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The Role for Female Sex Hormones in Idiopathic Pulmonary Fibrosis

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Abstract: *Idiopathic pulmonary fibrosis (IPF), a common disease in the spectrum of idiopathic interstitial pneumonia, is associated with poor prognosis.Emerging data suggests that female sex hormones play a role in these inflammatory airway conditions.In our study thirty patients of IPF were compared with thirty age matched controls who comprised of healthy population. Female sex hormonal profile were done with estradiol, progesterone, luteinizing hormone, follicle stimulating hormone and prolactin. In the study there was no significant difference in hormonal levels seen between both the population.The study states that the cases of IPF in females were more common among the postmenopausal age group which may suggest the role of low levels of post-menopausal estrogen, progesterone hormones in the pathogenesis of pulmonary fibrosis.*

Keywords : ILD - Interstitial Lung Disease, IPF - Idiopathic Pulmonary Fibrosis, FSH – Female Sex Hormone, LH- Leutinising Hormone, CF- Cystic Fibrosis, COPD- Chronic Obstructive Pulmonary Disease.

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I. Introduction

Interstitial Lung Diseases (ILDs) consists of a group of heterogenous diseases known as Idiopathic Interstitial Pneumonias (IIPs).[(1)]IPF is a particular form of chronic, progressive fibrosing interstitial pneumonia of unknown cause which occurs basically in older adults, limited to the lungs, and associated with the histopathologic and/or radiologic pattern of UIP.[(2-5)] While defining IPF exclusion of other forms of interstitial pneumonia including other idiopathic interstitial pneumonias and ILD associated with environmental exposure, medication, or systemic disease are necessary.[(3,4)]

Women generally appears to have worse prognosis than their male counterparts as it is more prevalent in the epidemiology of asthma, CF and COPD.[(6-8)]It is still uncertain about the exact mechanism of this process. Various studies have related the effect of female sex hormones in the development of inflammatory airway diseases such as asthma, chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF).[(9-11)] But there are only few animal studies to suggest the role of female sex hormones in idiopathic pulmonary fibrosis.[(12)]

II. Material And Methods

The present study was conducted for a period of 6 months in Kamla Nehru Chest Hospital, Dr S N Medical College, Jodhpur, a tertiary care centre for respiratory diseases in western part of Rajasthan. This is a cross sectional study to evaluate female sex hormonal abnormalities in patients of interstitial lung disease.

Patients either admitted or attending the Outpatient Clinic of the Department of Tuberculosis & Respiratory Diseases of our Hospital, who presented with signs, symptoms and history suggestive of ILD and willing to participate in the study were enrolled after proper counselling.

The protocol was explained to the patient/care provider before enrolment and informed consent was taken from each patient. Thirty patients of IPF were compared with thirty age matched controls who comprised of healthy population.

CRITERIA OF INCLUSION OF CASES UNDER STUDY

1. Diagnosed as per revised ATS/ERS/ALAT Classification of Idiopathic Interstitial Pneumonias.[(13)]
2. Patients clinically and radiologically diagnosed on HRCT as Idiopathic pulmonary fibrosis.[(2)]

CRITERIA OF EXCLUSION OF CASES UNDER STUDY

1. Patients with positivity for acid-fast bacilli (AFB) sputum by smear or culture or with past history of tuberculosis were excluded.
2. Chronic lung disease other than IPF such as other ILDs, Asthma, COPD, Bronchiectasis, Silicosis.
3. Patients immediately post partum .
4. Women on contraceptives.
5. Women with previous history of infertility and previous menstrual disturbances
6. Those not willing for the study.

The patient data including demographic information, past, personal and treatment history, physical examination findings (BMI, clubbing, crackles), and diagnostic studies (chest x-ray, sputum AFB smear, CBC, ESR, LFT, RFT, Blood Sugar, serum albumin, HIV, HBsAg, HCV, HRCT scan, pulmonary function testing) were collected. Then hormonal tests for S.FSH, S.LH, S. Prolactin, S. Estradiol and S. Progesterone were sent to Dept. of biochemistry, Dr S. N. medical college Jodhpur, for hormonal assay.

Female menstrual cycle is regulated by four main hormones: estradiol, progesterone, luteinizing hormone, and follicle stimulating hormone. Hormonal assay for female sex hormones was done by VIDAS FSH, VIDAS LH, VIDAS Estradiol 2, VIDAS Progesterone and VIDAS Prolactin tests.

STATISTICAL ANALYSIS

Quantitative data was expressed as mean and standard deviation. Difference in mean was inferred to using unpaired Student's t test for two group Comparison. A p value less than 0.05 was taken as statistically significant. Data was analysed using IBM SPSS Version 20.0 statistical software.

III. Results

In our study thirty patients of IPF were compared with thirty age matched controls who comprised of healthy population. Female sex hormonal profile was done with estradiol, progesterone, luteinizing hormone, and follicle stimulating hormone.

In our study 53.33% (16 patients) of study population were of age group of more than 55 years, only 6.66% (2 patients) were of age less than 40 years, 23.33% (7 patients) were of 46 to 50 years of age and 13.33% (4 patients) of age 51 to 55 years.

On measurement of female sex hormones the mean values of serum FSH was found to be 53.84±28.29 mlU/ml, S. LH was 23.85±16.18 mlU/ml, S. Prolactin was found to be 20.92±15.87 ng/ml, S. Progesterone was 0.43±0.36 ng/ml, S. Estradiol being 22.92±15.72 pg/ml. The hormonal levels reflected low estrogen, progesterone values in the study population. In the study patients of IPF were compared with age matched controls who comprised of healthy population and no significant difference in hormonal levels were seen between both the population.

Table No.1

AGE WISE DISTRIBUTION OF PATIENTS IN THE STUDY

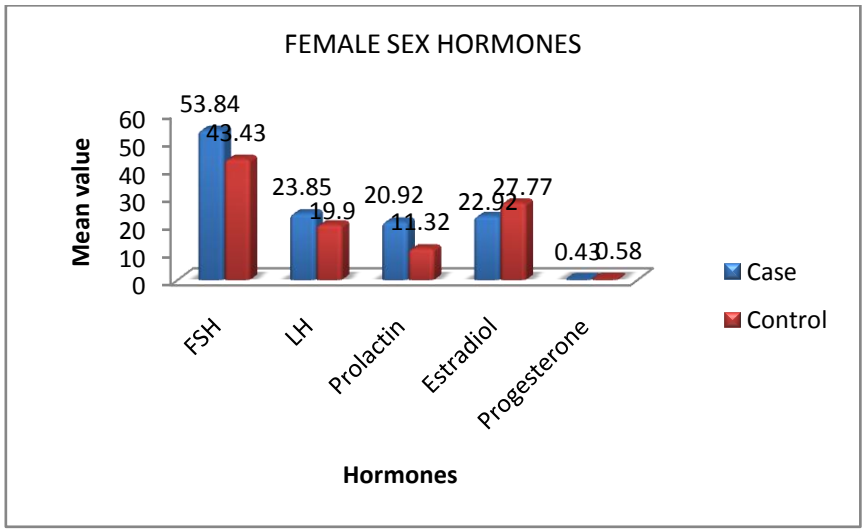
AGE GROUP (YEARS)	NO. OF PATIENTS	PERCENTAGE
≤40	2	6.66%
41-45	1	3.33%
46-50	7	23.33%
51-55	4	13.33%
>55	16	53.33%
Total	30	100%

Table No.2
COMPARISON OF HORMONAL LEVELS OF CASES WITH POST MENOPAUSAL VALUES

HORMONES	MENOPAUSE	STUDY POPULATION
FSH	17.0 – 95.0mlU/ml	53.84±28.29mlU/ml
LH	8.0 – 33.0mlU/ml	23.85±16.18mlU/ml
PROLACTIN	3 – 25ng/ml	20.92±15.87ng/ml
ESTRADIOL	<58pg/ml	22.92±15.72pg/ml
PROGESTERONE	<0.41ng/ml	0.43±0.36ng/ml

Table No.3
COMPARISON OF HORMONAL LEVELS OF CASES WITH AGE MATCHED CONTROLS

HORMONES	CASE (MEAN±SD)	CONTROL (MEAN±SD)	P VALUE
FSH	53.84±28.29	43.43±31.62	0.459
LH	23.85±16.18	19.90±14.73	0.686
PROLACTIN	20.92±15.87	11.32±0.90	0.309
ESTRADIOL	22.92±15.72	27.77±11.01	0.607
PROGESTERONE	0.43±0.36	0.58±0.26	0.478



IV. Discussion

The chronic disease spectrum of IPF affects elderly patients older than 60 years. Previous studies have shown that there is an increase in prevalence of IPF with increasing age, peak prevalence was observed as more than 75 years in a previous study.[14]In our study majority of the study population (53.33%) were of more than 55 years of age.

Emerging data suggests that female sex hormones play a role in inflammatory airway conditions. Anthony Tam et al. in the year 2011[15] conducted a study on role of female sex hormones on asthma , copd , cystic fibrosis which showed that estrogen promotes a TH2 response, while androgen promotes a TH1 response, which may be relevant in asthma. Estradiol inhibits Cl- secretion in the CF lung and up-regulates mucus production, which may be very relevant in CF. This may be relevant in the pathophysiology of COPD. Although

less well studied than estrogen, progesterone may also play relevant roles in inflammatory airway disease by amplifying airway inflammation.

A study done by lekgabe et al.[16] demonstrated an interesting synergism between the hormones relaxin and estrogen in the development of pulmonary fibrosis. They found that airway fibrosis is under the influence of both relaxin and estrogen and that estrogen can partially protect the lung from disease progression in the absence of relaxin.

In our study on measurement of female sex hormones the mean values of serum FSH was found to be 53.84±28.29 mlU/ml, S. LH was 23.85±16.18 mlU/ml, S. Prolactin was found to be 20.92±15.87 ng/ml, S. Progesterone was 0.43±0.36 ng/ml, S. Estradiol being 22.92±15.72 pg/ml. The patients of IPF were compared with age matched controls who comprised of healthy population.

The hormonal levels of study population were comparable to the postmenopausal hormonal levels. This indicates that the cases of IPF among female population were more prevalent among the postmenopausal age group and the decreased levels of serum estrogen and progesterone may be the contributing factor to the development of pulmonary fibrosis in these group of patients. It was also observed that there was no significant difference in female sex hormonal levels were seen between both the patients of IPF and age matched control group of healthy population.This necessitates furtherstudies in the field of sex hormonal influence in the pathogenesis of pulmonary fibrosis.

There is a need to evaluate the role of sex hormones in the etio-pathogenesis of pulmonary fibrosis which would help in early diagnosis and management of the same.We conclude that hormonal replacement therapy could play a role in delaying the occurrence of pulmonary fibrosis but further studies are needed in this regard.

LIMITATIONS OF OUR STUDY

1. This is a single centre study.
2. The invasive procedures of bronchoalveolar lavage and transbronchial biopsies were not performed for the confirmatory diagnosis of cases of IPF.
3. Sample size of the study group was small in number.

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