Vol 4 | Issue 40 |2023

PHYSICIAN CONNECT

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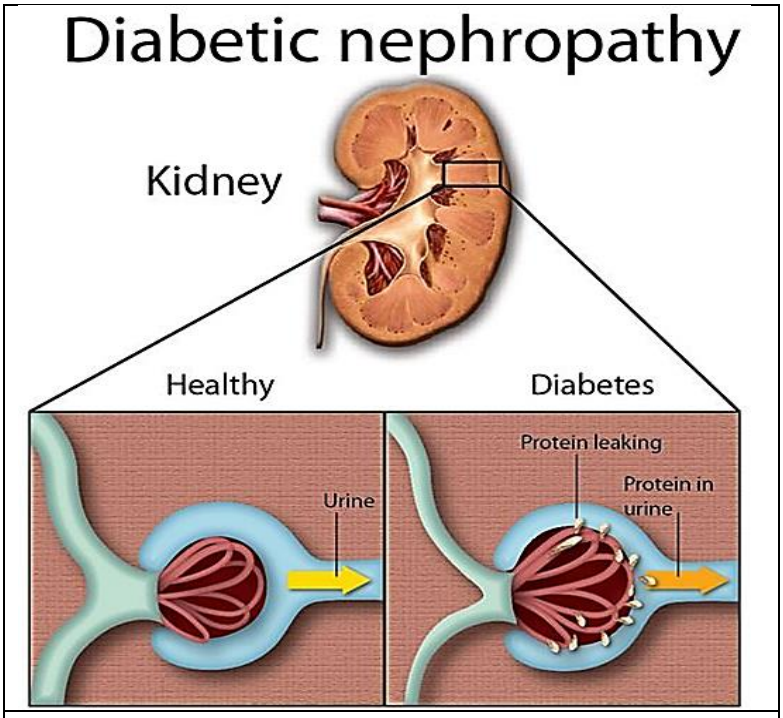
Association of renal damage and type 2 diabetic nephropathy patients' albumin, globulin, and albumin/globulin ratio levels

Introduction:

Diabetic Nephropathy (DN) is the most serious consequence of Diabetes Mellitus, with high morbidity and death. DN affects around one of every three diabetics. Increased glucose levels may cause inflammation and oxidative stress, resulting in nephropathy [(1)]. According to reports, DN accounts for 16.3% of end-stage renal diseases. Renal damage is so difficult to treat that it progresses to end-stage renal failure. As a result, early investigation, early diagnosis, and effective control of DN appear to be critical. The urinary albumin excretion rate (UAER) is commonly used to determine the extent of renal damage. Because of the time-consuming urine collection and the significantly increased UAER under urinary tract infection and menstrual state, UAER is vulnerable to influence from other causes. The albumin/globulin ratio (AGR) is a unique predictive indicator that can affect both inflammation and nutrition in the body. [(2)]. Globulin is a serum protein found in humans that is also known as immunoglobulin due to its immunological activity. Globulin is another reliable biomarker that is prevalent in the basal metabolome [(3)]. The purpose of this study was to assess the relationship between albumin (ALB), globulin (GLB), and albumin/globulin ratio (AGR) and renal damage in individuals with type 2 diabetes mellitus (T2DM).



Diabetic nephropathy

Methods:

A retrospective study was done on the clinical data of 82 patients with T2DM (Control group) and 110 patients with type 2 diabetic nephropathy (T2DN). According to urine albumin excretion rate (UAER), T2DN patients were divided into two groups: those with mild renal impairment (n=75) and those with moderate renal impairment (n=35). The general data of all groups were then compared. In addition, Pearson correlation was employed to examine the relationship between serum ALB, GLB, and AGR and UAER in the three groups. The diagnostic value of ALB, GLB, and AGR for mild renal damage in T2DN patients was assessed using a receiver operating characteristic curve (ROC).

Results:

Grouping	Control group ($n=82$)	Mild renal impairment group ($n=75$)	Moderate renal impairment group ($n=35$)	F	p
Albumin (mg/L)	4.13±0.38	3.84±0.43*	3.02±0.64*#	72.521	<0.001
Globulin (mg/L)	2.65±1.14	3.38±1.19*	3.73±1.56*	11.707	<0.001
albumin/globulin ratio	1.76±0.55	1.32±0.70*	0.94±0.41*#	25.858	<0.001

Table 1 Comparison of albumin, globulin and albumin/globulin ratio levels among the three groups

Significant variations existed across the three groups in terms of disease progression, a history of hypertension, levels of fasting plasma glucose, and glycosylated haemoglobin. Additionally, The ALB and AGR levels in the mild renal impairment and moderate renal impairment groups were lower, whereas GLB levels were greater, and the differences were statistically significant (p0.05) (table 1). The intermediate renal impairment group had lower ALB and AGR levels than the mild renal impairment group, but there was no significant difference in GLB levels between the two groups. The findings of Pearson correlation analysis showed not significant association between ALB and AGR levels and UAER in T2DN patients. Area under the curves (AUC) of ALB (0.88) and AGR (0.71) for predicting mild renal damage in T2DM patients were shown on ROC curves ($p<0.05$). GLB, however, does not significantly contribute to the diagnosis of mild renal damage in T2DN patients.

Discussion:

Diabetic Nephropathy (DN) causes a rapid decline in renal function that worsens over time and even proceeds to renal insufficiency and uraemia. A variety of causes can cause DN. Among these, genetic predisposition, renal hemodynamic alterations, cytokine diversity, and abnormalities of glucose metabolism all play significant roles [(2)]. Hypertension is also linked to renal impairment. In consistent to present study, previous studies by Ding JM et al and Zhong LN et al showed Diabetic individuals with hypertension have more severe insulin resistance and hyperinsulinemia, making them more susceptible to renal impairment [(4,5)].

Conclusion:

T2DN patients had lower levels of ALB and AGR expression when they are combined. Furthermore, ALB and AGR may be useful in clinical applications as a sensitive diagnostic for T2DN diagnosis.

In clinical settings, albumin (ALB) and albumin/globulin ratio (AGR) may be helpful as a sensitive diagnostic for the diagnosis of T2 Diabetic Nephropathy (DN).

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A study on exacerbation of Chronic Obstructive Pulmonary Disease Predicted by Blood Eosinophil Count

Introduction:

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide [(1)]. Acute exacerbation of COPD (AECOPD) is a sudden occurrence that worsens respiratory symptoms and necessitates changing one's course of treatment. Hospitalisations due to AECOPD are linked to a faster loss of lung function, a higher risk of recurring exacerbations, an increase in healthcare expenses, and a higher death rate [(2)]. According to the research, 30% to 40% of COPD patients suffer from eosinophilic airway inflammation, which is thought to be connected to the eosinophil count in the peripheral blood. When the illness is stable, increasing blood eosinophil levels are associated with an increased risk of exacerbation [(1)]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) document has been updated and now states that Inhaled corticosteroids (ICS)-containing regimens have little to no effect at a blood eosinophil count <100 cells/mm3, and that a threshold blood eosinophil count of less than ≥300 cells/mm3 or frequent exacerbations with a threshold blood eosinophil count of less than ≥100 cells/mm3 can [(3)]. The purpose of this study was to determine if blood eosinophil count serves as a reliable biomarker of COPD exacerbation and to evaluate the risk variables of COPD exacerbation.

Methods:

This is a one-year observational research that investigate into the risks of COPD exacerbation using real-world data. Patients with COPD were recruited, and their background information, spirometry data, laboratory test results, and moderate-to-severe exacerbation events were collected and analysed from their electronic medical records during the one-year follow-up period. The risk variables for COPD exacerbation were evaluated using univariate and multivariate logistic regression analysis.

Results:

Twenty-two (8.1%) of the 271 patients had a moderate-to-severe exacerbation. Exacerbation patients had worse pulmonary function, and study discovered that a high blood eosinophil count (350 cells/L; p =0.014), low forced expiratory volume (FEV1) (50%; p=0.002), increase in white blood cells (9000 cells/L; p=0.039), and use of home oxygen therapy (p=0.005) were risk factors for future exacerbations. The current investigation also showed an association between eosinophil count limitations and the chance of exacerbation (r 0.89, p<0.001). However, there was no correlation between exacerbation risk and COPD inhalation treatment. Exacerbators had greater blood eosinophil levels during the disease-stable phase, but the difference was not statistically significant (p = 0.436). The comparison of COPD comorbidities, such as benign prostatic hyperplasia (BPH), glaucoma, bronchial asthma (BA),

and interstitial pneumonia (IP), revealed no significant variations between the two groups. Table 1 displays the comparison of therapies between nonexacerbators and exacerbators.

Table 1: Comparison of therapies between nonexacerbators and exacerbators.

	Nonexacerbators (n = 249)	**Exacerbators (*n* = 22)**	**p value**
Component included			
ICS	89 (36%)	13 (59%)	**0.028**
LABA	197 (79%)	22 (100%)	**0.007**
LAMA	179 (72%)	14 (64%)	0.277
Inhalation therapy			
ICS mono	1 (0.4%)	0 (0%)	0.919
LABA mono	22 (9%)	4 (18%)	0.146
LAMA mono	31 (12%)	0 (0%)	0.061
ICS + LABA	29 (12%)	4 (18%)	0.272
LAMA + LABA	89 (36%)	5 (23%)	0.160
ICS + LABA + LAMA	57 (23%)	9 (41%)	0.057
Others			
Macrolide	32 (13%)	5 (23%)	0.164
Theophylline	23 (9%)	5 (23%)	0.061
LTRA	18 (7%)	6 (27%)	**0.007**
HOT	24 (10%)	9 (41%)	**<0.001**

Note. Data are shown as number of patients (percentage). Significant differences are marked using bold font. Macrolide and LTRA were administered orally. ICS, inhaled corticosteroid; LABA, long-acting β2-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; HOT, home oxygen therapy.

Discussion:

The current study identifies risk factors for COPD exacerbation in 271 COPD patients and found a peripheral blood eosinophil count of ≥350 cells/L, a low percentage of FEV1, and an increase in home oxygen therapy(HOT) and white blood cell count as risk factors for COPD exacerbation [(1)]. This was compared to the study by U. Kolsum et al found that Eosinophils have been found in sputum and Broncho alveolar lavage fluid [(4)]. Additionally, a study by P. Pignatti et al showed a connection between blood and sputum eosinophils. The association between blood and sputum eosinophils was influenced by age, high blood eosinophils, and hypertension. [(5)].

Conclusion:

According to current study findings, the peripheral blood eosinophil count is a reliable indicator of COPD exacerbation. Triple inhalation therapy is now relatively easy with single-inhaler devices, however for optimal COPD care, the peripheral blood eosinophil count in each patient's clinical history should be validated.

In this study, risk variables for COPD exacerbation were identified as peripheral blood eosinophil count ≥350 cells/L, poor FEV1 %, rise in home oxygen treatment (HOT), and white blood cell count.

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Examining the Genetic Relationship between Common Psychiatric Disorders and Thyroid Dysfunction

Introduction:

Thyroid hormones(TH) have an important role in brain development and neuronal function. Thyroid disorders and a variety of mental disorders are commonly associated· The THs are essential for the development and physiological function of the CNS. Their receptors are found throughout the central nervous system(CNS). THs are recognised to be essential for appropriate newborn brain development. Foetal THs are shown to be important in neural processing and integration, glial cell proliferation, myelination, and the production of critical enzymes necessary for neurotransmitter synthesis [(1)]. Thyroid hormone (TH) changes, even within the normal range, have been linked to an increased risk of developing common psychiatric diseases, while their causes are unknown. Both hypothyroidism and hyperthyroidism have been linked to an elevated risk of a variety of mental diseases, including depression, bipolar disorder, and anxiety disorders (ANXs) [(2)]. The objective of the current study was to evaluate phenotypic and genetic connections in large datasets of thyroid illnesses, TH levels, and three prevalent mental disorders associated with thyroid dysfunction, namely major depressive disorder (MDD), bipolar disorder (BIP), and anxiety disorder (ANX).

Methods:

This was a comprehensive investigation of different phenotypic and genotypic databases to gain fresh insight into the possibly common pathways causing thyroid dysfunction and mental illnesses. This study examined the connection between thyroid problems and depression, bipolar disorder (BIP), and anxiety disorders (ANXs) in 497,726 people. Following that, looked for genetic links between thyroid problems, thyrotropin (TSH), and free thyroxine (fT4) levels, and the genome-wide variables that predispose to mental illnesses. Finally, the identified global genetic associations were linked to particular local genomic areas.

Results:

Using International Classification of Diseases-10 (ICD) collected data from 502,489 in-patients, hypothyroidism was linked to an increased risk of major depressive disorder (MDD, OR= 1.31, $p = 5.29 \times 10^{-89}$), bipolar disorder (OR= 1.55, p = 0.0038), and anxiety (OR= 1.16, $p = 6.22\ 10^{-8}$). MDD (OR= 1.11, p = 0.0034) and ANX (OR= 1.34, $p = 5.99\ 10^{-6}$) were both linked with hyperthyroidism. Thyroid illness and severe depression ($r_g = 0.17$, $p = 2.7\ 10^{-4}$) and ANXs ($r_g = 0.17$, $p = 6.7\ 10^{-6}$) were found to have significant genetic coherence. This genetic association was extremely strong at the major histocompatibility complex locus on chromosome 6 ($p < 10^{-5}$), but additional investigation revealed that other sections of the genome also contributed to the overall impact. Notably, neither TSH nor fT4 levels were shown to be genetically associated to psychiatric health conditions. Table 1 shows the findings of a research

that looked at global genetic connections between thyroid characteristics, mood, and ANXs, as well as the observed single nucleotide polymorphism (SNP)-heritability estimates (h2-SNP). Hyperthyroidism exhibited the lowest SNP heritability (0.006) of the characteristics.

Table 1. Global Genetic Correlation Between Thyroid Hormone Levels and Thyroid Diseases with Affective Disorders

	h2 SNP	*ANX*, r_g (*p*)	*MDD*, r_g (*p*)
h2 SNP		0.08	0.07
Self-reported hypothyroidism (U.K. biobank)	0.05	0.17 (2.2×10^{-4})	0.17 (8.5×10^{-5})
TSH normal range	0.11	0.05 (0.43)	−0.05 (0.37)
TSH entire range	0.10	0.02 (0.67)	−0.03 (0.55)
fT4 normal range	0.15	−0.02 (0.71)	−0.04 (0.36)
Hypo and hyperthyroid disease[a]	0.03	0.16 (6.7×10^{-6})	0.13 (2.7×10^{-4})

ANX, anxiety disorder, MDD, major depressive disorder.

Discussion:

This study investigated the impact of common genetic variations in the complicated interactions between thyroid function, autoimmunity, and three major psychiatric diseases and also discovered significant genetic links between autoimmune hypothyroidism, MDD, and ANXs. One of the major molecular possibilities underlying the coexistence of several autoimmune disorders is that different organs have the same epitopes, which autoantibodies might crossreact with [(2)]. In this regard, Benvenga et al recently discovered a mysterious amino acid sequence similarity between thyroid autoantigens and central nervous system proteins, including TPO, autoantibodies to which serve as a diagnostic for Hashimoto's hypothyroidism [(3)].

Conclusion:

This study reveals an underlying link between autoimmune hypothyroidism and mood disorders that is not mediated by THs and in which autoimmunity plays a significant role. While these findings may provide fresh insight into the possible inefficiency of treating (small) changes in thyroid function in psychiatric illnesses, more investigation is required to identify the precise molecular pathways involved.

This study showed underlying association between autoimmunity and mood problems in autoimmune hypothyroidism, which is not mediated by Thyroid hormones (THs).

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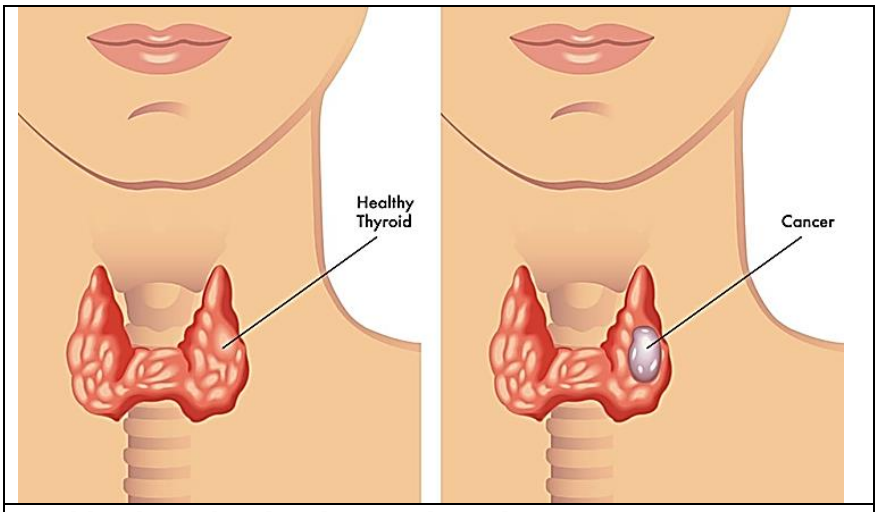
A rare case report of primary thyroid leiomyosarcoma with papillary thyroid carcinoma

Introduction:

A malignant tumour called leiomyosarcoma (LMS) develops from or has signs of differentiating towards smooth muscle. It is most frequently discovered in the retroperitoneal space, gastrointestinal system, or pelvic region [(1)]. They account for fewer than 1% of all adult cancers. Primary LMS can be seen in unusual locations such as the thyroid. Thyroid cancer is a frequent neoplasm, with 13.5 new cases per 100,000 people each year. Papillary thyroid carcinoma (PTC) responsible for 80% of thyroid malignancies [(2)]. Papillary thyroid carcinoma (PTC) is the most frequent kind of thyroid cancer. However, the presence of PTC and sarcoma in the same patient is unique [(3)]. This is the case presentation of a women who had both primary LMS in the left lobe, and PTC in the right lobe of her thyroid. This is the first reported case of both tumours in the same patient in the literature.



Healthy thyroid and malignant thyroid

Case presentation:

A 42-year-old woman who had been experiencing a swelling neck mass for a few months visited to clinic. No swallowing difficulties, compressive sensations, or other thyroid disease-related symptoms were present. Patient had previously undergone a cholecystectomy, sleeve gastrectomy, breast implantations, and the removal of benign uterine fibroids under close observation. She appeared normal upon examination, with no cachexia symptoms or scars. She developed a skinless rubbery submandibular goitre. thyroid stimulating hormone(TSH) was 1.22 mIU/L (reference range 0.5 to 5.0 mIU/L) and free T4 was 11.93 pmol/L (reference range 12 to 30 pmol/L). An ultrasound of the neck revealed a Thyroid Nodule Image Reporting and Data Systems (TI-RADS) 5 thyroid nodule measuring 3.89×2.4×2.1 cm in the left lobe, necessitating a fine needle aspiration (FNA) 2 days later, and a much smaller nodule measuring <1.1 cm. FNA findings indicated an atypia of unknown significance, classifying it as Bethesda category. She was recommended to have surgery to remove her left lobe. She had left hemi thyroidectomy a week later after carefully assessing the risks and benefits of the procedure. The procedure took around 2 hours and used a standard surgical technique with a midline

central incision. Gross examination revealed a white well-defined solid mass filling the bulk of the lobe and measuring 4.5 cm size. Microscopically, the mass was composed of aberrant spindle cells organised in a fascicular growth pattern. The spindle cells had eosinophilic fibrillary cytoplasm with focal granularity, but the nuclei were cigar-shaped with blunt ends and displayed varying degrees of atypia such as irregularity, hyperchromasia, and enlargement. There were more than 20 mitotic figures per 10 high power fields (>20/10 HPF) (Fig. 1, A-B). Smooth Muscle Actin (SMA), caldesmon, and desmin were all significantly positive, indicating a smooth muscle origin. While the presence of spindle cells suggested a differential diagnosis of medullary thyroid cancer, the calcitonin stain was negative. Thyroid-specific markers such Thyroid Transcription Factor (TTF-1) and Paired-box gene 8 (PAX-8) were also non-reactive. Other markers, including S-100, electroretinogram(ERG), myogenin, and signal transducer and activator of transcription 6 (STAT-6), were similarly negative, ruling out neurological and vascular markers, rhabdomyosarcoma, and solitary fibrous tumour. The results were consistent with a high-grade leiomyosarcoma. Because ultrasonography revealed tiny nodules in the residual lobe of her thyroid, she requested and underwent a complete thyroidectomy. The patient was recommended to have an oncology and gynaecology review. Her gynaecology assessment ruled out malignant uterine, cervical, and ovarian disease, suggesting that the tumour was primary. There had been no previous history of vaginal haemorrhage, menorrhagia, or dysmenorrhea. The Pap smear came back negative. A whole-body CT scan was performed and revealed no new lesions other than clinically insignificant previously known pulmonary nodules. A year later, the patient continues to be assessed on a regular basis.

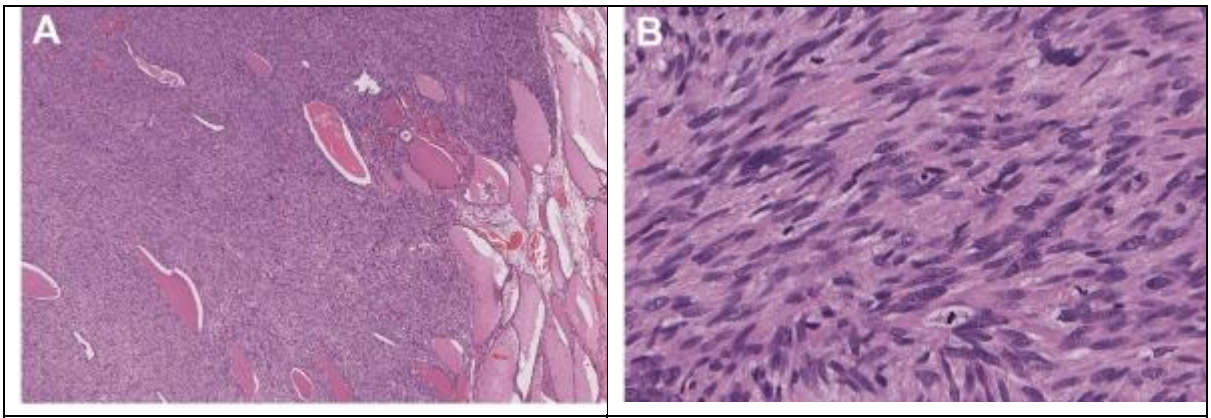


Fig. 1 A-B Leiomyosarcoma in left lobe. A Spindle cell tumor abutting and infltrating thyroid follicles (H&E*, original magnifcation×40).	Malignant spindle cells with frequent mitotic fgures (H&E*, original magnifcation×400).

Discussion:

Thyroid leiomyosarcoma (LMS) is an extremely uncommon cancer, and having it in conjunction with papillary thyroid cancer is even more unique. Vujosevic S et al and Dubrava J et al previously reported the leiomyosarcoma with papillary thyroid cancer and concluded the cause of LMS is uncertain, past malignancy and radiation should be considered risk factors. [4,5]. The majority of LMS patients (85%) appear with a neck mass, followed by compressive symptoms. In a study by Bashir MT et al LMS appeared with cervical lymphadenopathy [6].

Conclusion:

Thyroid LMS is a rare cancer with a worse prognosis compared to PTC. Before categorising it as primary thyroid cancer, a complete workup must be performed to rule out metastases.

Thyroid leiomyosarcoma (LMS) is a rare malignancy, and having it together with papillary thyroid cancer is even more unusual.

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