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RESEARCH ARTICLE

TO STUDY HIV SEROPOSITIVITY IN PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AT NATIONAL INSTITUTE OF TUBERCULOSIS AND RESPIRATORY DISEASES

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Abstract

Background: HIV (Human Immunodeficiency Virus) attacks the immune system and thereby weakens body's natural defence mechanism against various diseases. Several pulmonary complications have been documented in HIV infected people among which Chronic Obstructive Pulmonary Disease (COPD) carries special importance. It has been postulated that COPD occurs more frequently in HIV infected people and occurs in younger aged HIV infected people than non HIV population.

Methods: It was a cross sectional observational study, and convenience sampling method was adopted. COPD cases were selected from outpatient department. HIV testing was done as per national guideline with the HIV kits supplied by NATIONAL AIDS CONTROL ORGANIZATION (NACO).

Objective: To study the occurrence of HIV seropositivity in the adult (older than 18 years of age) patients of COPD attending National Institute of Tuberculosis and Respiratory Diseases (NITRD).

Results: HIV positivity was found in 4% of COPD patients. COPD developed at an earlier age in HIV positive patients. Median age was 37.5 years in HIV positive patients compared to median age of 50 years in HIV negative patients. Smoking and nutritional status of the patients did not show any significant relationship with HIV.

Final conclusion: Keeping in mind the limitations of this study we concluded that HIV testing may be helpful in young aged, uncontrolled COPD patients. But further studies are required with larger sample sizes to confirm these observations.

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Introduction:-

The **Human Immunodeficiency Virus (HIV)** is a lentivirus (a subgroup of retrovirus) that causes HIV infection and over time acquired immunodeficiency syndrome (AIDS). It attacks the immune system, which is our body's natural defence against illness⁽¹⁾. The virus destroys CD4 cells and makes copies of itself inside them. As per reports of National AIDS Control Organization (NACO), the National Institute of Health and Family Welfare and the

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National Institute of Medical Statistics (a body under ICMR) national adult HIV prevalence in India is approximately 0.36 percent⁽²⁾.

Abnormalities of pulmonary function associated with HIV were first noted by the Pulmonary Complications of HIV Infection Study (PCHIS)⁽³⁾. Lung pathologies associated with HIV infection are found to be an important cause for comorbidity⁽⁴⁾.

The early days of the HIV/AIDS epidemic were marked by frequent and often deadly infectious pulmonary complications. But newer data suggest that chronic, non-infectious lung diseases, especially chronic obstructive pulmonary disease (COPD), are emerging problems among HIV patients⁽⁴⁾.

While the best-established COPD risk factor is cigarette smoking⁽⁵⁾, emerging data suggest HIV infection also independently increases COPD risk⁽⁶⁾. The mechanisms by which HIV might increase COPD risk remain quite unclear. Postulated mechanisms include respiratory infections, abnormal inflammatory responses, oxidative stress etc.

COPD is an important co-morbidities of HIV and several studies have established that this disease occurs at an early age in HIV affected person than non-HIV person⁽⁴⁾. However, to the best of our knowledge, observation of HIV occurrence in COPD patients had not been studied earlier in India. Diagnosing HIV in COPD at an earlier stage may help in early and appropriate management leading to reduce morbidity.

This study was aimed to detect HIV seropositivity in diagnosed cases of COPD.

Patients and Methods:-

This study was a cross sectional observational study to find out the seropositivity of HIV in diagnosed cases of COPD who attended the out-patient department at NITRD for their management. Case selection was done irrespective of their age, sex, disease status, economical condition and health factor. Active tuberculosis was excluded before as tuberculosis itself is a risk factor for HIV/AIDS. This study was conducted from August 2015 to May 2016, over a duration of 10 months. A total of 102 COPD cases were enrolled with convenience sampling method. HIV testing were done as per national guideline with NACO supplied CombAids kit for detecting HIV positivity and positive patients further tested for type specification (HIV 1 or HIV 2 detection) with NACO supplied Meriscreen HIV kit. This study was approved by the Ethical committee of the Institute.

As per inclusion criteria we have enrolled diagnosed cases of COPD who attended the hospital for management and having age more than or equal to 18 years, and were willing to participate in the study and having no active tuberculosis.

Diagnosis of COPD was based upon GOLD guidelines⁽⁵⁾. It consisted of medical history, physical examination and spirometry. COPD was suspected and confirmed by performing spirometry if any of the indicators mentioned below were present in an individual viz. dyspnoea which was exertional, progressive and persistent, chronic cough (may be intermittent, may be un-productive), chronic sputum production, history of exposure to risk factor (eg. tobacco smoke, smoke from home cooking and heating fuels, occupational dusts and chemicals), family history of COPD. The presence of multiple key indicators increases the probability of a diagnosis of COPD. As per GOLD guidelines post bronchodilator FEV₁/FVC should be <0.70 to diagnose COPD.

Diagnosed COPD cases were enrolled and all the patients were taken to the Integrated and Confidential Counselling and Testing Centre (ICTC) in the NITRD. From the collected data, the total number of seropositive patients was calculated.

Statistical analysis

All analyses were performed on SPSS software (Windows version 17.0). Frequency tables were made. Continuous data were summarized as Mean $\pm$ SD (standard deviation) while discrete (categorical) in number and percentage. The statistical tests used for analysis were Fischer's Exact Test as number of HIV-COPD cases are very small. p value less than 0.05 ($p < 0.05$) was considered statistically significant.

Results:-

The demographic characteristics of COPD patients were analysed. Sex distribution shows male and female ratio is 2.6:1. Mean smoking index was found to be 383.803. Analysis of data of two groups viz. patients of COPD with HIV and COPD without HIV, is shown in the following table:

Parameters	COPD with HIV(n=4)	COPD without HIV(n=98)	p value
Age Median(range)	37.5(33-70)	50(13-75)	-
Sex (M:F)	3:1	2.5:1	-
Socio-economic status (according to Kuppuswami scale)	Upper lower(2)	Upper lower(33)	-
	Lower middle(2)	Lower middle(44)	-
BMI Median(range)	20.15(15.8-22.9)	21.1(12.4-34.4)	p value=0.29
Hypertension	NIL	NIL	
Diabetes	NIL	NIL	-
Smoking Index Median(range)	60(0-225)	250(0-1000)	p value=0.62
High risk behaviour	50%	0%	p value=0.001

In our study four COPD cases were found to be positive for HIV which accounts for approximately 4% of the subjects. Two of these patients had history of smoking with smoking index <300 (225 and 120). Three patients belong to age group <40 and two were having BMI within normal limit. Three patients fell into GOLD 4 severity staging according to their PFT report. These three patients were having high risk behaviour.

One patient of HIV positive group belonged to the age group of more than 40 years but had no history of smoking. As per BMI he was in malnutrition group and according to the spirometric severity staging he was in GOLD 2.

Data analysis revealed that smoking was not significantly related in COPD-HIV cases. Same was true for the nutrition status where p value showed not significant relation. High risk behaviour was the only factor which was found statistically significant in COPD-HIV cases.

Discussion:-

As per WHO reports⁽⁷⁾ worldwide HIV prevalence is 0.8% (0.7-0.9) and prevalence in south-east Asia including India is 0.3%. National data also shows that the prevalence of HIV in India is 0.36%, and prevalence in Delhi is around 0.3%⁽⁸⁾. In this study HIV positivity came out to be approximately 4% which is more than ten times higher than normal in India.

COPD in HIV infected people has been extensively studied⁽⁹⁾, and it is postulated that COPD occurs at younger age if the person is having HIV. In this study COPD was found to be developed in younger age group with low smoking index.

The mechanism of early COPD in HIV patient is still a topic of controversy. Some postulated mechanisms are: Risk behaviour⁽⁶⁾, Infections⁽⁶⁾, Apoptosis, Altered oxidant-antioxidant balance. These are explained in the following paragraphs.

Many HIV-infected populations have a high degree of behaviours associated with COPD risk, including cigarette and marijuana smoking as well as injectable drug use. However, it is likely that these risk factors are not the only explanation for accelerated COPD because emphysema and pulmonary function abnormalities are seen in HIV-infected non-smokers as well. It is likely that these behaviours interact with the effects of HIV and increase the risk of HIV-associated COPD.

In those without HIV infection, smoking leads to structural remodelling, which results in increased risk of microbial colonization or decreased ability to clear subclinical infection. In persons with HIV infection, defective immune responses to infections could also contribute, alone or combined with smoking, to an increased likelihood of

developing colonization. Once colonization is established, the organism or organisms recruit white blood cells to the lungs, stimulating the release of inflammatory cytokines and chemokines as well as proteases. The inability to clear the inciting organism perpetuates the cycle, ultimately resulting in tissue destruction, airway thickening, and clinical COPD.

It has been postulated that lung endothelial and epithelial cell apoptosis are critical steps in COPD development in the non-HIV-infected population^(10, 11). HIV-infected persons might have increased susceptibility to apoptosis because the HIV proteins Tat (Transcriptional transactivator) and Nef (Negative Factor) may induce endothelial cell apoptosis⁽¹²⁾. It is also possible that HIV may cause apoptosis directly^(13, 14).

Increased oxidative stress is another potential mechanism linking HIV and COPD. Non-HIV-infected persons with COPD have increased markers of oxidative stress systemically and in the lungs⁽¹⁵⁾. Oxidative stress can worsen COPD in several ways. Increased oxidation results in inactivation of antiproteases, activation of MMPs (Matrix metalloproteinase), and direct damage to the lung matrix and decreases the lung's ability to repair itself⁽¹⁵⁾. HIV infected individuals have altered systemic and lung oxidant/antioxidant balance, with decreases in antioxidant levels such as superoxide dismutase and glutathione and increases in oxidants that may result from HIV proteins⁽¹⁶⁻¹⁹⁾.

Conclusion:-

Current study observed that HIV seropositivity in COPD patient is approximately 4%. It is more than 10 times higher than normal population. Among HIV positive patients COPD developed earlier compared to HIV negative patients. Smoking was not a significant risk factor in HIV-COPD cases. This study indicates that HIV in COPD has immense clinical significance. Observation of HIV seropositivity in COPD patients had not been studied earlier. Limitations of this study includes the convenience sampling method and small sample size. Keeping in mind the results and the limitations of the study, we cannot recommend HIV testing in all COPD patients, however it can be said with certainty that we need further studies in this topic.

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