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Diabetes Update

Vol. 2 | Issue 32| 2021

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.

- Type 2 diabetes and the risk of cardiovascular events in patients with peripheral arterial disease compared to those with coronary artery disease
- Leukocyte Counts and T-Cell Frequencies among diabetes subgroup and their association with Metabolic Parameters and Biomarkers of Inflammation

  A Retrospective Cohort study on association between aspartate aminotransferase to alanine aminotransferase ratio and incidence of type 2 diabetes mellitus in Japanese population

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

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Type 2 diabetes and the risk of cardiovascular events in patients with peripheral arterial disease compared to those with coronary artery disease

A high risk of cardiovascular events is indicated by the presence of coronary artery disease (CAD), and even more so by the presence of peripheral artery disease (PAD), especially in presence of type 2 diabetes mellitus (T2DM). T2DM patients with CAD or PAD are at an extremely high risk of cardiovascular events. However, because the individual and combined effects of CAD, PAD, and T2DM on the event rate have not been explored, it is unknown how the cardiovascular risk of PAD patients who do not have T2DM compares to the risk of CAD patients with T2DM.

This study compared the cardiovascular risk between coronary artery disease and peripheral artery disease in patients with type 2 diabetes mellitus.

A total of 923 patients with CAD and 292 patients with PAD were enrolled in this study. Height and weight, as well as waist and hip circumferences, were measured at the start. The Riva-Rocci method was used to assess systolic and diastolic blood pressures following a one-hour rest in a sitting position on the day of hospital admission. T2DM was diagnosed in accordance with the American Diabetes Association's clinical practise guidelines. Patients with CAD but no diabetes, those with both CAD and T2DM, those with PAD but no diabetes, and those with PAD and T2DM were all included in this study. Patients with PAD were compared to those

with CAD, and those with T2DM were compared to those without diabetes. The impact of the severity of CAD on the occurrence of MACE was also discussed.

During the study's 10.04.7-year follow-up period, 366 MACE occurred (including 163 cardiovascular deaths, 108 non-fatal myocardial infarctions, and 95 non-fatal strokes). As a result, the primary research endpoint had a 30.0 percent incidence rate, or 3.0 percent every year. MACE was substantially greater in CAD+/T2DM+ patients (3.96 events per 100 person-years; p0.001), PAD+/T2DM patients (3.68 events per 100 person-years; p=0.022), and PAD+/T2DM+patients (7.10 events per 100 person-years; p0.001). The presence of T2DM (HR=1.44 (95 percent CI 1.09 to 1.92; p=0.012) and the existence of PAD vs CAD (HR=1.48 (95 percent CI 1.15 to 1.91; p=0.002) were mutually independent predictors of cardiovascular events, according to Cox regression analysis after multivariate adjustment.

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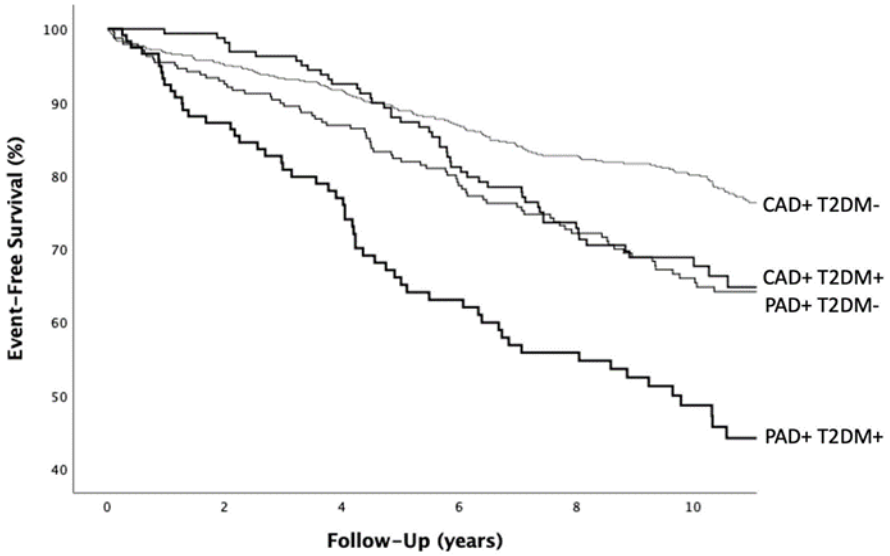

Figure 1: Incidence of MACE. CAD, coronary artery disease; MACE, major cardiovascular event; PAD, peripheral artery disease; T2DM, type 2 diabetes mellitus.

	HR unadjusted	P value	HR adjusted*	P value
3-point MACE	1.78(1.44to 2.19)	<0.001	1.44(1.09to1.92)	0.012
Vascular mortality	2.17 (1.62 to 2.91)	<0.001	1.73 (1.15 to 2.60)	0.008
Stroke	1.65 (1.13 to 2.40)	0.009	1.20 (0.72 to 2.02)	0.489
MCI	1.46 (1.03 to 2.06)	0.034	1.27 (0.80 to 2.02)	0.308
All-cause mortality	1.70 (1.42 to 2.03)	<0.001	1.29 (1.00 to 1.65)	0.050

Table 1: Results from Cox regression models for T2DM− versus T2DM+

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	CAD		PAD	
	T2DM-	T2DM+	T2DM-	T2DM+
3-point MACE	-	1.57(1.21to 2.03)	1.50 (1.09 to 2.06)	2.94 (2.18 to 3.97)
3-point MACE*	-	1.27 (0.93 to 1.79)	1.28 (0.91 to 1.79)	2.18 (1.49 to 3.18]
Vascular mortality	-	2.00 (1.40 to 2.85)	1.46 (0.91 to 2.33)	3.22 (2.13 to 4.89)
Vascular mortality*	-	1.70 (1.08 to 2.70)	1.30 (0.78 to 2.16)	2.13 (1.25 to 3.63)
Stroke	-	1.36 (0.84 to 2.20)	1.73 (1.01 to 2.97)	2.24 (1.93 to 5.43)
Stroke*	-	1.05 (0.57 to 1.92)	1.47 (0.82 to 2.61)	2.00 (1.02 to 3.91)
MCI	-	1.32 (0.84 to 2.08)	2.32 (1.48 to 3.65)	3.03 (1.86 to 4.95)
MCI*	-	1.17 (0.68 to 2.01)	1.88 (1.15 to 3.07)	2.44 (1.33 to 4.49]
All-cause mortality	-	1.60 (1.29 to 2.00)	1.69 (1.29 to 2.20)	2.67 (2.04 to 3.48)
All-cause mortality*	-	1.30 (0.98 to 1.72)	1.37 (1.03 to 1.82)	1.58 (1.13 to 2.20)

Table 2: Results from Cox regression models in subgroups considering both the presence of CAD versus PAD and the presence of T2DM

This study demonstrated Type 2 diabetes and the prevalence of peripheral artery disease and coronary artery disease are mutually independent predictors of cardiovascular events. Patients with PAD and type 2 diabetes have a significantly increased risk of cardiovascular events.

Reference:

Sprenger L, Mader A, Larcher B, et alType 2 diabetes and the risk of cardiovascular events in peripheral artery disease versus coronary artery diseaseBMJ Open Diabetes Research and Care 2021;9:e002407

Leukocyte Counts and T-Cell Frequencies among diabetes subgroup and their association with Metabolic Parameters and Biomarkers of Inflammation

Immune cells play a key part in the development of diabetes and the difficulties that come with it. Hyperglycemia and disease development are driven by T cell–

mediated -cell death in type 1 diabetes. Subclinical inflammation is characterized by greater numbers of leukocytes in the peripheral blood in people with type 2 diabetes compared to people with type 1 diabetes and healthy controls. Immune cell frequencies are linked to not just incident type 2 diabetes, but also metabolic parameters including fasting glycemia, insulin resistance, and plasma lipid levels, as well as the likelihood of comorbidities like cardiovascular disease and peripheral neuropathy in diabetics.

This study aimed to evaluate immune cell profiles among diabetes subgroups in people and see if differences in immune cell profiles are partially explained by changes in anthropometric, clinical, and biochemical profiles between clusters. In addition, the study investigates how distinct immune cell types correlated with inflammation biomarkers in the German Diabetes Study (GDS).

The findings are based on data from people with recent adult-onset diabetes who took part in the GDS, a prospective observational cohort research that is still ongoing. Age, BMI, HbA1c, β-cell function (HOMA2-B) and insulin resistance (HOMA2-IR) and GAD antibodies (GADA) were used to divide patients into diabetic subgroups. This study includes 708 participants who were divided into subgroups. Anthropometric measurements and metabolic variables were measured using normal laboratory techniques. The Sysmex KX21 or XP300 were used to perform automated white blood cell counts. Leukocytes from fresh whole blood were analysed using flow cytometry. A dual laser FACSCalibur cytometer was used to analyse the samples (Becton Dickinson). The Cellquest software was used to collect the samples (Becton Dickinson). FlowJo software was used to examine the samples. The

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Inflammation panel from Olink Proteomics was used to assess protein biomarkers in the serum of fasting GDS patients.

Severe insulin-resistant diabetes (SIRD) and mild obesity-related diabetes (MOD) had the greatest leukocyte counts, while severe autoimmune diabetes had the lowest (SAID). CD4+ T-cell frequencies were greater in SIRD compared to SAID, MOD, and mild age-related diabetes (MARD), and CCR4+ regulatory T-cell frequencies were higher in SIRD compared to SAID, MOD, and MARD compared to SAID. Disparities in clustering factors explained some of the pairwise differences between groupings. CD4+ T cell frequencies were associated with age, BMI, HOMA2 estimate of -cell function (HOMA2-B), and HOMA2 estimate of insulin resistance (HOMA2-IR), while CCR4+ regulatory T cell frequencies were associated with age, HOMA2-B, and HOMA2-IR.

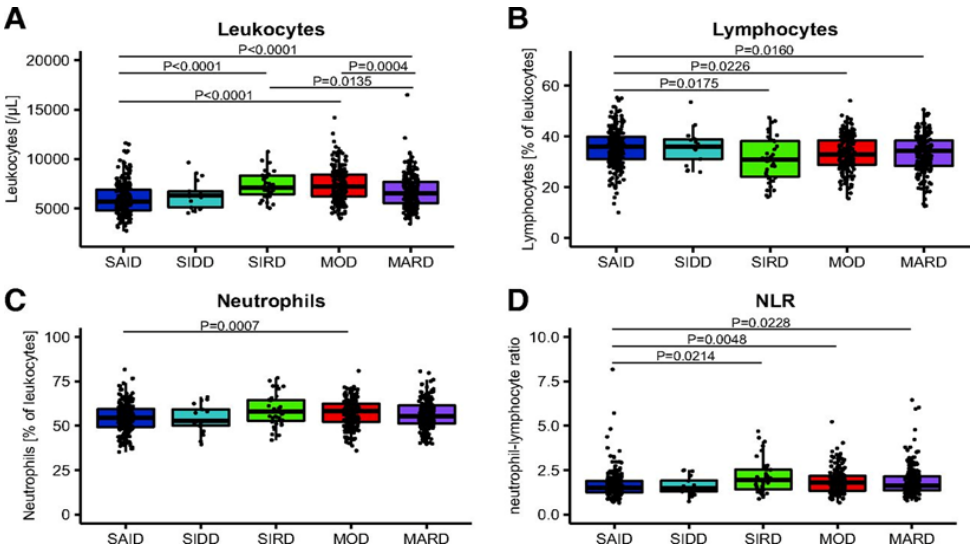

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Figure 2: Distribution of automated blood cell counts among different diabetes subgroups

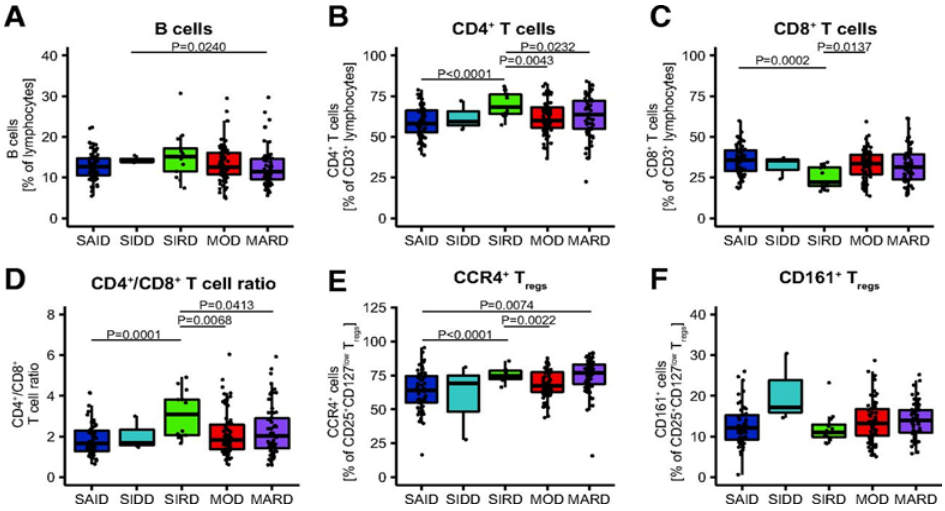

Figure 3: Distribution of lymphocyte frequencies among different diabetes subgroups

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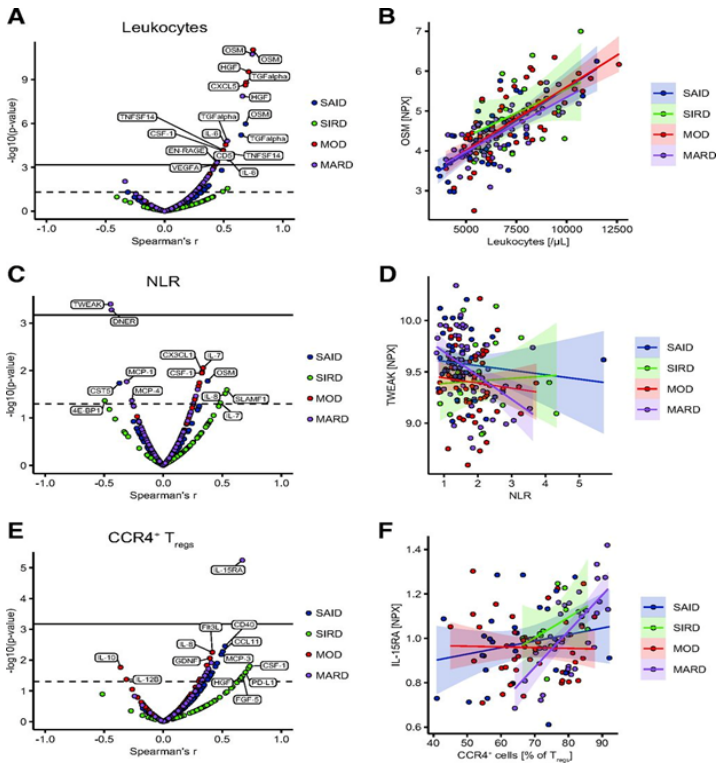

Figure 4: Correlations of blood cell counts and immune cell frequencies with protein biomarkers measured in serum.

This study demonstrated that immune cell frequencies in the blood differ amongst diabetes subgroups. Different T-cell frequencies in diverse subgroups of type 2 diabetes show that these diabetes subgroups have different inflammatory mechanisms associated to adaptive immunity.

Reference:

Ratter-Rieck JM et al. Diabetes. 2021 Nov;70(11):2652-2662.

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A Retrospective Cohort study on association between aspartate aminotransferase to alanine aminotransferase ratio and incidence of type 2 diabetes mellitus in Japanese population

The levels of liver enzymes such as aspartate transaminase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (GGT) have been shown to predict the incidence of type 2 diabetes mellitus (T2DM) in a number of investigations. One of the best surrogate indications for NAFLD was the AST/ALT ratio. In non-obese Chinese, Zou et al found that the ALT/AST ratio was an independent predictor of new non-alcoholic fatty liver disease (NAFLD) episodes (HR: 2.10, 95 percent CI: 1.88–2.36).

This study aimed to conduct an analysis based on online data to explore whether there was an association between the AST/ALT ratio and incident T2DM among a large number of Japanese people.

The research was carried out as a retrospective cohort study. A total of 15,291 people took part in this investigation. Physical examination assessments, HbA1c 6.5 percent, fasting plasma glucose 7.0 mmol/L, or self-reported T2DM were included in the baseline data. The AST/ALT ratio measured at baseline was the target-independent variable. The occurrence of T2DM during the follow-up period was defined as the study's endpoint. Selection and observation bias were reduced because this was a retrospective cohort research. The association between the AST/ALT ratio and T2DM occurrences was investigated using Cox proportional-hazards regression, generalised additive models, and subgroup analysis.The AST/ALT ratio determination coefficient was 0.9 percent. The AST/ALT ratio was found to be inversely linked with incident T2DM in a crude model (HR = 0.179,

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95 percent confidence interval (CI): 0.118, 0.272, P <0.00001). The trend was virtually the same in the minimum adjusted model (HR=0.349,95 percent CI: 0.226–0.540, P <0.00001). The AST/ALT ratio could be utilised to predict the incidence of T2DM independently in the full adjusted model (HR = 0.617, 95 percent CI: 0.405 to 0.938, P = 0.0239).

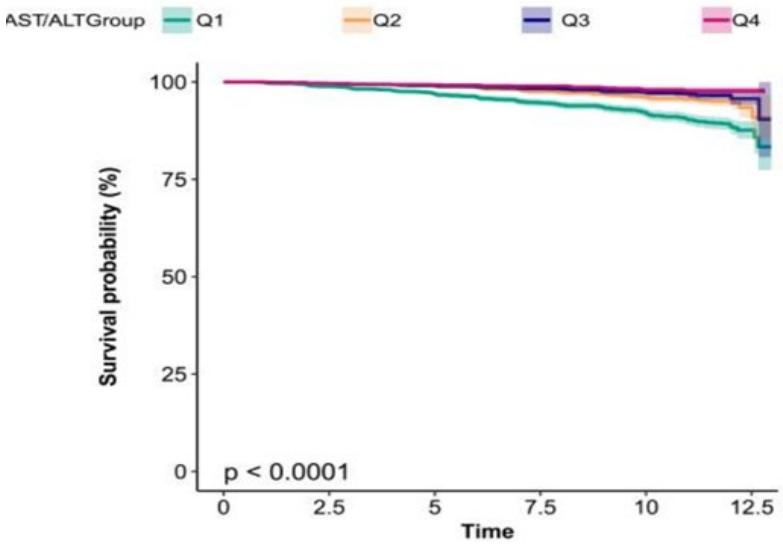

Figure 5: Kaplan–Meier event-free survival curve based on AST/ALT ratio quartiles and the incidence of T2DM.

The inflection point was 0.882, and there was a non-linear relationship and saturation impact between them. When the AST/ALT ratio was smaller than the inflection point, it was found to be inversely linked with incident T2DM (HR = 0.287, 95 percent CI: 0.126–0.655, p = 0.0030). Exercise had an effect on their relationship (P for interaction = 0.0024), and persons who did not exercise had a substantial association (HR = 0.464 95 percent CI: 0.290–0.741).

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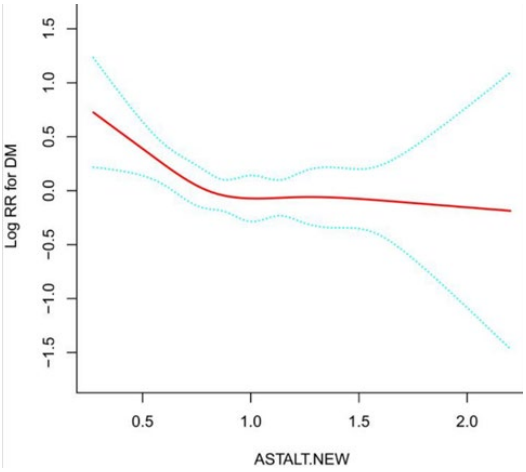

Figure 6: The non-linear relationship between AST/ALT and the incidence of diabetes.

In conclusion, the association between the AST/ALT ratio and the risk of T2DM was nonlinear, with an inflection point of 0.882. When the AST/ALT ratio was less than 0.882, it was linked to the development of type 2 diabetes. In the population that did not exercise, there was a stronger link.

Reference:

Chen L et al Diabetes Metab Syndr Obes. 2021 Nov 9;14:4483-4495.