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PHYSICIAN CONNECT

Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Physician Connect" which contains latest and interesting news.

This issue contains:

A molecular analysis onassociation between *Mycobacterium tuberculosis* genotype and diabetes mellitus/hypertension.

Noncommunicable diseases (NCDs), particularly cardiovascular illnesses and diabetes, have been identified as the main cause of death globally. The major NCDs are responsible for over 60% of all fatalities and 47% of the global burden of illness. Poor patient control is a major factor to the rising burden of morbidity and mortality from NCDs.[1] Diabetes mellitus (DM), hypertension, and associated risk factors have all been linked to the development of tuberculosis caused by *Mycobacterium tuberculosis*. There have been few investigations on the genetic link between tuberculosis (TB) patients with non-communicable diseases (NCDs) and *Mycobacterium tuberculosis* (MTB) infections with higher virulence and anti-TB drug resistance than those without NCDs. The aim of the study was to determine the most common genotype, as well as the relationship between MTB genotypes, NCD status, and treatment resistance.[2]

This study conducted a molecular analysis in 105 TB patients based on a cross-sectional study focusing on the comorbid link between chronic illnesses and TB among 1773 people. Face-to-face interviews with the individuals were conducted, followed by NCD screening. MTB isolates' DNA was collected before genotyping with 24 MIRU-VNTR loci. Following that, phylogenetic trees were used in conjunction with statistical power tests, Chi-square or Fisher tests, and multivariate logistic regression analysis.

The Lineage 2 (East Asia) was the most common genotype, accounting for 43.8% (46/105), followed by Uganda I (34.3%, 36/105), and the NEW-1 (9.5%, 10/105) strains from Lineage 4 (Euro-America). With a statistical power test value of 24.3%, the proportion of Beijing strain in patients with and without NCDS was 28.6% (8/28) and 49.4% (38/77), respectively. There was no evidence of a link between MTB genotype and NCD status. A low clustering rate (2.9%) was discovered, with only two clusters. Global, mono-, poly-, and multi-drug resistance rates were respectively 16.2% (17/105), 14.3% (15/105), 1.0% (1/105), and 4.8% (5/105). TB drug resistance rates were 6.7% (7/105), 11.4% (12/105), and 5.7% (6/105, respectively. The Beijing genotype of Lineage 2 was shown to be substantially related with isoniazid resistance (19.6 percent versus 5.1%). Table 1 summarizes the relationships between the Beijing genotype and specific NCDs as well as gender and age brackets. In the univariate analysis, no significant association was found among the most variables related to NCD status contributing to Beijing genotypes of MTB. The males were more likely to be infected by the family (East Asia) compared to females, who were mainly infected by Uganda I genotype.

Table 1: Lineages of MTB among patients by NCDs and other factors (n, %)								
Variables		**Total**	**Beijing**	**Non-Beijing**			**OR**	**P value**
				Ugandal	**NEW-1**	**Other Lineages**		
Total		105	46	36	10	13		
Diabetes Mellitus	No	87	36 (41.4)	30 (34.5)	10 (11.5)	11(12.6)	Ref.	0.482
	Yes	18	10 (55.6)	(33.3)	0 (0.0)	2 (1.1)	1.030	
Hypertension	No	93	40 (43.0)	31 (33.3)	9(9.7)	13(14.0)	Ref.	0.649
	Yes	12	6 (50.0)	(41.7)	1(8.3)	0 (0.0)	1.330	
Other NCDs	No	96	41 (42.7)	34 (35.4)	10 (10.4)	11(11.5)	Ref.	0.540
	Yes	9	5 (55.6)	2 (22.2)	0 (0.0)	2(22.2)	1.030	
Gender	Female	37	12 (32.4)	17 (45.9)	7 (18.9)	1(2.7)	Ref.	0.003
	Male	68	34 (50.0)	19 (27.9)	3(4.4)	12(17.6)	1.040	
Age (year-old)	15~34	40	17 (42.5)	13 (32.5)	6(15.0)	4(10.0)	Ref.	0.285
	35~59	35	12 (34.3)	14 (40.0)	2(5.7)	7(20.0)	0.520	
	60~100	29	17 (58.6)	9 (31.0)	1 (3.4)	2 (6.9)	0.730	

Other lineages Uganda II, Delhi/CAS LAM, TUR, Cameroon, Haarlem, and S, OR Odds ratio, DM Diabetes, HTN Hypertension, COPD Chronic Obstructive Pulmonary Disease, NCDs non-communicable chronic diseases, refers to DM, HTN, dyslipidemia, heart disease and COPD, Other NCDs dyslipidemia, heart disease and COPD

The Lineage 2 (East Asia) was the most common genotype, followed by Lineage 4 (EuroAmerica) MTB strains, with endogenous infection being the most common. The percentage of patients with NCDs who had Beijing strain was lower than that of those who did not have NCDs. There was no evidence of a link between NCD status and MTB genotype. Isoniazid resistance was found to be linked to the Beijing genotype.[2] Diabetes was linked to an increased risk of disease caused by strains with resistance mutations, according to Ruesen C et al.[3]

The findings of this study provide insight into the epidemiological and molecular characteristics of individuals with MTB who also have NCDs, laying the groundwork for future interdisciplinary research on TB and chronic non-communicable illnesses, particularly during the COVID-19 pandemic.

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Plasma lipopolysaccharide-binding protein biomarker for Venous thromboembolism

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are both symptoms of venous thromboembolism (VTE). VTE affects between 104 and 183 people per 100,000 on a yearly basis. In high-risk patients, the incidence can reach 68 per 1,000. The most common complication of post thrombotic syndrome is venous ulcers, which are the most serious.[1] VTE should be suspected and clinically evaluated if there is pain, swelling, edoema, or risk factors in the leg or upper extremity. Female reproductive factors play a big role in the sex gap in VTE risk, and oestrogen signalling boosts inflammatory gene expression, the researchers used a sex-stratified analysis to confirm their discovery of plasma lipopolysaccharide binding protein (LBP) as a DVT biomarker in women in a larger nested case-control study.[2] The aim of this study was to re-analyze the mass spectrometry (MS)-based proteomic dataset in order to find predictive biomarkers for VTE with varying effect sizes across DVT and PE, as well as those that were affected by regression bias and to perform targeted candidate validation.

The general population was surveyed for a VTE case-control discovery investigation and a nested case-control validation study. Plasma was taken at the start of the trial, and VTE episodes were tracked until 2007. For candidate discovery, untargeted proteome data was re-analyzed. The enzyme-linked immunosorbent test was used to validate the lipopolysaccharide-binding protein (LBP).

In women with fewer than 3 years between blood collection and DVT, elevated LBP was revealed as a potential DVT biomarker (Figure 1). For women with fewer than 3 years between blood collection and DVT, the odds ratio (OR) for DVT was 2.03 (95% confidence intervals [CI]: 1.53–2.74) per standard deviation (SD) rise in LBP in the validation trial. The OR was reduced to 1.79 (95% CI: 1.25–2.62) per SD after adjusting for age, BMI, and C-reactive protein. When compared to the lowest quartile, men in the 25th to 50th percentiles had an OR for VTE of 0.47 (95% CI: 0.28–0.77) in the validation study.

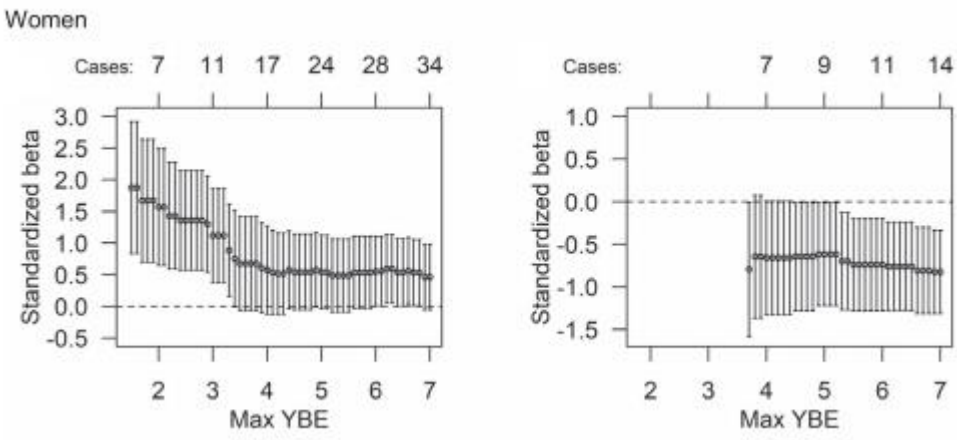

Figure 1: Mass spectrometry–based measurement of the relative plasma levels of lipopolysaccharide-binding protein was used to calculate the follow-up-time-dependent standardized beta coefficients for deep vein thrombosis (DVT). Sex-stratified analysis is

shown for women.
The maximum allowed time in years from blood sampling to venous thromboembolism event (YBE) is indicated on the x-axis.

LBP was identified as a plasma biomarker candidate for future DVT in women after re-analyzing data from our untargeted VTE biomarker discovery project. The findings were confirmed in a larger nested case-control research. When the follow-up duration was limited to three years, women had a twofold greater OR for DVT for each SD increase in LBP plasma level. After adjusting for age, BMI, and CRP, the link between LBP and DVT in women was less but still significant. Males in the lowest quartile of LBP, on the other hand, had a higher risk of VTE than men in the second quartile.[2] LBP is a biomarker for the lipopolysaccharide (LPS) burden in blood, which is mostly caused by gut leakage and infection. Infection is a well-known cause of VTE, and new proteomic and metabolomic investigations have suggested that the gut microbiota may play a role in hypercoagulability and VTE development.[3,4]

Increased LBP was found and verified as a predictive biomarker for DVT in women in this investigation. Men in the lowest quartile of LBP had a higher risk of VTE.

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A study on association between plasma aldosterone concentration and renal impairment in patients with both hypertension and abnormal glucose metabolism

Chronic kidney disease (CKD) is linked to a variety of metabolic abnormalities due to risk factors such as oxidative stress, chronic inflammation, and endothelial dysfunction. In patients with chronic renal disease, insulin resistance (IR) has been recognised as a risk factor for cardiovascular morbidity and mortality.[1] Patients who have both hypertension and diabetes mellitus have a higher risk of developing CKD than those who just have one.[2] The activation of aldosterone and mineralocorticoid receptors has been shown to contribute to the progression of CKD via haemodynamic and direct cellular effects. The aim of this study was to see if there was a link between high blood pressure and poor glucose metabolism and renal impairment (AGM).

A total of 2033 hypertensive people with AGM who did not have chronic kidney disease (CKD) at the start of the trial were included in the longitudinal observational study. CKD was defined as an eGFR of less than 60 ml/min per 1.73 m2 and/or positive proteinuria. Adjusted sets were identified using directed acyclic graphs and least absolute shrinkage and selection operator (LASSO) regression analysis. The connection of plasma aldosterone concentration (PAC) with CKD and its components, such as reduced renal function (DRF) and proteinuria, was studied using Cox proportional hazard models and linear regression. The effect of blood pressure (BP) in the relationship between the two was investigated using mediation analysis.

A total of 291 participants acquired CKD with a total follow-up of 5951 person-years with a median follow-up of 31 months. The results of DAGs describing the connection between PAC and CKD, based on literature reports and empirical confirmability, are shown in (Figure 1). With an increase in tertile PAC, the risk of CKD rose (Figure 2). In a multivariable Cox model, PAC was linked to an elevated risk of CKD (hazard ratio ¼ 76 for natural log-transformed PAC, P< 0.001), as well as an increased risk of DRF and proteinuria (Figure 2). SBP was responsible for 7.5–17.9% of the link between PAC and renal impairment. By removing those with questionable primary aldosteronism, too short follow-up time, and

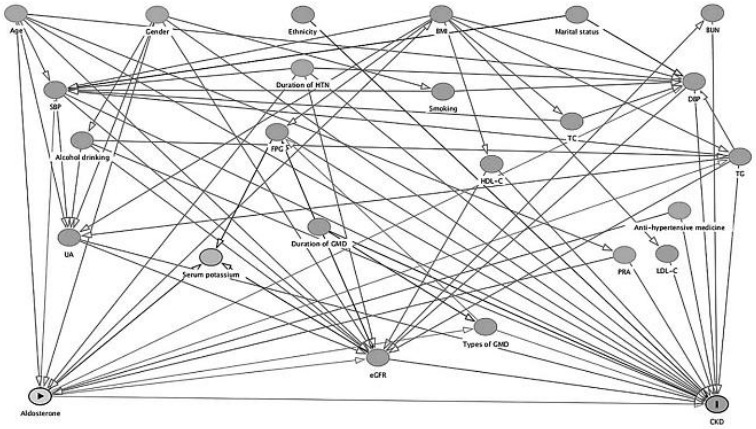

Figure 1: Directed acyclic graph of causal assumptions. *Nodes represent variables and arrows represent causal associations.Gray-coloured nodes represent possible confounding factors. AGM, abnormal glucose metabolism; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; PRA, plasma renin activity; TC, total cholesterol; TG, triglyceride; UA, uric acid.*

mineralocorticoid receptor antagonist use, the overall results remained consistent and significant in sensitivity analysis.

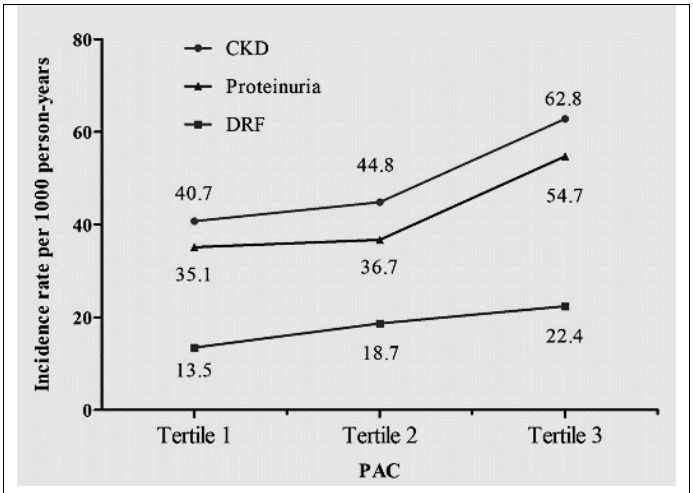

Figure 2: Incidence rate of chronic kidney disease, decreased renal function and proteinuria across tertile plasma aldosterone concentration. CKD, chronic kidney disease; DRF, decreased renal function; PAC, plasma aldosterone concentration.

Even in the absence of primary aldosteronism, the current longitudinal study finds that PAC is positively and independently related with an elevated risk of CKD in individuals with both hypertension and AGM. A positive correlation exists between PAC and DRF and proteinuria, indicating that this population has both functional and structural renal impairment.[2]Minakuchi H et al demonstrated that plasma aldosterone level was an independent risk factor for renal dysfunction development and that MRA might slow the pace of deterioration in eGFR in CKD patients with high PAC.[3]

In hypertensive people with AGM, higher PAC is related with an increased risk of CKD, including renal functional and structural impairment, even in the absence of primary aldosteronism. As a result, aldosterone could be a therapeutic target for CKD prevention in this high-risk group.

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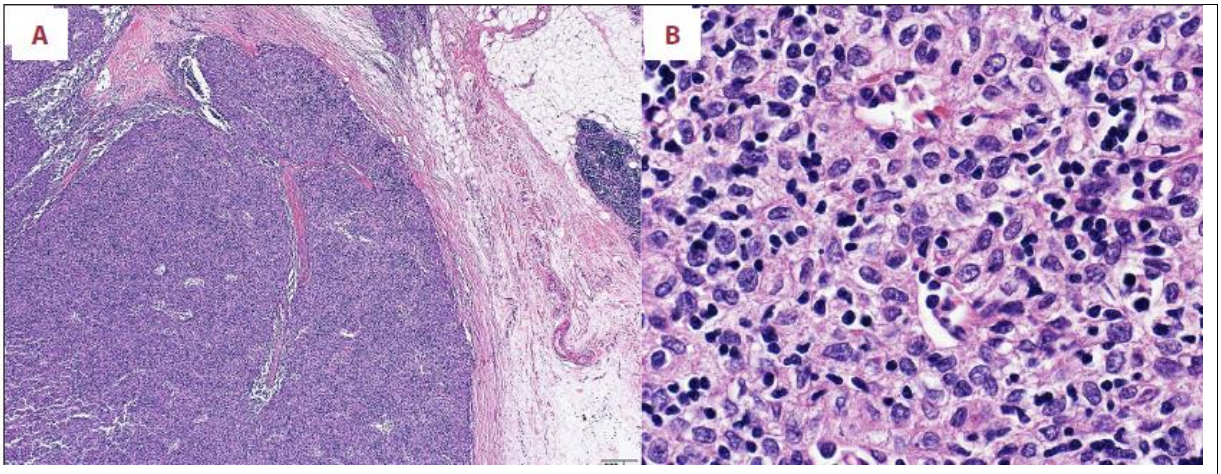
A woman with increased salty taste perception and decreased sweet taste perception prior to a diagnosis of Thymoma Associated Myasthenia Gravis

Myasthenia gravis (MG) is an autoimmune illness that causes striated muscular weakening, particularly in the oculobulbar muscles. Antibodies against postsynaptic proteins disrupt neuromuscular junction transmission, resulting in weakness. The treatment includes anticholinesterases, thymectomy, immunosuppressive and immunomodulatory drugs.[1] With an estimated yearly incidence of 810 cases per million, it has an overall prevalence of 150–250 cases per million. Because of the well-known and well-characterized autoantigens, it is considered a model of organ-specific autoimmune disease.[2] Not all tastes are impacted by MG-related dysgeusia. A decrease in or loss of sweet taste perception is common in patients with MG-associated dysgeusia, which could be linked to an autoimmune process. This article describes the case of a 47-year-old woman with MG who developed not only a decreased sense of sweet taste but also an increased perception of salty taste 3 months before her motor symptoms appeared.[3]

A 47-year-old woman had a decreased sweet taste perception and an increased salty taste perception. Meanwhile, she had extended thymectomy after being diagnosed with thymoma-associated widespread MG. Her anti-acetylcholine receptor (AChR) antibody (Ab) titer grew to 70 nmol/L three months later, when she had entirely lost her sweet taste sense and had obtained a dramatically heightened salty taste sensibility. Her partial dysgeusia gradually improved after prednisolone and tacrolimus were added to the medicine. The sweet taste disturbance went away when the AChR Ab titer dropped, while a minor decrease remained. The heightened salty taste perception reverted to normal.



Photomicrographs of the surgical specimen. (A) Low-power image demonstrated lymphocyte-rich thymoma. (B) High-power image showed tumor composed of polygonal epithelial cells set in a background of numerous lymphocytes indicating type B2 thymoma

A growing body of research demonstrates that hormones influence taste function. Angiotensin II reduces nerve responses to sweets while suppressing amiloride-sensitive taste responses to sodium chloride. It has no influence on potassium chloride, sour, bitter, or umami tastant reactions.[4] The study postulated that immunologic and endocrinologic mechanisms induced hypogeusia to sweet flavour, but only an endocrinologic mechanism generated hypergeusia to salty taste. As a result, when the AChR Ab titer reached its maximum, the degree of dysgeusia to salty taste may have been lower than that to sweet flavour, but dysgeusia to sweet taste lingered after the dysgeusia to salty taste vanished as a result of MG treatment.[3]

This is a unique case of an MG patient who developed an increased salty taste perception and a decreased sweet taste perception three months before her motor symptoms appeared. In patients with partial dysgeusia but no motor symptoms, its believed that MG should be investigated as a differential diagnosis.

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