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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:

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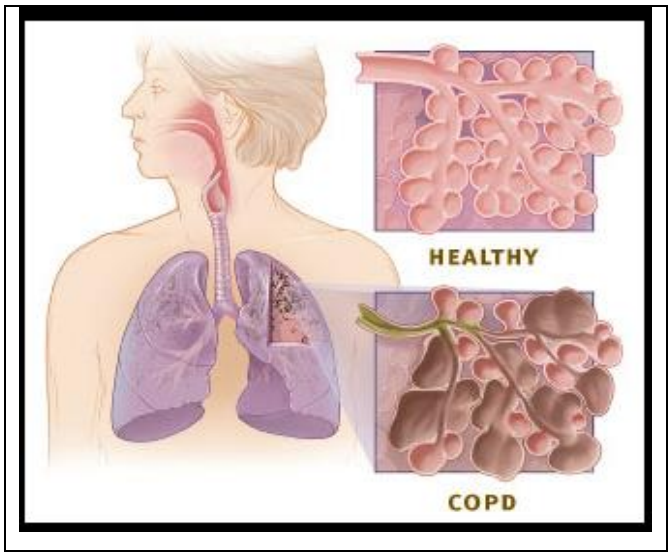
Best Regards,

Medical Team, Micro Labs Limited.

1. Association between childhood smoking and COPD prevalence

Introduction:

Chronic obstructive pulmonary disease (COPD) is a slow-developing, incurable lung illness that causes airflow limitation and can lead to complications like pulmonary heart disease and respiratory failure. COPD is caused by a complex interaction between genes and the environment. Cigarette smoking is the most significant environmental risk factor for COPD. Besides these, COPD is also influenced by various risk factors such as age, gender, lung growth and development, exposure to particles, socioeconomic level, asthma, airway hyper-reactivity, chronic bronchitis, and infections.[1] According to a recent study, adults who started smoking cigarettes before the age of 15 had a significantly greater prevalence of chronic obstructive pulmonary disease (COPD), regardless of whether they currently smoke, how many years they have smoked, or how long they have smoked.[2] This study examined whether the relationship between COPD and childhood smoking is independent of lifetime smoking, current smoking status, smoking intensity, and second-hand smoke exposure.



Methods:

In this large nationally representative study, data has been collected from Wave 5 of the PATH research, a nationwide longitudinal cohort survey. Adults who had ever smoked cigarettes were asked what age they started smoking on a regular basis. A multivariable Poisson regression model was used to determine the likelihood of self-reported COPD diagnosis in children under 15 years old while adjusting for current smoking, cigarette pack years or smoking duration, second-hand smoke exposure, and sociodemographic factors. The primary analysis included a three-category age of initiation variable, with 15+ as the reference group. A secondary analysis included the age of initiation variable, which was divided into four categories, with 20+ serving as the reference category. A third study used

the 9-category variable to stratify the 3-category age of cigarette smoking initiation by smoking status and intensity.

Results:

The majority of participants (77.0%) were from cities, 53.4% were female, and 80.2% were white. Overall, 13.4% answered that they had COPD. COPD prevalence was 7.5% for persons who never smoked, compared to 29.0% and 21.1% for those who started smoking at ages <15 and 15+ years, respectively. Adults who started smoking before the age of 15(versus 15+) had a higher prevalence of current smoking (45.9% vs. 33.3%), longer smoking duration (mean 34.2 vs. 27.3 years), more cigarette pack years (mean 48.8 vs. 30.8), and more exposure to second-hand smoke (p's<0.05) (Table 1). In a multivariate analysis, there was about 1.27 (95% confidence interval=1.06, 1.51) relative risk of COPD for those who started smoking before the age of 15, compared to those who started after that age.

	Weighted % (weighted mean)			
	Overall (N=10,126)	Never Smoking (N=2752)	Cigarette Initiation <15 Years (N=935)	Cigarette Initiation 15+ Years (N=4423)
Lifetime COPD Diagnosis[a]				
Yes	13.4	7.5	29.0	21.1
No	86.6	92.5	71.0	78.9
Smoking Status[a]				
Never	47.2	100.0	-	-
Former	35.3	-	54.1	66.7
Current	17.5	-	45.9	33.3
Cigarette Pack Years[a]	(14.6)	-	(48.8)[b]	(30.8)[b]
Cigarettes/Day[c]	(26.1)	-	(21.5)	(23.4)
Smoking Duration (years)[c]	(12.9)	-	(34.2)[b]	(27.3)[b]
Secondhand Smoke Exposure (hours in past 7 days)[a]	(3.4)	(1.2)	(10.1)	(5.7)

[a]Statistically significant difference from tests comparing adults who initiated cigarette smoking <15 years to 15+ years using Chi-square tests for categorical variables and independent-samples *t*-tests for continuous variables ($p<0.05$)
[b]Adults reporting current and former established cigarette smoking
[c]Only among adults reporting current smoking.

COPD=chronic obstructive pulmonary disease

Table 1: Smoking-Related Factors of the Overall Sample and by Status of Childhood Smoking

Discussion:

This study found that, regardless of cigarette pack-years, current smoking status, second-hand smoke exposure, and smoking duration, age of onset for cigarette smoking before the age of 15 was substantially related to COPD risk. This study supports the association between childhood smoking and an increased risk of COPD.[2] A previous investigation concluded that the association between childhood cigarette smoking and COPD was independent of current smoking or cigarette smoking history. Among adults over 40, one-fifth of those who smoked as children had COPD.[3]

Conclusion:

Childhood smoking significantly elevated the risk of COPD, regardless of cigarette pack-years, duration, second-hand smoke exposure, or current smoking status. This study supports the association between childhood smoking and an increased risk of COPD.

Smoking during childhood is associated with an increased risk of COPD.

Reference:

1. Cuixue W et al. Progress in the mechanism and targeted drug therapy for COPD. Signal Transduction and Targeted Therapy. 2020;5(1):248
2. Ozga JE et al. Childhood Cigarette Smoking and Risk of COPD in Older United States Adults: A Nationally Representative Replication Study. Chronic Obstr Pulm Dis. 2024 Nov 22;11(6):549-557.
3. Sargent JD et al. Childhood Cigarette Smoking and Risk of Chronic Obstructive Pulmonary Disease in Older U.S. Adults. Am J Respir Crit Care Med. 2023 Aug 15;208(4):428-434.

2. A retrospective analysis of visceral adiposity as an independent risk factor for diabetic peripheral neuropathy in people with type 2 diabetes mellitus

Introduction:

Diabetic peripheral neuropathy (DPN) is the term used to describe peripheral nerve damage that develops in diabetic individuals after all other causes have been ruled out. The condition can damage both central and peripheral nerves, with DPN accounting for around one-third of peripheral neuropathy cases. The most typical signs of DPN are distal symmetrical limb numbness and loss of feeling. Additionally, DPN can cause neuropathic pain in 20% of diabetics.[1] About 50% of those with Type 2 diabetes mellitus (T2DM) have DPN, which can result in serious consequences like amputations and foot ulcers. Notably, it is becoming more well recognised that visceral adiposity plays a crucial role in raising the risk of DPN.[2] So, this study was conducted to assess the relationship between DPN and obesity-related body

composition, namely visceral fat, in order to assist in the early detection of high-risk T2DM patients.

Methods:

This cross-sectional investigation included T2DM patients from the Department of Endocrinology and Metabolism at the Second Affiliated Hospital. Patients with DPN (DPN group) and those without DPN (NDPN group) were divided into two groups. This study used bioelectrical impedance analysis (BIA) to quantify body weight and visceral fat area, as well as collect clinical and biochemical data. Data analysis was done using logistic regression.

Results:

This study included 113 T2DM patients, with 50 in the DPN group and 63 in the NDPN group. The visceral fat area of the DPN and NDPN groups differed statistically significantly, according to the study (p = 0.048). The visceral fat area was found to be an independent risk factor for DPN in T2DM patients using multivariate logistic regression analysis (OR 1.027; 95% CI 1.004–1.051, p = 0.022) (Table 1). Additionally, the duration of diabetes was identified as an independent risk factor for DPN (OR 1.009 [95% CI 1.002, 1.016], p = 0.007). Patients with diabetic retinopathy had a significantly increased risk of developing DPN than those without retinopathy (OR 3.909 [95% CI 1.373, 11.127], p = 0.011).

Independent variables	OR (95% CI)	*p* value
Duration of diabetes	1.009 (1.002, 1.016)	**0.007**
Glycated hemoglobin	1.120 (0.890, 1.410)	0.334
Fasting plasma glucose	1.115 (0.939, 1.323)	0.214
Uric acid	1.004 (0.999, 1.009)	0.100
Body mass index	0.811 (0.627, 1.049)	0.110
Visceral fat area	1.027 (1.004, 1.051)	**0.022**
Diabetic retinopathy	3.909 (1.373, 11.127)	**0.011**
Gender	2.351 (0.825, 6.702)	0.110

Table 1: Multivariate logistic regression analysis of diabetic peripheral neuropathy in Type 2 diabetes patients.

Discussion:

In this study, in T2DM patients, the VFA measured by BIA, and its association with DPN was examined. Compared to the NDPN group, the DPN group had a noticeably increased prevalence of diabetic retinopathy. Multivariate logistic regression analysis revealed that among individuals with type 2 diabetes, diabetic retinopathy is a risk factor for DPN.[2] According to a previous study, patients with DPN have an increased risk of acquiring diabetic retinopathy than people without DPN.[3] This is likely due to common pathology foundations including glucose metabolism disorder, microvascular difficulties, and microcirculatory abnormalities.[2]

Conclusion:

In people with type 2 diabetes, visceral fat is a unique risk factor for DPN. The prevention and treatment of DPN may depend on the implementation of strategies to evaluate and control visceral obesity. This demonstrates the need for early intervention tools like BIA in clinical and community settings.

Reference:

1. Zhu J et al. Diabetic peripheral neuropathy: pathogenetic mechanisms and treatment. Frontiers in endocrinology. 2024 Jan 9;14:1265372.
2. Wu RL et al. Visceral Adiposity as an Independent Risk Factor for Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus: A Retrospective Study. J Diabetes Res. 2024 Nov 11;2024:9912907.
3. Li J et al. Correlations among Diabetic Microvascular Complications: A Systematic Review and Meta-analysis. Sci Rep. 2019 Feb 28;9(1):3137.

Visceral fat is a distinct risk factor for diabetic peripheral neuropathy in individuals with type 2 diabetes.

3. Prevalence and Risk factors of Pulmonary Embolism in COPD patients with secondary polycythemia

Introduction:

Chronic obstructive pulmonary disease (COPD) is a chronic lung disease where its pathophysiologic causes are complicated, involving both innate and adaptive immune cells as well as elevated levels of inflammatory cytokines. Cigarette smoking and aging both contribute to this abnormal inflammatory pathophysiology and are two of the most powerful risk factors for the development and progression of COPD.[1] About 2–10% of patients with COPD have secondary polycythemia (SP), a comorbidity of the disease caused by chronic and prolonged hypoxia. It is directly linked to an elevated risk of pulmonary hypertension, mortality, and venous thromboembolism (VTE). The majority (>90%) of pulmonary embolism (PE) cases are pulmonary thromboembolism, which is the most prevalent type of PE. Studies indicate that COPD patients are four times more likely to get PE, and those with both conditions have a much higher mortality rate. Patients with COPD had a significantly higher incidence of PE, indicating that COPD is an independent risk factor for PE. Still, there is a lack of data on the pathophysiology and risk factors of PE in COPD patients with SP.[2] The purpose of this study was to determine the prevalence of PE in SP and COPD, as well as to investigate the risk factors for PE in these patients.

Methods:

This observational cohort study examined the prevalence of PE in hospitalized COPD patients with SP. Inclusion criteria were being ≥45 years old and had COPD, COPD with SP, or COPD with SP secondary PE. Exclusion criteria included cancer, cardiovascular illness, surgery within a year, paralysis, and immobility. Patients were divided into three groups: COPD+SP+PE, COPD+SP, and control. Laboratory testing, biomarkers, echocardiography, and pulmonary function tests were conducted. Biomarkers were assessed seven days following clinical treatment for patients in the COPD+SP group. To perform statistical analysis, SPSS 23.0 was utilized.

Results:

PE was present in 5.21% of patients with COPD and SP. In comparison to the COPD+SP group, COPD+SP+PE group exhibited significantly higher levels of erythrocyte distribution width (RDW), platelet volume distribution width (PDW), mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), monocyte to large platelet ratio (MLPR), 5-hydroxytryptamine (5-HT), activated protein C (APC), urokinase-type plasminogen activator (u-PA), thrombomodulin (TM), interleukin-38 (IL-38), tissue factor (TF), and fractalkine (FKN). For COPD patients with SP who are complicated by PE, biomarkers such FKN, β-thromboglobulin (β-TG), APC, u-PA, TM, TF, and IL-38 were risk factors. Patients with COPD+SP who received clinical treatment had significantly lower levels of β-TG, IL-38, APC, endothelin-1 (ET-1), u-PA, FKN, TM, 5-HT, and neutrophil extracellular traps (NETs) (Table 1).

Indicators	OR	*P* value	95% CI
5-HT	1.011	0.132	0.997–1.026
β-TG	1.098	0.013*	1.020–1.182
APC	1.006	0.002*	1.002–1.010
ET-1	1.013	0.301	0.988–1.038
u-PA	1.006	0.000*	1.003–1.009
tPA	1.003	0.060	1.000–1.006
TM	1.684	0.004*	1.186–2.393
TF	1.034	0.000*	1.001–1.005
TFPI	1.009	0.191	0.966–1.022
IL-38	1.001	0.001*	1.000–1.001
FKN	1.004	0.020*	1.001–1.008
NETs	1.033	0.104	0.993–1.073

Note: *P < 0.05 was considered statistically significant.
Abbreviations: 5-HT, 5-hydroxytryptamine; β-TG, β-thromboglobulin; APC, activated protein C; ET-1, endothelin-1; u-PA, urokinase-type plasminogen activator; t-PA, tissue plasminogen activator; TM, thrombomodulin; TF, tissue factor; TFPI, tissue factor pathway inhibitor; IL-38, interleukin-38; FKN, fractalkine; NETs, neutrophil extracellular traps.

Table 1: Risk Factor Analysis Using Binary Logistic Regression for COPD Patients with PE-Complicated SP

Discussion:

This study found that COPD patients had a PE incidence of 1.73%, while COPD patients with SP had an incidence of 5.21%. Also, this study showed that the COPD+SP+PE group had significantly greater levels of RDW, PDW, NLR, PLR, LMR, and MLPR compared to the COPD+SP group.[2] Wang et al. showed a significant increase in the RDW of COPD patients with PE, suggesting that the RDW could predict the likelihood of PE in COPD patients.[3]

Conclusion:

Patients with SP and COPD had a considerably increased risk of PE. Routine blood and cardiac marker detection, blood gas analysis, and pulmonary function tests may be helpful in identifying patients with PE in COPD with SP. In patients with COPD and SP, APC, u-PA, TF, FKN, TM, and IL-38 are risk factors for PE, and this risk can be successfully decreased with clinical treatment.

Reference:

1. Miller PG et al. Association of clonal hematopoiesis with chronic obstructive pulmonary disease. Blood, The Journal of the American Society of Hematology. 2022 Jan 20;139(3):357-68.
2. Li J et al. Prevalence and Risk Factors of Pulmonary Embolism in COPD Patients Complicated with Secondary Polycythemia. Int J Chron Obstruct Pulmon Dis. 2024 Nov 3;19:2371-2385.
3. Wang J et al. Predictive Value of Red Blood Cell Distribution Width in Chronic Obstructive Pulmonary Disease Patients with Pulmonary Embolism. Anal Cell Pathol (Amst). 2020 Jul 21;2020:1935742.

Patients with secondary polycythemia and Chronic obstructive pulmonary disease had a significantly higher incidence of pulmonary embolism (PE).

4. Case report on yellow nail syndrome associated with mediastinal lipoma

Introduction:

Yellow nail syndrome (YNS) is an uncommon condition that often appears above the age of 50. It is characterized by common yellow nail discolorations, lower limb lymphedema, and pulmonary symptoms such as persistent cough, bronchiectasis, and pleural effusion. Additionally, it might be linked to cancer, autoimmune diseases, and other uncommon lymphatic conditions such as primary intestinal lymphangiectasia or lymphedema-distichiasis syndrome.[1] Samman and White first described YNS in 1964. It has an estimated prevalence of fewer than one in a million, making it a rare condition. The pathophysiology of YNS is typically explained in terms of poor lymphatic drainage. This may be caused by an obstruction of the thoracic duct, which drains the chyle of the small intestines and the lymphatic fluid of the lower extremities, or by an increase in chyle production. Only one more sign of lymphedema or a respiratory condition is needed to confirm the diagnosis, even though yellow nails are a must.[2] This case report describes a patient with all three clinical symptoms of YNS who underwent percutaneous lymphatic embolization after conservative therapy failed.

Case presentation:

A 73-year-old Caucasian male patient presented to clinic with new-onset dyspnea and orthopnea. He experienced symmetrical swelling in his lower extremities for 3 years, as well as yellow discoloration of his fingers and toes for 2 years. The physical examination revealed diminished breath sounds in the lower lung fields, dullness to percussion, peripheral edema in the feet and toes, and yellow staining of the nails (Fig. 1 and 2).

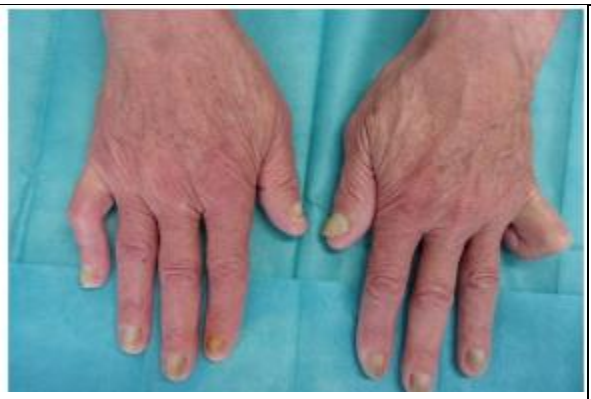


Figure 1: Yellow discolouration and cuticle loss in fingernails

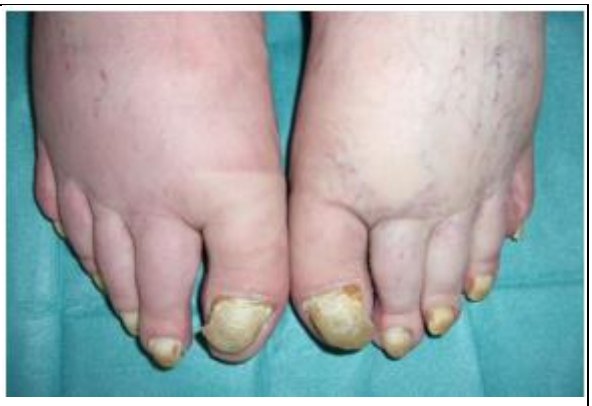


Figure 2: Onycholysis, thickness, and yellow discolouration of the toenails

The electrocardiogram was normal, except for the low voltage amplitude. Echocardiography revealed a 6 mm circumferential pericardial effusion during diastole, but no significant hemodynamic changes were seen. Pulmonary function tests revealed decreased forced expiratory volume (FEV1) of 1.6 l (51.2%) and reduced forced vital capacity (FVC) of 1.6 l (69.5%), with preserved ratio. The patient's medical history includes chronic bronchitis, epilepsy, one-sided amaurosis, hypothyroidism, resection of a retrobulbar meningioma, and multiple lumbar spine surgeries. This patient took levetiracetam, l-thyroxine, valsartan, cholecalciferol, and a tiotropium/olodaterol inhaler. The laboratory assessment of routine values was unremarkable. Nail biopsies tested negative for onychomycosis on periodic acid-Schiff stain (PAS) but showed nail thickening and extensive subungual stroma on H&E staining. Chest X-ray revealed significant pleural effusion in the left hemithorax with meniscus signs on both sides. An ultrasound-guided puncture on the left side was used to extract a non-viscous fluid from the chylous. A drainage catheter was inserted subscapulary into the ninth intercostal gap. Laboratory analysis of the pleural fluid revealed high levels of triglycerides and cholesterol, with a triglyceride to cholesterol ratio of 1.3, confirming the diagnosis of a chylothorax. Protein and lactate dehydrogenase (LDH) concentrations were indicative of an exsudate based on Light's criterion. The cytopathological investigation revealed foam cells on H&E staining (Fig. 3) and positive for fat-specific staining with Sudan Red.

A CT scan of the chest revealed a 7×4.5 ×3 cm^3 paratracheal lipoma with no infiltrative development or compression of the surrounding mediastinum. The first week shown a minor decrease in the drained volume of roughly 500 ml per day because of using a dietary treatment strategy and start total parenteral feeding with middle-chain triglycerides (MCT). Despite treatment adherence, this patient experienced a weight loss of around 6 kg, persistent lymphedema, and nail discolouration. An abnormal lymphatic drainage with chylolymphatic refux into mediastinal lymphatic vessels was observed during lymphangiography, which was performed to assess additional treatment options. The following day, lipidol was used to perform percutaneous lymphatic embolization through an inguinal access point. Radiographic examination, including CT thorax, showed good results, with no post-interventional problems and a drop in drained volume to around 100 ml daily during the next week. Lymphedema was treated with compression bandages, manual drainage, and a mechanical decongestive device. To promote nail regeneration, this patient was prescribed topical tocopherol (vitamin E) and oral zinc supplementation.

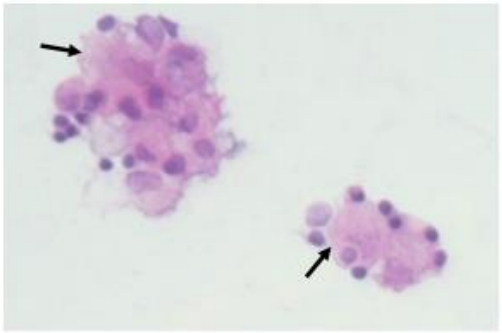


Figure 3: Hematoxylin and eosin staining with arrows indicating foam cells

Discussion:

YNS is diagnosed based on its clinical signs and exclusion of other common disorders. In the present case, YNS was managed with 5% vitamin E solution and 30 mg zinc once daily.[2] In a previous case by Pozzo-Magana et al, YNS was treated with itraconazole and vitamin E.[3]

Conclusion:

This case presentation highlights common pathogenesis and treatment options, in addition to displaying specific diagnostic findings.

References:

1. Walz-Eschenlohr U, Witt S, Dieterle T. A 9-Year-Old Patient with Yellow Nail Syndrome. connective tissue. 2023 Jun 26;51(2):42516- 42520.
2. Muller C, Stricker I, Hykel P, Dellweg D. Yellow nail syndrome linked to a mediastinal lipoma: a case report. J Med Case Rep. 2024 Dec 11;18(1):599.

3. Del Pozzo-Magana BR. Yellow nail syndrome treated with itraconazole and vitamin E: A case report. Dermatologica Sinica. 2024 Jul 1;42(3):242-3.

Percutaneous lymphatic embolization was employed as an interventional strategy when conservative treatment failed to significantly alleviate the initial YNS symptoms.