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# Prevalence of Subclinical Peripheral Neuropathy in Chronic Obstructive Pulmonary Disease.

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## ABSTRACT

**Background:** Present study aimed to assess peripheral neuropathy in stable COPD patients, its prevalence, type and distribution and correlate the changes with severity of COPD. **Methods:** Study comprised of 60 healthy adults and 60 stable nonalcoholic and normo-glycemic COPD patients (30-70yrs) with no clinical symptoms and signs of neuropathy. Severity of COPD was classified as per WHO GOLD criteria. Nerve conduction study of four motor and four sensory nerves of upper and lower limb was done and parameters like distal latency, amplitude and conduction velocity was studied. **Results:** Study revealed prolonged distal latency, reduced conduction velocity and reduced amplitude in COPD patients as compared to controls. More number of nerves involved with increasing severity of disease. The observations revealed that demyelinating motor and axonal sensory neuropathy can be seen in COPD patients and neuropathy occurred even in mild COPD patients. **Conclusion:** Sensory polyneuropathy predominant in lower limb was present in majority of patients.

***Key words***: COPD, Peripheral neuropathy

## INTRODUCTION

COPD a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lungs to noxious particles or gases. Exacerbations and comorbidities contribute to overall severity in individual patients.[1] According to WHO, 65 million people have moderate to severe COPD and it is the fourth leading cause of death in the world.[2] There are approximately 30 million COPD patients in India.[3]

COPD is a multisystem disorder that is frequently associated with significant extra-pulmonary manifestations.[4] Peripheral neuropathy is a known systemic manifestation of COPD. COPD leads to hypoxemia due to ventilation perfusion mismatch. Hypoxemia is thought as a possible cause of peripheral neuropathy.[5]

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Electrophysiological studies reveal mostly sensory type neuropathy more in distal parts of extremities but in severe cases it is characterized by loss of axons and demyelination also.[6]

With this background the study was undertaken to evaluate electrophysiological variables of peripheral sensory and motor nerves and their correlation with severity and duration of illness, pack years of smoking and Spiro metric indices.

## MATERIALS AND METHODS

Sixty clinically diagnosed COPD patients (49 male, 11 female, not suffering from diabetes mellitus, hypertension, uremia, asthma, unstable angina and not on any neurotoxic drug) were selected for the study. They were subjected for detailed clinical and neurological examinations followed by spirometry and nerve conduction studies.

Participants were divided into four subgroups- mild, moderate, severe, very severe grade of COPD (15 patients in each group) as per WHO GOLD criteria. COPD patients were either current smokers (76.6%) or non smokers (23.3%).smoking pack years were calculated using Dr N.J. Masters and Catherine Tutt smoking pack year calculator.[7,8]

Healthy age and sex matched, nonsmoker volunteers (n=60) were also selected from attendants of patients and subjected to spirometry and nerve conduction study. There was no evidence of any neurological deficit on history and clinical examination. On

spirometry FEV1/FVC was more than 70%. The exclusion criteria of patient group were also used for controls.

Spirometry was done by using RMS-Helios 401 spirometer and best of three consecutive tests were taken into consideration. Patients were advised to stop bronchodilators and anticholinergic drugs for a period of 12 hours before spirometry. Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1) and the ratio of FEV1/FVC, peak expiratory flow during middle half of FVC (FEF 25-75 or MMEFR) were measured. Pre and post bronchodilator study was done in all and there was no significant reversibility after bronchodilators in COPD patients.

Nerve conduction study (NCS) was done using RMS EMG Aleron 201. NCS was done in two parts- motor and sensory nerve conduction studies. The nerves studied were:

1. Median nerve motor &sensory
2. Ulnar nerve motor &sensory
3. Tibial nerve motor & sensory
4. Peroneal nerve motor
5. Sural nerve sensory
6. Superficial peroneal nerve sensory

Parameters recorded were distal latency for motor and sensory nerves, nerve conduction velocity for motor (MNCV) and sensory nerves (SNCV), compound muscle action potential (CMAP) and sensory nerve action potential (SNAP).

Motor NCS were performed by stimulation of a peripheral nerve and recording from a muscle supplied by this nerve. The time taken for the electrical impulse to travel from the stimulus to the recording site was measured this is called distal latency, measured in milliseconds. The size of response called the amplitude was also measured. Motor amplitude are measured in millivolts. By stimulating in two or more different locations along the same nerve, the nerve conduction velocity (m/sec) across different segments were determined. Calculations were performed using the distance between different stimulating electrodes and difference in latencies. A supra-maximal stimulation was given to prevent hyper-polarization of anode and anodal conduction block. After placing all electrodes in positions a biphasic action potential with initial negativity is thus recorded.

Sensory NCS were performed by electrical stimulation of a peripheral nerve and recording from a purely sensory portion of nerve, such as on a finger. Latency measured in milliseconds and amplitude in microvolt. Conduction velocity was calculated based upon the latency and the distance between the stimulating and recording electrodes.

Statistical analysis: All values were expressed as Mean ± Standard Deviation. Student t-test and one way ANOVA were used to compare groups. Bivariate correlations between variables were evaluated by Pearson's correlation. Statistical analysis was done using SPSS-16.0 (statistical package for social science)

## RESULTS

Analysis of electrophysiological variables recorded showed significantly prolonged ($p<0.05$) distal latency and/or reduced conduction velocity of Median nerve, Tibial nerve and left Peroneal nerves in COPD group as compared to controls. Significantly reduced amplitude($p<0.05$) was identified in right Peroneal nerve ,while both significantly prolonged distal latency and reduced amplitude of Ulnar nerve was seen in COPD group. Significant reduction in amplitude of left median nerve and left peroneal nerve ($p<0.05$) as compared to controls was established. Sensory nerve conduction parameters of control and COPD group and their changes with severity were also studied. Electrophysiological variables recorded showed significantly prolonged distal latency ($p<0.05$) in COPD cases as compared to controls in Sural nerve, Peroneal nerve and left Ulnar nerve. Significantly decreased amplitude ($p<0.05$) was found in right Ulnar nerve, left Sural nerve and Superficial peroneal nerve in COPD group as compared to controls. Sensory nerve conduction velocity of right peroneal nerve was significantly reduced ($p<0.05$) in COPD pts. Although the distal latency of median sensory nerve in COPD patients was prolonged as compared to that of control group the change was not statistically significant.

An attempt was also made to identify changes in electrophysiological variables with increasing severity of COPD ,for which COPD pts were classified on the basis of FEV1>50% (group I) and FEV1<50% (group II).

In left peroneal nerve significant reduction of conduction velocity was found with increasing severity of disease .With increasing severity of disease more number of motor nerves i.e. left median, ulnar and peroneal were also observed to have neuropathy. With increasing severity of airway obstruction more number of sensory nerves i.e. median nerve (16.6% in group II), left ulnar nerve (63.3% in group II and right superficial peroneal nerve (86.6% in group II) were involved.

An attempt was made to find out the distribution of peripheral neuropathy in motor nerves and sensory nerves of COPD pts. In motor nerves, in upper limb

mixed peripheral neuropathy was predominant in ulnar nerve (right ulnar 46.6%, left ulnar 36.6%).In lower limb motor demyelinating neuropathy was predominant in tibial nerve and peroneal nerve(51.6% right tibial, 55% left tibial and 48.3% right peroneal, 46.6% left peroneal nerve). In sensory nerves predominant axonal neuropathy was detected in nerves of lower limbs. (46.6%and 70% in right and left Sural nerve, 45% and 68.3% cases in right and left superficial peroneal nerve respectively). In upper limb nerves, left ulnar sensory nerve showed axonal degeneration in 25% of cases.

**Table 1**: Relevant baseline characteristics of study population.

| S. No. | Variables | Controls n=60 | Cases (COPD patients) n=60 | | | | |
|---|---|---|---|---|---|---|---|
| | | | Entire group n=60 | Mild n=15 | Moderate n=15 | Severe n=15 | Very severe n=15 |
| 1. | Age(years) | 53.1±13.4 | 54.5±11.4 | 55±11.9 | 56.1±12.5 | 52.3±8.8 | 54.6±12.0 |
| 2. | BMI(kg/m$^{2)}$ | 24.1±2.5 | 23.9±4.2 | 24.4±3.8 | 23.1±4.0 | 23.3±4.4 | 24.9±4.6 |
| 3. | Pulse(bpm) | 73.4±4.1 | 81.7±11.8 | 82.9±9.2 | 75.4±15 | 82.0±9.8 | 86.6±10.4 |
| 4. | Respiratory rate (pm) | 14.2±1.9 | 18.0±3.5 | 18.6±4.1 | 17.4±2.7 | 18.2±4.2 | 18±2.9 |
| 5. | SBP(mm hg) | 113.2±2.9 | 129.3±9.1 | 129.2±9.1 | 128.3±10.5 | 130.6±8.4 | 129.3±9.5 |
| 6. | DBP(mm hg) | 73.4±2.9 | 83.5±6.6 | 84.1±9.1 | 80.8±6.7 | 84.6±4.9 | 84.5±4.6 |
| 7. | Pack years | - | 29.5±25.3 | 23.7±15.8 | 25.8±21.2 | 30.9±34 | 37.9±30 |
| 8. | Duration of COPD symptoms | - | 10.9±6.7 | 2.66±1.79 | 8.6±2.2 | 12.5±1.9 | 20.1±2.6 |

All the vital parameters in COPD patients were found to be on higher side compared to control.

**Table 2**: Spirometric indices and saturation of oxygen of COPD patients and control:

| | FEV1(%predicted) | FEV1/FVC (%) | FVC (%) | PEFR (predicted) |
|---|---|---|---|---|
| **Control (n=60)** | 95.9±34.2 | 88.8±11.1 | 92.5±24.3 | 88.7±39.6 |
| **COPD patients (n=60)** | 53.5±26.4 | 52.9±11.3 | 73.3±20.6 | 45±18.9 |
| **t** | 7.5 | 17.6 | 4.6 | 7.7 |
| **p** | 0.0001 | 0.0001 | 0.0001 | 0.0001 |

**Table 3:** Comparison of motor nerve conduction parameters in control and study group

| Nerve | Electrophysiological Variable | Control group(n=60) | | COPD group(n=60) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Right I | Left II | Right III | Left IV | $T_1$ IvsIII | $T_2$ IIvsIV | $P_1$ IvsIII | $P_2$ IIvsIV |
| **Median** | Distal latency(ms) | 2.5±0.6 | 2.5±0.6 | 2.7±0.6 | 3.1±0.8 | 2.5 | 4.1 | 0.01 | 0.0001 |
| | CMAP(mV) | 6.9±2.1 | 6.9±1.7 | 8.7±2.8 | 8.2±2.6 | - | - | -- | - |
| | MNCV(m/s) | 53.4±5.2 | 52.9±3.4 | 51.5±3.9 | 52.7±5.6 | 2.7 | 0.2 | 0.001 | NS |
| **Ulnar** | Distal latency(ms) | 2.1±1.5 | 1.6±0.5 | 2.2±0.9 | 2.6±1.1 | 0.4 | 6.9 | NS | 0.0001 |
| | CMAP(mV) | 7.6±1.5 | 6.9±0.5 | 5.8±1.5 | 5.9±1.7 | 6.3 | 3.9 | 0.0001 | 0.0001 |
| | MNCV(m/s) | 54.9±5.5 | 53.9±3.9 | 48.9±6.1 | 50.3±8.4 | 5.6 | 2.9 | 0.0001 | 0.0038 |
| **Tibial** | Distal latency(ms) | 3.1±1.1 | 4.1±1.1 | 4.6±1.1 | 4.4±1.2 | 8.3 | 1.9 | 0.0001 | 0.05 |
| | CMAP(mV) | 6.4±1.9 | 6.1±1.6 | 8.5±3.7 | 9.1±4.1 | - | - | - | - |
| | MNCV(m/s) | 48.2±6.1 | 45.4±4.6 | 41.5±14.2 | 40.2±11.5 | 3.4 | 3.3 | 0.001 | 0.001 |
| **Peroneal** | Distal latency(ms) | 3.8±1.5 | 2.7±1.2 | 2.9±1.6 | 3.7±1.3 | - | 4.6 | - | 0.0001 |
| | CMAP(mV) | 4.61.4 | 3.3±0.8 | 3.1±1.5 | 3.4±1.8 | 5.2 | - | 0.0001 | - |
| | MNCV(m/s) | 48.2±3.0 | 47.4±3.1 | 45.4±8.9 | 43.2±5.2 | 2.3 | 5.3 | 0.02 | 0.0001 |

**Table 4:** Comparison of sensory parameters in study and control group

| Nerve | Electro-physiological variable | Control group (n=60) | | COPD group (n=60) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Right I | Left II | Right III | Left IV | $T_1$ IvsIII | T2 IIvs IV | $P_1$ IvsIII | $P_2$ IIvsIV |
| **Median** | Distal latency | 2.4±0.9 | 2.1±0.6 | 2.6±0.7 | 2.3±0.6 | 1 | 1.9 | NS | NS |
| | SNAP(µV) | 26.8±4.7 | 29.6±8.3 | 33.2±15.6 | 30.0±18.6 | - | - | - | - |
| | SNCV(m/s) | 54.0±4.4 | 54.6±5.9 | 59.0±12.8 | 60.6±14.9 | - | - | - | - |
| **Ulnar** | Distal latency | 1.9±0.6 | 1.8±0.6 | 2.0±0.5 | 2.30.8 | 0.7 | 3.9 | NS | 0.0002 |
| | SNAP(µV) | 26.7±9.1 | 21.3±4.0 | 20.0±9.6 | 26.3±18.6 | 3.9 | - | 0.0002 | - |
| | SNCV(m/s) | 54.6±5.4 | 55.0±5.3 | 53.3±11.8 | 56.7±19.4 | 0.8 | - | NS | - |
| **Sural** | Distal latency | 2.2±1.0 | 2.3±0.9 | 2.7±0.9 | 2.8±0.9 | 2.9 | 2.7 | 0.004 | 0.007 |
| | SNAP(µV) | 7.3±2.3 | 7.7±2.7 | 6.9±4.9 | 3.7±3.9 | 0.5 | 6.5 | NS | 0.0001 |
| | SNCV(m/s) | 52.87.4 | 46.67.1 | 53.417.7 | 48.0±9.6 | - | - | - | - |
| **Sup. peroneal** | Distal latency | 2±0.9 | 2.3±0.9 | 3.0±1.1 | 3.2±1.6 | 5.6 | 3.8 | 0.0001 | 0.0002 |
| | SNAP(µV) | 6.8±0.9 | 6.8±1.1 | 4.5±5.8 | 4.2±5.2 | 3.0 | 3.7 | 0.002 | 0.0003 |
| | SNCV(m/s) | 48.1±6.0 | 47.±16.7 | 44.4±9.7 | 47.5±11.7 | 2.5 | 0.2 | 0.01 | NS |

Table 5: Changes in electrophysiological variables with increasing severity of disease

| Nerve | Electrophysiological variable | Motor | | | | Sensory | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Group I $FEV_1$>50% (n=30) | Group II $FEV_1$<50% (n=30) | t | p | Group I $FEV_1$>50 % (n=30) | Group II $FEV_1$<50 % (n=30) | t | p |
| **Right median** | Distal latency | 2.7±0.5 | 2.9±0.7 | 1.3 | NS | 2.5±0.6 | 2.6±0.7 | 0.5 | NS |
| | amplitude | 9.1±2.8 | 8.2±2.7 | 1.2 | NS | 35.2±13.3 | 31.1±17.6 | 1.0 | NS |
| **Left median** | Distal latency | 3.1±0.7 | 3.10.9 | 0.1 | NS | 2.2±0.6 | 2.4±0.6 | 1.0 | NS |
| | amplitude | 8.9±2.3 | 7.4±2.6 | 2.3 | 0.2 | 33.9±14.7 | 26.1±21.5 | 1.6 | NS |
| | Conduction velocity | 53.8±4.5 | 51.6±6.3 | 1.5 | NS | 62.2±17.1 | 58.6±12.3 | 1.0 | NS |
| **Right ulnar** | Distal latency | 2.2±1.2 | 2.2±0.7 | 0.04 | NS | 1.9±0.5 | 2.1±0.5 | 0.9 | NS |
| | amplitude | 6.1±1.6 | 5.5±1.5 | 1.4 | NS | 21.3±8.3 | 18.8±10.7 | 1.0 | NS |
| | Conduction velocity | - | - | - | - | 54.5±6.4 | 52.1±15.5 | 0.8 | NS |
| **Left ulnar** | Distal latency | - | - | - | - | 2.2±0.7 | 2.5±0.9 | 1.2 | NS |
| | amplitude | 6.4±1.5 | 5.6±1.8 | 1.7 | NS | - | - | - | - |
| | Conduction velocity | 51.0±9.8 | 49.7±6.7 | 0.6 | NS | 61.8±21.3 | 51.6±16.1 | 2.1 | 0.04 |
| **Right tibial** | amplitude | 9±4.7 | 8.1±2.3 | 0.9 | NS | - | - | - | - |
| **Left tibial** | Distal latency | 4.3±1.2 | 4.5±1.3 | 0.6 | NS | - | - | - | - |
| | Conduction velocity | 40.3±15.1 | 39.4±6.1 | 0.5 | NS | - | - | - | - |
| **Right peroneal & sup peroneal** | Distal latency | 2.8±2.0 | 3.1±1.0 | 0.7 | NS | - | - | - | - |
| | amplitude | 3.8±1.6 | 2.4±0.9 | 4.2 | .0001 | 4.8±7.6 | 4.2±3.3 | 0.4 | NS |
| | Conduction velocity | 47.1±10.2 | 43.7±7.2 | 1.5 | NS | 46.2±10.3 | 42.6±9.1 | 1.4 | NS |
| **Left peroneal** | Distal latency | 4.0±1.3 | 3.5±1.2 | 1.7 | NS | | - | - | - |
| | Conduction velocity | 44.6±5.2 | 41.9±4.8 | 2.1 | 0.04 | | - | - | - |
| **Left sural** | Distal latency | - | - | - | - | 2.5±0.9 | 2.9±0.8 | 1.7 | NS |
| | Conduction velocity | - | - | - | - | 51.0±11.3 | 45.1±6.3 | 1.4 | NS |

**Table 6**: Distribution of peripheral neuropathy in motor and sensory nerves

| Nerves | Motor | | | Sensory | | |
|---|---|---|---|---|---|---|
| | Axonal | Demyelinating | Mixed | Axonal | Demyelinating | Mixed |
| **Rt Median** | 0 | 14 | 0 | 2 | 0 | 6 |
| **Lt Median** | 6 | 9 | 0 | 9 | 2 | 6 |
| **Rt Ulnar** | 3 | 17 | 28 | 6 | 12 | 6 |
| **Lt Ulnar** | 7 | 20 | 22 | 15 | 9 | 10 |
| **Rt Tibial** | 2 | 31 | 1 | - | - | - |
| **Lt Tibial** | 5 | 33 | 4 | - | - | - |
| **Rt Sural** | - | - | - | 28 | 0 | 5 |
| **Lt Sural** | - | - | - | 42 | 0 | 5 |
| **Rt Peroneal & s peroneal** | 3 | 29 | 6 | 27 | 12 | 10 |
| **Lt Peroneal & s peroneal** | 0 | 28 | 9 | 41 | 4 | 6 |

## DISCUSSION

Chronic respiratory insufficiency has been implicated as one of the factors for peripheral neuropathy in various studies.[9-15] In previous studies there are marked variations in prevalence of neuropathy which might be due to less number of nerves studied, in few studies only two, three[16]or different[17] nerves were investigated. In the present study four motor nerves and four sensory nerves of upper and lower limbs bilaterally were tested. In COPD, usually sensory axonal polyneuropathy were reported by many authors.[17,18]

In present study also sensory axonal neuropathy was predominantly found in nerves of lower limb (Sural nerve, superficial peroneal nerve) whereas predominantly demyelinating neuropathy was identified in motor nerves. In the upper limb mixed neuropathy of ulnar motor nerve was found.

Posterior tibial nerve as the most affected nerve has been reported in a previous study.[19]Electrophysiological variables recorded revealed reduced or un-recordable SNAP and slowing of MNCV and prolongation of DL of motor nerves in majority of COPD cases. Segmental demyelination and remyelination in addition to axonal degeneration might be the major pathologic abnormality.

In the present study motor nerve conduction velocity of all nerves of upper (median nerve, ulnar nerve) and lower limb (posterior tibial, peroneal nerve) was significantly reduced as compared to control group. Slowing of conduction velocity of motor nerves was reported in other studies as well.[19,20]

Study aimed to investigate the presence of peripheral neuropathy in the study group as there is dearth of evidence and awareness of subclinical neuropathy in stable COPD patients.[21] Present study included 60 stable COPD pts in age group 35-75yrs, having no obvious clinical evidence of neuropathy. In the present study polyneuropathy was identified in all the cases studied. Prevalence rate of neuropathy has been reported from 16 to 95%.

Hypoxia probably the most common cause of peripheral neuropathy affecting nerve fibers either directly or by enhancing the effects of other neurotoxic factors or deficiencies.[14] Neuropathies have been reported in diabetic patients associated with obesity. The obese patients included in this study were non-diabetic.

Hypoxia, tobacco smoke, alcoholism and certain drugs are also believed to be the etio-pathogenic factor.[14] Improvement in peripheral nerve function has been noted in some pts following treatment of malnutrition, suggesting metabolic abnormalities in Schwann cell or malnutrition as a probable cause of peripheral neuropathy.[16]

Chronic exposure to polluted air has been identified as the vital cause of COPD.[22,23]Environmental pollution may be the probable cause of neuropathy as well in few COPD pts.[14]

Present study also established involvement of both motor and sensory components of median nerve, ulnar nerve and Peroneal nerve in more number of cases with increasing severity of disease. It was detected in the present study that even in cases with mild obstruction considerable motor and sensory nerve involvement was present suggesting a need of nerve conduction study even in early stages of disease.

## CONCLUSION

Our study showed that individuals with COPD had neurophysiological alterations in comparison with control group. Nerve conduction study revealed presence of impaired nerve functions in pts of COPD with no clinical evidence of neuropathy.

Lower extremities were involved more commonly and sensory polyneuropathies was present in majority of cases. Left sural nerve was most commonly affected sensory nerve.

Demyelinating motor and axonal sensory peripheral neuropathy can be seen in patients of COPD and subclinical motor and sensory polyneuropathies may be present at higher frequency than symptomatic in these cases.

Study suggested that peripheral neuropathy occurred in association with even mild chronic respiratory insufficiency. Therefore it is crucial to evaluate neuropathy both clinically and electro-physiologically even in mild COPD patients for early detection and management of neurophysiological impairment.

## REFERENCES


1. Hillas G, Perlikos F, Tsiligianni I, Tzanakis N. Managing comorbidities in COPD. International Journal of Chronic Obstructive Pulmonary Disease. 2015;10:95-109.
2. Mannino DM, Kiri VA. Changing the burden of COPD mortality. International Journal of Chronic Obstructive Pulmonary Disease. 2006;1(3):219-233.
3. Salvi S, Agarwal A. India needs a national COPD prevention and control program. J. Assoc physicians India. 2012;60 (Suppl):5-7.
4. Vijayan V. Chronic Obstructive Pulmonary Disease .Indian J Med Res 2013;137:251-269.
5. Asal G, Cakan A ,Erbayku A, Dereli S, Ozsoz A ,Edipoglu H ,Ozer B. Electromyographic evaluation of peripheral nerves in Chronic obstructive pulmonary disease .Turkish Respiratory journal 2003;4(2):51-6.
6. Sipahiolu B, Kzltan M, Hachekimolu A. COPD and neuropathy Solunum 1995;19:960-6.
7. Hake SD, Patil ML, Shah TM, Gokhale PM, Suvarna V. Practical challenges in conducting respiratory studies. Perspect Clin Res 2015;6:15-9.
8. Shrivastava A, Dave R, Sharma B, Shrivastava S. Correlation of Visual Evoked Potential Changes with Severity of COPD. Int J Bas App Physiol 2014;3(1):342-8.
9. Valli G, Barbieri S, Sergi P, Fayoumi Z, Berardinelli P. Evidence of motor neuron involvement in chronic respiratory insufficiency. Journal of Neurology, Neurosurgery and psychiatry, 1984,47:1117-1121.
10. Moore N, Lerebours G, Senant J, Ozenne G, David PH, Nouvet G. Peripheral neuropathy in chronic obstructive lung disease. Lancet 1985;II:1311.
11. Vila A ,Reymond F ,Paramelle B ,Stoebner P, Ouvrard-Hernandez AM , Muller P, Pollak P. Neuropathies and chronic respiratory insufficiency: electro-physiologic study. Rev Electroencephalogry Neurophysiology Clin, 1986;15:331-40.
12. Nowak D, Bruch M, Arnaud F, Fable H, Kiessling D, Notle D et al. Peripheral neuropathies in chronic obstructive pulmonary disease: a multicentre prevalence study. Lung 1990;168:43-51.
13. Kiessling D, Langenbahn H, Fabel H, Magnussen H, Notle D, Overlack A. Prevalence of polyneuropathies in patients with chronic obstructive lung disease. Pneumologie 1990;44(1):441-3.
14. Gupta PP, Agarwal D. Chronic Obstructive Pulmonary Disease and Peripheral Neuropathy. Lung India 2006;23:25-33.
15. Ulubay G, Ulasli S, Bozbas S, Ozdimirel T, Karatas M. Effects of peripheral neuropathy on exercise capacity and quality of life in patients with chronic obstructive pulmonary disease. Arch Med Sci, 2012;8:296-302.
16. Appenzeller O, Parks RD, Macgee J. Peripheral neuropathy chronic disease of respiratory tract. Am J Med 1968;44:873-80.
17. Faden A, Mendoza E, Flynn F. Subclinical neuropathy associated with chronic obstructive pulmonary disease. Arch Neurol 1981;38:639-42.
18. Pfeifer G, Kunze K, Bruch M, Kutzner M, Ladurner G, Malin JP, Trackman WP. Polyneuropathies associated with hypoxemia: Prevalence in patients with chronic obstructive pulmonary disease. J Neurol 1990;237:230-3.
19. Hamdan F, Mohammed F, Hashim M. Prevalence of neuropathy in patients with chronic obstructive pulmonary disease. Al- Kindy Col Med J 2004;2(1):13-8.
20. Narayan M, Ferranti R. Nerve conduction impairment in patients with respiratory insufficiency and severe chronic hypoxemia. Arch Phys Med Rehabil 1978;59:188-92.
21. Agarwal D, Vohra R, Gupta P, Sood S. Subclinical peripheral neuropathy in stable middle aged patients with chronic obstructive pulmonary disease. Singapore Med J 2007;48(10):887.
22. Sunyer J. Urban air pollution and chronic obstructive pulmonary disease: A Review. Eur Respir J 2001;17:1024-33.
23. Karakatsani A, Andreadaki S, Katsouyanni K. Air pollution in relation to chronic pulmonary disease: A Nested case control study in Athens, Greece. Eur J Epidemiol 2003;18:45-53.


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