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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:

1. Assessment of functional outcomes as a clinical endpoint in a cohort of patients with acute hypoxemia
2. A cross-sectional study on the relationship between monocytes to high-density lipoproteins and the prevalence of prediabetes
3. Evaluation of the correlation between nocturnal blood pressure, night-time dipping patterns, and the occurrence of major adverse events in individuals with coronary heart disease and hypertension
4. Case report on Graves' Disease with Initial Symptoms of Thyrotoxic Periodic Paralysis

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

Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

Assessment of functional outcomes as a clinical endpoint in a cohort of patients with acute hypoxemia

Introduction:

Hypoxemia occurs when arterial blood has low oxygen levels (partial pressure or saturation). Commonly used criteria for arterial blood include partial pressure of oxygen (PaO2) less than 60 mmHg and oxygen saturation (SaO2) less than 90%. In contrast, hypoxia is defined as an insufficient oxygen flow to organs and tissues.[1] In critically sick patients, hypoxia is a common and possibly fatal condition. However, little is known about the occurrence, treatment, and consequences of hypoxemia in non-selected ICU patients.[2] The impact of oxygen treatment on survival and other patient-relevant outcomes in patients with acute hypoxemia admitted to emergency care was unknown due to the lack of randomized studies. Data on mortality and intubation rates in hypoxemic patients vary based on the underlying condition. Hypoxemic individuals with community-acquired pneumonia and COPD exacerbations had an 8% mortality rate 28 days after admission. Despite increasing attention to oxygen utilization, observational data on functional impairment in hospitalised patients with acute hypoxemia were limited.[1] This study aimed to assess functional deterioration in patients with acute hypoxemia using the WHO scale as a clinical endpoint. It was part of a nationwide clinical trial evaluating various oxygen goals. This trial's secondary objective was to determine the necessary inclusion criteria and outcome variables to generate a suitable sample size.

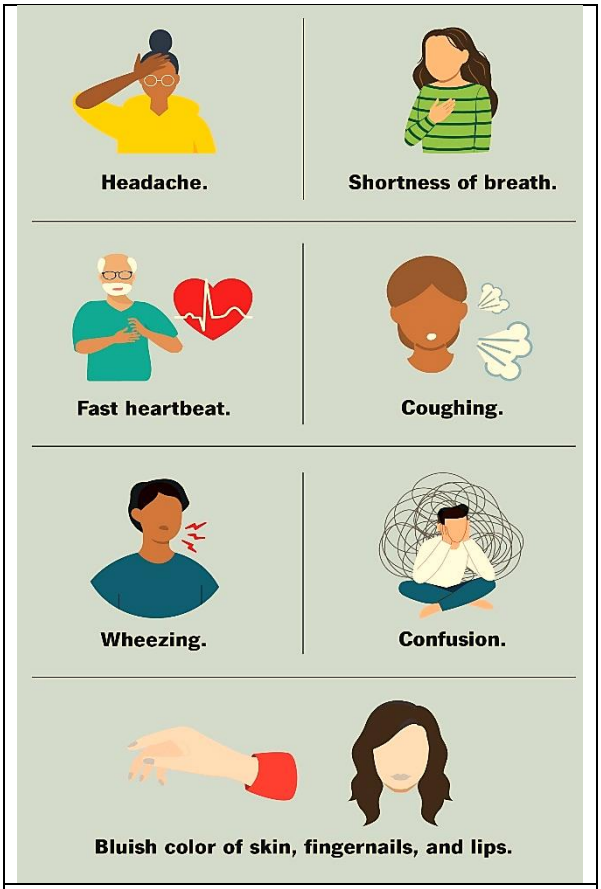

Figure 1. Symptoms of hypoxemia

Methods:

A multicentre prospective observational study was done on individuals experiencing new-onset hypoxemia. The WHO scale was used to measure patients' functional state 4 weeks before to admission and at discharge. Data was collected on oxygen therapy type and duration, hospital length of stay, survival rates, and risk of hypercapnic failure. The primary objective of this study was to monitor the functional results of hospital admissions resulting in acute hypoxemia at discharge. This trial's secondary objective was to determine the proper inclusion criteria and outcome variables in order to determine the necessary sample size.

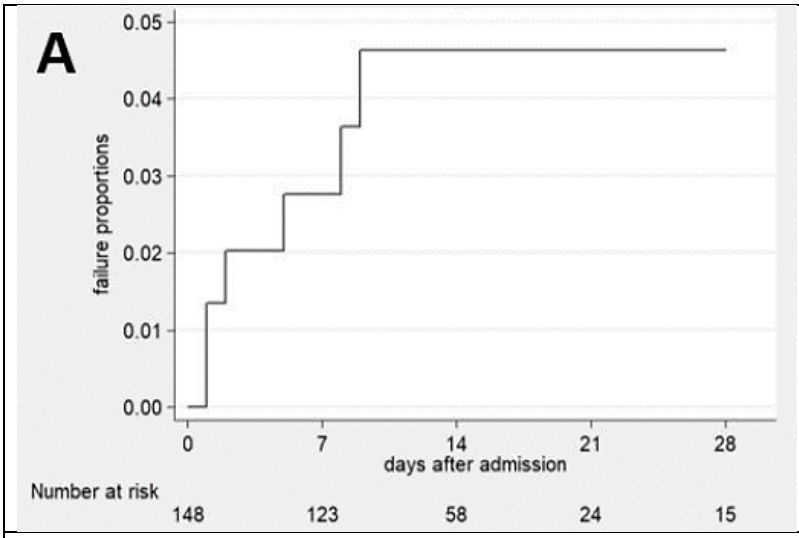

Figure 2A. Time to intubation on the Kaplan-Meier failure graph within 28 days

Results:

The study comprised 151 individuals, with a median age of 74 years. The majority of patients hospitalized with hypoxemia were elderly (median age 74), with 51% having previously acceptable performance status (WHO grade 0 or 1). Patients were hospitalized for a variety of reasons, including respiratory infections (29%), COPD exacerbations (14%), decompensated heart failure (28%), and cancer progression (11%). At discharge, two-thirds experienced a drop in functional status of at least one grade. Functional decline was more likely in those with high functional status (OR 4.849, 95% CI 2.209-10.647) and progressing cancer (OR 6.079, 1.197-30.881). The majority of patients (n = 95, 62%) received standard oxygen treatment. In-hospital mortality and intubation rates were both 8%. The mean length of oxygen treatment was 12 (25, 75% percentile 7, 18)

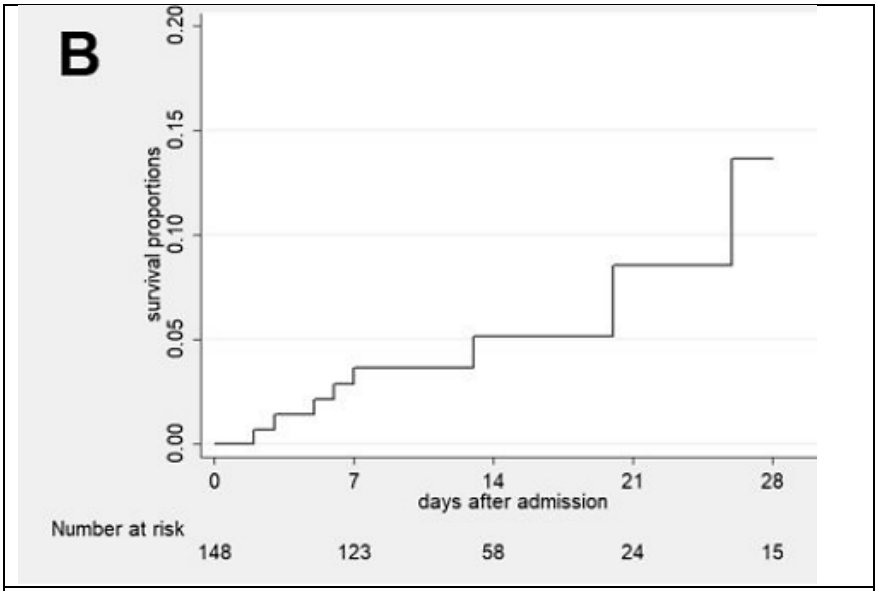

Figure 2B. Time to death on Kaplan–Meier failure graphs within 28 days

days (Figure 2A). The median hospital stay was 12 days (25, 75% percentile 8, 18). Twelve patients (8%) died in the hospital, with a median stay of 17 days (Figure 2B).

Discussion:

This study demonstrated that new-onset hypoxemic respiratory failure significantly affects functional deterioration at hospital discharge in two-thirds of patients. Twenty-nine percent of the participants in this study were hospitalized because of pneumonia.[1] A recent study of 1054 hospitalized patients with community-acquired pneumonia found that elderly patients had a 23% higher mortality rate after 30 days.[3] In this cohort, 10 individuals were diagnosed with community-acquired pneumonia and 2 died in the hospital, which was consistent with previous findings.

Conclusion:

Patients with acute hypoxemia in the emergency room have a worse functional status following discharge. There might be several factors causing this decline.

Acute hypoxemia patients in the emergency department had worse functional statuses after they discharge from the hospital.

Reference:

1. Simon S, Gottlieb J, Burchert I, Abu Isneineh R, Fuehner T. Outcomes and Functional Deterioration in Hospital Admissions with Acute Hypoxemia. Advances in Respiratory Medicine. 2024 Mar 6;92(2):145-55.
2. SRLF Trial Group. Hypoxemia in the ICU: prevalence, treatment, and outcome. Ann Intensive Care. 2018 Aug 13;8(1):82.
3. Theilacker C, Sprenger R, Leverkus F, Walker J, Häckl D, von Eiff C, Schiffner-Rohe J. Population-based incidence and mortality of community-acquired pneumonia in Germany. PloS one. 2021 Jun 15;16(6):e0253118.

A cross-sectional study on the relationship between monocytes to high-density lipoproteins and the prevalence of prediabetes

Introduction:

Prediabetes is a condition when blood glucose levels exceed the normal range but do not yet meet the diagnostic criteria for diabetes. The annual conversion rate from prediabetes to diabetes was estimated to be 5-10%, making it a significant risk factor for the condition.[1] Prediabetes was diagnosed using laboratory measurements of fasting blood glucose (FBG), glycosylated hemoglobin (HbA1C), or 2-hour post load blood glucose (2hBG). Prediabetes increases cardiometabolic risk factors and leads to poor outcomes.[2] Early treatments are critical for preventing prediabetes from progressing to diabetes and its consequences. Inflammatory factors, including neutrophil-to-lymphocyte ratio (NLR), white blood cell (WBC), C-reactive protein (CRP), NLRP3 inflammasome, interleukins (IL-1β, IL-6, TNF-α, and IL-18), and increased monocyte activation, have been linked to prediabetes risk. The monocyte-to-high-density lipoprotein cholesterol (MHR) ratio has been associated with metabolic diseases. However, there was minimal information on the link between MHR and prediabetes.[1] The purpose of this study was to investigate the relationship between MHR and prediabetes prevalence.

Methods:

This was a cross-sectional observational study that included routine health check-up data from 3,652,054 individuals. The association between MHR and prediabetes was investigated using multivariable regression, subgroup analyses, and interaction testing. A generalized additive model (GAM) and smoothing splines were used to investigate the non-linear relationship between MHR and risk of prediabetes. The threshold effect study of MHR on the risk of prediabetes was used to identify the turning point.

Results:

The clinical characteristics of 85,293 subjects were categorized according to the presence or absence of prediabetes. The average age was 50.29 ± 13.24 years, and 63.88% were male. About 33,992 individuals (39.85%) were diagnosed with prediabetes. After controlling for covariates, the study found a positive correlation between MHR and prediabetes (OR =1.64, 95% confidence interval (CI), 1.48-1.82). Subgroup analyses revealed a stronger correlation between MHR and prediabetes in individuals with lower age, SBP, DBP, TG, TC, and higher BMI and LDL-C values compared to their counterparts. The relationship between MHR and the risk of prediabetes was non-linear, with a turning point of -0.4 (Log-Likelihood Ratio, $P < 0.001$). The effect of variables on the two sides of the turning point was 1.94 (1.72, 2.19) and 0.88 (0.69, 1.14) (Table 1).

	Prediabetes OR (95% CI)	P value
Fitting model by standard linear regression	1.64 (1.48, 1.82)	<0.001
Fitting model by two-piecewise linear regression		
Inflection points of MHR	−0.40	
≤ −0.40	1.94 (1.72, 2.19)	<0.001
> −0.40	0.88 (0.69, 1.14)	0.348
P for log likelihood ratio test	0.001	

Note: Each model was adjusted for age, gender, BMI, SBP, DBP, Scr, UA, TG, TC, LDL-C, FPG, WBC.
Abbreviations: OR, odds ratio; CI, confidence; MHR, monocyte-to-high-density lipoprotein ratio, MHR value was log10-transformed.

Table 1. Two-Piecewise Linear Regression Model-Based Threshold Effect Analysis of MHR on Prediabetes

Discussion:

This cross-sectional study demonstrated that greater MHR values were associated with an increased likelihood of prediabetes. This study was the first to identify a link between MHR and prediabetes, providing potential for primary preventive strategies.[1] In a previous study by Li C et al. concluded that MHR levels were associated with in-hospital MACE and long-term bleeding episodes in T2DM patients with NSTE-ACS undergoing PCI.[3]

Conclusion:

MHR was shown to have a non-linear positive connection with prediabetes risk, with MHR ≤ −0.4 indicating a significant link.

When MHR was less than -0.4, there was a significant positive connection with prediabetes risk.

Reference:

1. Ruan C, Li Y, Ran Z, Liu G, Li W, Zhang X, Shao S, Li Y. Association Between Monocyte-to-High-Density Lipoprotein Ratio and Prediabetes: A Cross-Sectional Study in Chinese Population. Diabetes, Metabolic Syndrome and Obesity. 2024 Dec 31:1093-103.
2. Echouffo-Tcheugui JB, Selvin E. Prediabetes and what it means: the epidemiological evidence. Annual review of public health. 2021 Apr 1;42:59-77.
3. Li C, Fan H, Liu Y, Zeng L, Chen P, Duan C, Liang H, He P. The monocyte to high-density lipoprotein cholesterol ratio and outcomes in type 2 diabetes mellitus patients with non-ST-segment elevation acute coronary syndrome. Ann Transl Med. 2021 Nov;9(21):1627.

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Evaluation of the correlation between nocturnal blood pressure, night-time dipping patterns, and the occurrence of major adverse events in individuals with coronary heart disease and hypertension

Introduction:

Coronary heart disease (CHD), a major cardiovascular disease, is the leading cause of mortality and disability worldwide. CHD was linked to atherosclerosis, and the presence of atherosclerotic plaques in coronary arteries can reduce myocardial perfusion. CHD includes persistent and unstable angina, myocardial infarction (MI), and sudden cardiac death. Obesity, smoking, excessive consumption of alcohol, and salt intake were few of the risk factors for coronary heart disease.[1] Hypertension is regarded as a major risk factor for CHD and has a high worldwide prevalence. Accurately diagnosing and managing hypertension is critical for CHD patients. Ambulatory blood pressure monitoring (ABPM) gives vital information on 24-hour, daytime, and nightly blood pressure, as well as diurnal changes. Blood pressure typically rises throughout the day and decreases at night, with a normal drop of less than 20% and at least 10%. This is referred to as a dipping pattern. Other patterns include excessive dipping (over 20% drop), non-dipping (less than 10% reduction), and riser patterns (any riser) based on SBP decrease at night versus daylight. The riser pattern has been linked to a much poorer outcome for stroke and cardiovascular events. Limited study has investigated whether the riser pattern was linked to a worse outcome in individuals with CHD and hypertension, regardless of overnight SBP levels.[2] This study aimed to investigate the link between nocturnal blood pressure, overnight dipping patterns, and significant adverse events in individuals with CHD and hypertension.

Methods:

This prospective clinical trial comprised 568 hospitalized patients with CHD and hypertension. During hospitalization, all patients were monitored for ambulatory blood pressure (BP) every 24 hours. Using multivariate adjusted Cox proportional hazard models, the relationships between dipping status and nocturnal blood pressure and primary endpoint events were investigated. Harrell's C-statistics were used to assess the discriminative capacity of each model. The study's primary outcome included the first incidence of all-cause mortality or total nonfatal cardiovascular disease (CVD) events.

Results:

The study included 1467 participants with CHD and hypertension. Among them, a total of 568 patients were categorized into three groups based on their nocturnal SBP dipping pattern. During the one-year follow-up, 64 (11.3%) primary endpoint events were observed, with 55 (9.7%) being atherosclerotic cardiovascular disease (ASCVD) (Figure 1). Even after controlling for demographic and clinical risk factors, nocturnal SBP was linked to an increased risk of primary endpoint events (hazard ratio (HR) = 1.775, 95% confidence interval (CI) 1.256-2.507). The riser pattern group had a substantially greater risk of primary endpoint events compared to the dipper pattern group, even after adjusting for office SBP (HR: 2.687, 95% CI: 1.015-7.110, p =0.047). Adding nocturnal SBP or dipping status to the original model resulted in substantial increases in C-statistic values (p =0.036, p =0.007). Adding night-time SBP and dipping status did not improve the model's ability to predict primary endpoint events and ASCVD events (p =0.053 and p =0.054, respectively), indicating that the riser pattern group did not have a significantly higher risk for primary endpoint events than the dipper pattern group after controlling for night-time SBP.

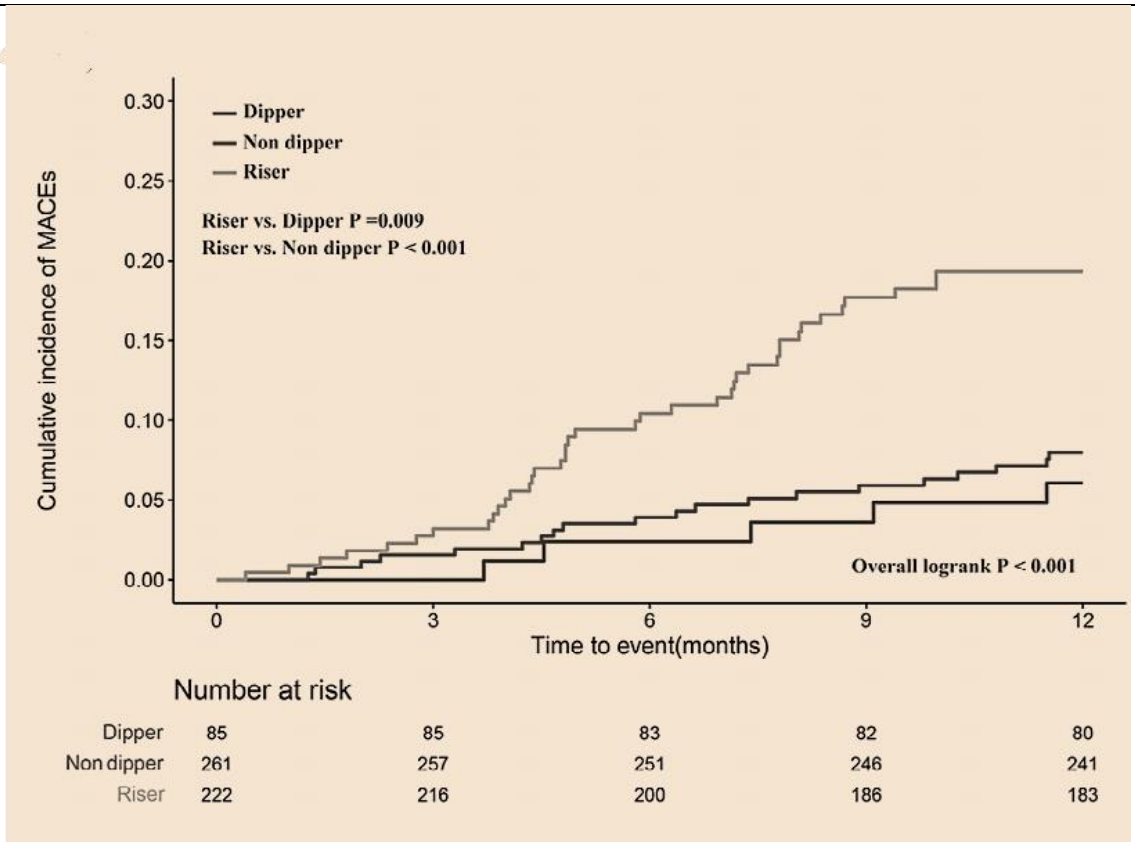

Figure 1. Cumulative incidence of total and ASCVD events among three groups. Kaplan-Meier graphs illustrate the cumulative incidence of all ASCVD events.

Discussion:

This study assessed the relationship between the prognosis and overnight blood pressure characteristics in individuals with hypertension and congestive heart failure. Patients with CHD and hypertension were more affected by increased night-time SBP and dipping status than by daytime SBP.[2] This was similar to the findings of the previous study by Kazuomi Kario et al. found that night-time blood pressure levels and a riser pattern were found to be independently linked with the overall cardiovascular event rate, particularly for heart failure.[3]

Conclusion:

Nocturnal SBP and riser pattern were associated with a worse prognosis in individuals with CHD and hypertension. Notably, nocturnal SBP was a more reliable predictor than dipping status.

People with Coronary heart disease (CHD) and hypertension who have nocturnal SBP and a riser pattern were likely to have a worse prognosis.

Reference:

1. Liang X, Huang Y, Han X. Associations between coronary heart disease and risk of cognitive impairment: A meta-analysis. Brain and Behavior. 2021 May;11(5):e02108.
2. Du Y, Zhu B, Liu Y, Zhou W, Du Z, Yang W, Gao C. Association between nocturnal blood pressure phenotype and adverse cardiovascular prognosis in patients with coronary heart disease and hypertension. The Journal of Clinical Hypertension. 2024 Mar 7;1-11.
3. Kario K, Hoshide S, Mizuno H, Kabutoya T, Nishizawa M, Yoshida T, Abe H, Katsuya T, Fujita Y, Okazaki O, Yano Y, Tomitani N, Kanegae H; JAMP Study Group. Nighttime Blood Pressure Phenotype and Cardiovascular Prognosis: Practitioner-Based Nationwide JAMP Study. Circulation. 2020 Nov 10;142(19):1810-1820.

Case report on Graves' Disease with Initial Symptoms of Thyrotoxic Periodic Paralysis

Introduction:

Thyrotoxic periodic paralysis (TPP) is caused by environmental variables in the setting of thyrotoxicosis, resulting in abrupt muscular weakness or paralysis and hypokalemia. TPP is more prevalent in Asians with hyperthyroidism, with a prevalence of up to 2%. In non-Asian populations, the reported incidence is 0.1-0.2%.[1] TPP develops in people with excessive levels

of thyroid hormone or hyperthyroidism. Graves' disease is the leading cause of hyperthyroidism linked with TPP. Other causes of thyrotoxicosis include toxic multinodular goiter, iodine-induced thyrotoxicosis, excessive thyroxine usage, solitary toxic adenoma, lymphocytic thyroiditis, and amiodarone-induced thyrotoxicosis. TPP is reversible with correction of hypokalemia and thyrotoxicosis, but its rare presentation may delay diagnosis and therapy.[2] In this case report, a 24-year-old male experienced proximal muscular weakness, leading to frequent falls and inability to walk for three days.

Case presentation:

A 24-year-old male with a history of atrial fibrillation and autoimmune thyroid disease presented to the emergency department with severe muscular weakness. For three days, the patient complained of gradually worsening widespread muscular weakness, and as his condition got worse, he lost the ability to walk. His weakness led to repeated falls and inability to move himself from a seated posture, forcing friends to take him to the emergency department. The weakness did not improve with rest. Upon arrival at the emergency department, he was in a wheelchair and unable to walk. Other prominent symptoms included sporadic and non-persistent episodes of tremors and heat sensitivity. The patient claimed temporary lactose sensitivity and loose stools after consuming dairy products. The patient reported no unexplained weight loss, palpitations, hair, skin, or eyesight abnormalities. He reported no back discomfort, numbness, or paresthesia, and no recent fever or viral infections. Family history was notable for a mother with Hashimoto's thyroiditis. The patient's physical exam revealed sinus tachycardia, a heart rate of 120 bpm, a temperature of 98.8°F, blood pressure of 140/84 mm Hg, and a respiratory rate of 16 bpm. He had a BMI of 23 (kg/m^2) and weighed 68 kg. The physical test revealed bilateral 2/5 muscular strength, including flexion and extension in the hips, knees, shoulders, and forearms. He also possessed two-fifths grip strength bilaterally. Bilateral patellar and biceps reflexes were missing, although both extremities had normal sensation to mild touch. Laboratory findings showed potassium at 1.8 mmol/L (3.3-5.0 mmol/L) and magnesium at 1.8 mg/dL (1.6-2.6 mg/dL). The patient's thyroid stimulating hormone (TSH) level was < 0.01 (0.3-4.00 mU/L), free thyroxine was 5.0 ng/dL (0.8-1.7 ng/dL), total triiodothyronine was 301 ng/dL (80-200 ng/dL), and TSH receptor antibody was 10.17 IU/L (<= 1.75 IU/L). Creatine kinase was 890 U/L (20–200 U/L). The patient was treated with careful potassium repletion, receiving 40 mEq oral potassium, 40 mEq IV potassium, and 2 grams IV magnesium. After serum potassium levels reached 4.4 mmol/L, the patient's weakness resolved quickly. He did not need further potassium replenishment. The patient was also given propranolol 40 mg BID and methimazole 20 mg daily. After two days of hospitalization, the patient was discharged with improved mobility and activity (Table 1). After three months of treatment, the patient's thyroid function improved and methimazole was reduced to 10 mg daily. The patient gained 4kg and no longer experienced hyperthyroidism symptoms. He experienced no recurrence of thyrotoxicosis or weakness. After a 12-month follow-up, the patient continued on methimazole and did not experience any recurrence but after that lost to follow-up.

Timeline	Symptoms	Diagnostic test	Treatment
Initial presentation	Non-ambulatory. Severe proximal muscle weakness 2/5. Heat intolerance. Diarrhea. Tremors.	K+ 1.8 mmol/L	40 meq KCl PO
		Mg 1.8 mg/dL	40 meq KCl IV
		TSH <0.01 mU/L	2 grams MgSO4 IV
		FT4 5.0 ng/dL	Methimazole 20 mg daily
		TT3 301 ng/dL	Propranolol 20 mg BID
+ 7 hours	Weakness improved 4/5 and patient is ambulatory.	K+ 4.4 mmol/L	Monitored in hospital
+ 36 hours	Muscle strength improves 5/5.	K+ 4.2 mmol/L	Discharged from hospital
+ 1 month	Weakness resolved. Mild tremor remains.	FT4 3.1 ng/dL	Increased Methimazole to 30 mg daily
		TT3 203 ng/dL	
+ 3 months	Asymptomatic.	K+ 3.9 mmol/L	Decreased Methimazole to 10 mg daily
		TSH 0.01 mU/L	
		FT4 1.0 ng/dL	Stopped Propranolol
		TT3 91 ng/dL	
+ 12 months	Asymptomatic. No recurrence of muscle weakness.	TSH 10.15 mU/L	Decreased Methimazole to 5 mg daily
		FT4 1.3 ng/dL	

Table 1: Timeline of events
TSH; thyroid stimulating hormone, FT4; free thyroxine, TT3; total triiodothyronine, K+; potassium, KCL; potassium chloride, Mg; magnesium, MgSO4; magnesium sulfate.

Discussion:

TPP can be identified by thyrotoxicosis, abrupt hypokalemia, and muscular weakness that may lead to paralysis. Paralysis often begins symmetrically in the lower extremities and progresses to quadriplegia. In the present case, the patient was treated with careful potassium repletion, receiving 40 mEq oral potassium, 40 mEq IV potassium, and 2 grams IV magnesium. The patient was also given propranolol 40 mg BID and methimazole 20 mg daily.[2] In a previous case report on TPP by Shourya Tadisina et al. demonstrated that emergency treatment to avoid cardiopulmonary consequences involves cautious potassium replenishment. Non-selective beta blockers, such as propranolol, can be administered orally at a high dosage of 3-4 mg/kg, either with potassium chloride or alone, to prevent acute episodes.[3]

Conclusion:

Diagnosing TPP can be complicated because of its many clinical presentations. However, early detection and treatment may prevent life-threatening consequences. The treatment objective was to achieve and maintain euthyroidism to avoid hyperthyroidism consequences including muscular weakness. To prevent rebound hyperkalemia, treat hypokalemia with beta blockers and carefully administer low-dose potassium replacement therapy if necessary.

Thyrotoxic periodic paralysis (TPP) is an uncommon disorder that can be difficult to diagnose. However, a comprehensive medical history, physical exam, and biochemical examination can help identify and treat this condition.

References:

1. Rivas AM, Thavaraputta S, Orellana-Barrios MA, Payne JD, Sotello D, Vinan-Vega M, Lado-Abeal J. Thyrotoxic periodic paralysis and complicated thyrotoxicosis, two presentations of hyperthyroidism with notable differences in their clinical manifestations: an experience from a tertiary care hospital in the United States. Endocrine Practice. 2020 Jul 1;26(7):699-706.
2. Petty L, Kaput K. Graves' Disease with Initial Presentation of Thyrotoxic Periodic Paralysis. Cureus. 2023 Nov 27;15(11):e49524.
3. Tadisina S, Asad R, Varakantam A, Weide L, Drees B. Thyrotoxic periodic paralysis as an ongoing diagnostic challenge: a case report and literature review. Cureus. 2023 Sep;15(9):e46272.