844	1.122 (0.766-1.643)	0.554	1.000 (0.524-1.908)	0.999
Highest group	78 (12.2%)	1.547 (1.091-2.193)	0.014	1.651 (1.146-2.378)	0.007	2.293 (1.260-4.171)	0.007
NLR							
Lowest group	55 (7.8%)	1.00 (reference)		1.00 (reference)		1.00 (reference)	
Middle group	65 (9.4%)	1.185 (0.825-1.704)	0.358	1.234 (0.850-1.793)	0.269	1.358 (0.770-2.397)	0.291
Highest group	73 (10.6%)	1.327 (0.932-1.890)	0.117	1.466 (1.013-2.122)	0.043	1.415 (0.781-2.565)	0.252

Note: Model 1: adjustment for gender, age, BMI; model 2: model 1 plus adjustment for HbA1C, ALT, history of HBP, total cholesterol, triglyceride, HDLcholesterol, LDL-cholesterol. Abbreviations: ALT, alanine transaminase; BMI, body mass index; CI, confidence interval; HbA1C, glycosylated hemoglobin; HBP, high blood pressure; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein; NLR, neutrophil-to-lymphocyte ratio.

Diabetes Update

Vol. 3 | Issue 37 | 2022

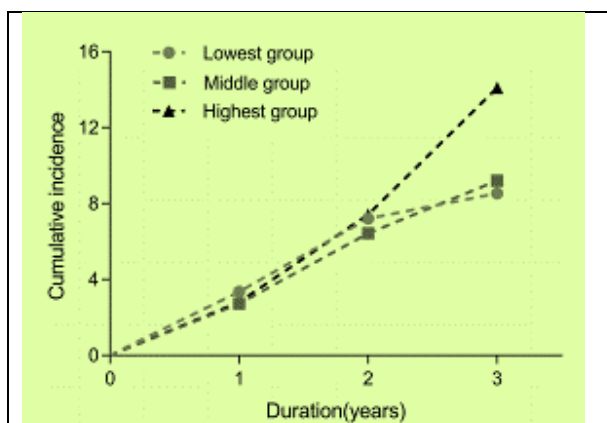


Figure 1: Cumulative incidence of nephropathy by tertile of neutrophil count in the cohort study.

The first study with a sizable sample size to independently link neutrophil count—rather than WBC, lymphocyte count, or NLR—with the progression of CKD in patients with diabetes is this cross-sectional investigation and retrospective cohort analysis.² The main elements of the WBC count are the lymphocyte and neutrophil counts, and an increase in WBC in CKD would primarily be attributable to an increase in neutrophils. The increased NLR was most likely caused by higher neutrophil counts and lower lymphocyte counts since NLR is the ratio of neutrophil count to lymphocyte count. Neutrophils, which make up the majority of white blood cells, play a role in long-lasting, meta-inflammatory conditions such as obesity, insulin resistance, type 2 diabetes, gestational diabetes mellitus, and coronary artery disease.^{2,3}

According to this study, neutrophil count is a standalone risk factor for CKD advancement in diabetic patients.

Diabetes Update

Vol. 3 | Issue 37 | 2022

References:

1. Bonner R, Albajrami O, Hudspeth J, Upadhyay A. Diabetic Kidney Disease. Prim Care. 2020 Dec;47(4):645-659.
2. Zhang R, Chen J, Xiong Y, Wang L, Huang X, Sun T, Zha B, Wu Y, Yan C, Zang S, Zhou Q, Huang Z, Liu J. Increased neutrophil count Is associated with the development of chronic kidney disease in patients with diabetes. J Diabetes. 2022 Jul;14(7):442-454.
3. Sun T, Meng F, Zhao H, Yang M, Zhang R, Yu Z, Huang X, Ding H, Liu J, Zang S. Elevated First-Trimester Neutrophil Count Is Closely Associated With the Development of Maternal Gestational Diabetes Mellitus and Adverse Pregnancy Outcomes. Diabetes. 2020 Jul;69(7):1401-1410.

Early clinical outcome and stent restenosis following carotid artery stenting: Effect of diabetes mellitus

It has been demonstrated that in people with diabetes, the prevalence of carotid atherosclerosis (CA) is strongly correlated with cardiovascular events. It was discovered that patients with asymptomatic carotid artery stenosis (CAS) and diabetes have a very high chance of dying from cardiovascular causes. It is estimated that 8 to 15 percent of ischemic strokes are caused by internal CAS, a major contributing factor.¹ In this study, the effectiveness of percutaneous carotid revascularization was compared in diabetic and nondiabetic individuals, and the effects of DM on the results of CAS were also assessed.²

Patients who underwent percutaneous treatment for carotid artery stenosis were the subject of this retrospective, two-center investigation. In the database, patients were sorted into two groups and studied. Patients without diabetes made up the first group, while those with diabetes made up the

Diabetes Update

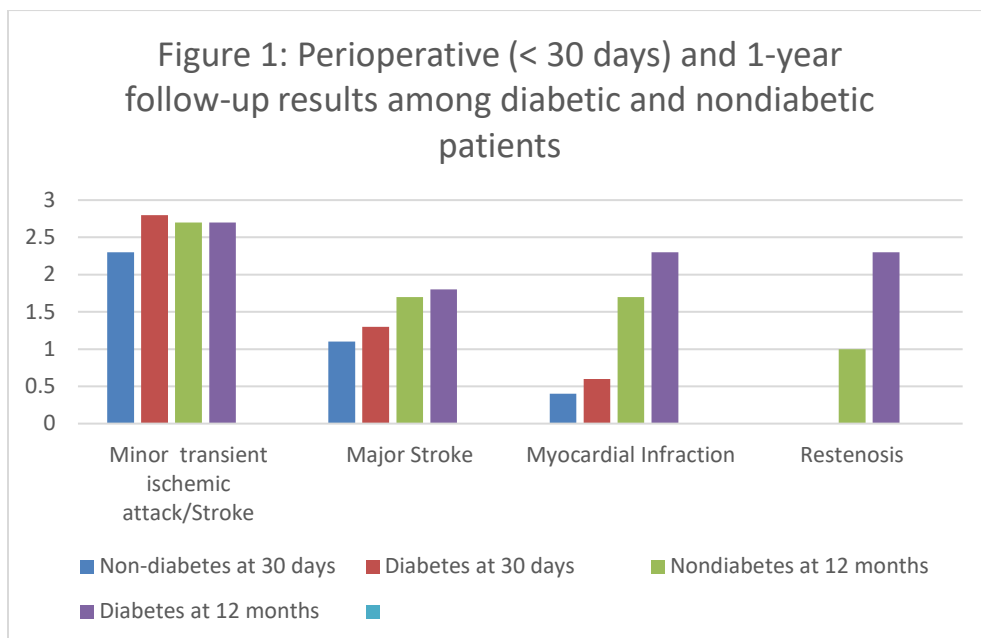
Vol. 3 | Issue 37 | 2022

second. All patients who had previously received a diagnosis of diabetes mellitus were regarded as diabetics (oral or insulin controlled glycaemia). Clinical problems, interventional devices, stent type, procedure results, and baseline demographic and clinical variables were noted. The combined risk of any stroke, MI, or death within 30 days was the main result (perioperative). The incidence of stroke, mortality, and restenosis one year after the surgery served as secondary end points. It was also examined how the restenosis rate related to other important parameters including stent design, postdilatation, antiplatelet, and/or statin medication.

There were 730 diabetic patients present, and their BMI, blood pressure, frequency of chronic dialysis, and dyslipidemia were all significantly higher ($p < 0.05$). In terms of early and late MACCEs (composed of transient ischemic attack, major stroke, myocardial infarction, and death), there was no significant difference between the two groups, with an early rate of 3.5 percent for non-diabetics vs. 5.3 percent, $p = 0.08$ and 2.4 non-diabetics vs. 2.3 percent diabetics, $p = 0.1$ at 12 months. The restenosis rate was greater in the diabetes population (2.3 percent vs. 1 percent, $p = 0.04$) and the overall stroke/death rate in the asymptomatic individuals was 2.4 percent. (Figure 1).

Diabetes Update

Vol. 3 | Issue 37 | 2022



This study demonstrated that when carotid stenting is used as a treatment, patients with diabetes and severe carotid stenosis share similar periprocedural stroke and death risks as nondiabetic patients (perioperative stroke and death rate: nondiabetics 1.7 percent vs. diabetics 2.0 percent; $p = 0.08$). The 30-day stroke/death rates following CEA in asymptomatic insulin-dependent DM patients exceeded worldwide vascular societies' guideline thresholds for acceptable outcomes in asymptomatic individuals, especially those with anatomic high-risk criteria, making the study's findings even more pertinent. In a 2000-chinese cohort described by Jiao et al., general metabolic syndrome was also a risk for short-term MACCEs following CEA, but not CAS. However, it must be acknowledged that these data originate from an observational, retrospective study and that we did not distinguish between insulin-dependent and non-insulin-dependent diabetics in our analysis.^{2,3}

Diabetes Update

Vol. 3 | Issue 37 | 2022

An acceptable elevated periprocedural risk for CAS was linked to diabetes, but no new risks surfaced throughout the course of longer-term follow-up. The rate of early in-stent restenosis may increase as a result of diabetes.

Reference:

1. Klimontov VV, Koroleva EA, Khapaev RS, Korbut AI, Lykov AP. Carotid Artery Disease in Subjects with Type 2 Diabetes: Risk Factors and Biomarkers. J Clin Med. 2021 Dec 24;11(1):72.
2. Achim A, Lackó D, Hüttl A, Csobay-Novák C, Csavajda Á, Sótónyi P, Merkely B, Nemes B, Ruzsa Z. Impact of Diabetes Mellitus on Early Clinical Outcome and Stent Restenosis after Carotid Artery Stenting. J Diabetes Res. 2022 Jul 11;2022:4196195.
3. Bai XS, Feng Y, Wang T, Zhang X, Yang CL, Wang YB, Hua Y, Lu J, Zhu FS, Chen YF, Gao P, Yang RJ, Ma Y, Jiao LQ. Impact of metabolic syndrome on short-term outcome of carotid revascularization: a large sample size study in Chinese population. Chin Med J (Engl). 2020 Nov 20;133(22):2688-2695.

A Study on Relationship between subclinical atherosclerosis and the blood creatinine to cystatin C ratio in people with type 2 diabetes

A common consequence of type 2 diabetic mellitus (T2DM) is atherosclerosis (AS). In order to effectively control T2DM, early AS identification and intervention are crucial.¹ In the elderly population, T2DM has apparently been linked to a 1.55-fold increased risk of sarcopenia. Sarcopenia index (SI), which is determined by multiplying (serum creatinine/cystatin C) by 100, is said to be related to sarcopenia.² The relationship between SI and subclinical atherosclerosis has only been briefly studied. This investigation examined the relationship between SI and brachial-ankle pulse wave velocity-measured preclinical atherosclerosis (baPWV).³

Diabetes Update

Vol. 3 | Issue 37 | 2022

In this cross-sectional study, 174 patients with type 2 diabetes were included. The Pearson correlation coefficient was used to evaluate the connection between SI and baPWV. Receiver operator characteristic (ROC) analysis was carried out to determine the SI's area under the ROC curve (AUC) for the presence of subclinical atherosclerosis, defined as baPWV >1800 cm/s. After controlling for confounders, logistic regression analyses were used to determine how SI affected the prevalence of subclinical atherosclerosis.

The mean age, length of diabetes, baPWV, and SI were, respectively, 66.9 (10.1), 17.7 (11.6), 1802 (372) cm/s, and 77.6 (15.8) years old. SI and baPWV were associated (men: $r=-0.25$, $p=0.001$, and women: $r=-0.37$, $p=0.015$). The ideal SI cut-off value for the presence of subclinical atherosclerosis was 77.4 (sensitivity = 0.72; specificity = 0.58; $p < 0.001$; AUC = 0.66; 95% CI: 0.57 to 0.74). (Figure 1). The prevalence of subclinical atherosclerosis was also linked to SI (adjusted OR 0.95, 95 percent CI: 0.91 to 0.99, $p=0.015$).

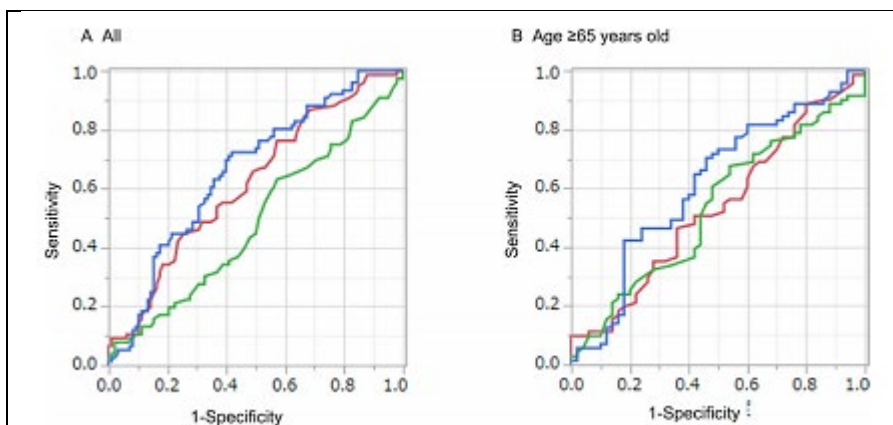


Figure 1: Receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) of cysteine C, creatinine, or sarcopenia index for subclinical atherosclerosis.

Red line represents cysteine C (AUC 0.62, 95% CI 0.53 to 0.70), green line represents creatinine (AUC 0.49, 95% CI 0.40 to 0.57), and blue line represents sarcopenia index (AUC 0.66, 95% CI 0.57 to 0.74)

Diabetes Update

Vol. 3 | Issue 37 | 2022

This study demonstrated a relationship between SI and the prevalence of subclinical atherosclerosis in people with type 2 diabetes mellitus (T2DM). It also made clear that there is a relationship between SI and baPWV.3 According to a study by Zeng F et al, anaemia and sarcopenia both increase the risk of cardiovascular disease (10-year CVD risk) in people with type 2 diabetes. Loss of muscle mass can predict CVD risk in diabetic individuals independently.⁴

Conclusion: In people with type 2 diabetes, SI is related to the occurrence of subclinical atherosclerosis.

Reference:

1. Li J, Shanguan H, Chen X, Ye X, Zhong B, Chen P, Wang Y, Xin B, Bi Y, Zhu D. Advanced glycation end product levels were correlated with inflammation and carotid atherosclerosis in type 2 diabetes patients. *Open Life Sci.* 2020 Jun 11;15(1):364-372.
2. Takahashi F, Hashimoto Y, Kaji A, Sakai R, Okamura T, Kitagawa N, Okada H, Nakanishi N, Majima S, Senmaru T, Ushigome E, Hamaguchi M, Asano M, Yamazaki M, Fukui M. Sarcopenia Is Associated With a Risk of Mortality in People With Type 2 Diabetes Mellitus. *Front Endocrinol (Lausanne).* 2021 Nov 11;12:783363.
3. Hashimoto Y, Takahashi F, Okamura T, Osaka T, Okada H, Senmaru T, Majima S, Ushigome E, Nakanishi N, Asano M, Hamaguchi M, Yamazaki M, Fukui M. Relationship between serum creatinine to cystatin C ratio and subclinical atherosclerosis in patients with type 2 diabetes. *BMJ Open Diabetes Res Care.* 2022 Jun;10(3):e002910.
4. Zeng F, Huang L, Zhang Y, Hong X, Weng S, Shen X, Zhao F, Yan S. Additive Effect of Sarcopenia and Anemia on the 10-Year Risk of Cardiovascular Disease in Patients with Type 2 Diabetes. *J Diabetes Res.* 2022 Jan 24;2022:2202511.

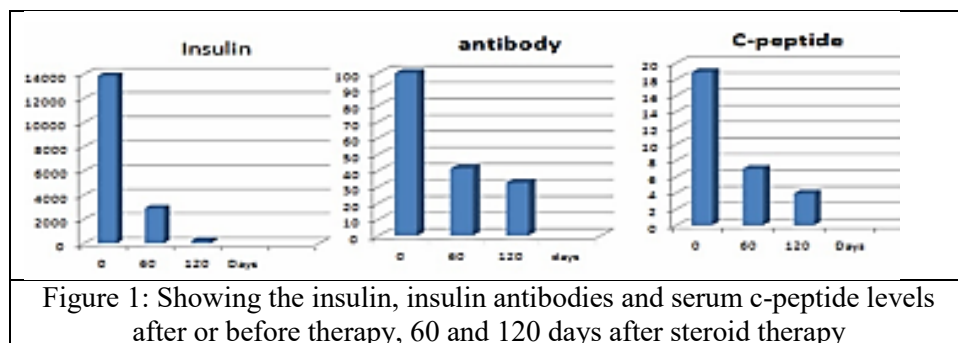
Diabetes Update

Vol. 3 | Issue 37 | 2022

A Case Study on Autoimmune Hypoglycaemia

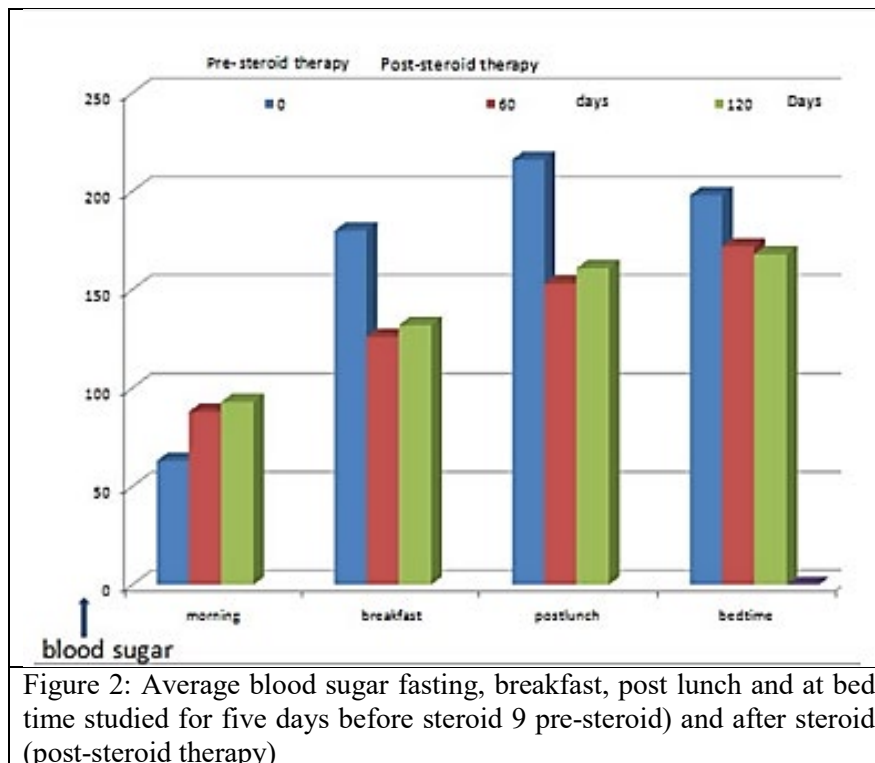
Insulin autoimmune syndrome (IAS), also referred to as Hirata's disease or insulin autoimmune hypoglycemia, is a rare autoimmune condition that can result in fasting and/or postprandial hypoglycemia, high serum concentrations of total immunoreactive insulin, and the presence of insulin autoantibodies in people who have never taken exogenous insulin before.¹ This paper is reporting a typical IAS instance.²

A 50-year-old man complained of experiencing frequent giddiness, sweating, palpitations, tremors, and a sense of impending death for the previous 14 months. After eating food or sweets, these symptoms subsided. A neurologist and six other doctors examined him. He received anti-platelet medication and had a brain MRI, but neither procedure had any positive effects. 18.88 ng/mL of C-peptide was present in his serum (normal 0.90-7.1). Our initial assumption was an insulinoma, but the pancreas' MRI (appendix) was normal and there was no acanthosis nigricans. Serum insulin antibody was present and greater than 100 u/mL. The level of D-hydroxybutyrate (a ketone body) was 0.02 mmol/L. (normal 0.02-0.27). The most accurate indicator of ketosis, D-3 hydroxybutyrate, made up 78% of the ketone bodies found in blood. He began oral steroid medication at 1 mg/kg body weight with the understanding that autoimmune hypoglycemia might be present. The average body weight before and after receiving 1 mg/kg of steroids tapered during a six-week period (Figures 1 and 2).



Diabetes Update

Vol. 3 | Issue 37 | 2022



Hirata originally described the illness in Japan in 1970. Despite this, IAS is challenging to identify in patients with newly-onset hypoglycemia because it is frequently concealed by other conditions like sepsis, alcohol intoxication, starvation, insulin resistance, and drug overdose. Hypoglycemia can also result from a number of anatomical issues, such as adrenal insufficiency, excessive insulin production from an insulinoma, and islet hyperplasia.¹ IAS can be treated by stopping the offending medication, following a low-carbohydrate diet, or frequently by using glucocorticoids.³

In conclusion, it is important to check the fasting serum insulin levels, insulin antibodies, and responsiveness to steroid medication in patients who experience recurring sweating, giddiness, and weakness that improve with the consumption of sweets.

Diabetes Update

Vol. 3 | Issue 37 | 2022

References:

1. Wu HY, Chen IH, Lee MY. Case report: hypoglycemia secondary to methimazole-induced insulin autoimmune syndrome in young Taiwanese woman with Graves' disease. *Medicine (Baltimore)*. 2022 Jun 24;101(25):e29337.
2. Bawaskar H et al. "Hirata Diseases: Autoimmune Hypoglycaemia." *Clin Case Rep* 12(2022): 1487.
3. Yoshino H, Kawakami K, Kohriyama K, Yoshino G, Matsunaga S, Takechi H. Long-term follow-up of insulin autoimmune syndrome in an elderly patient. *Clin Case Rep*. 2020 Sep 14;8(12):2941-2944.

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