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Original Research Paper

General Medicine

STUDY OF PULMONARY ARTERIAL HYPERTENSION IN PATIENTS OF CHRONIC KIDNEY DISEASE STAGE 5.

Dr. Ravi Allichandi MBBS, MD, Assistant Professor, Department of General Medicine, S.N. Medical College Bagalkote, India.

Dr. Nagesh Babu. C MBBS, MD Resident, Department of General Medicine, S.N. Medical College, Bagalkote, India.

ABSTRACT

Pulmonary hypertension (PAH) contributes to cardiovascular disease and mortality in patients with chronic kidney disease (CKD), but the pathophysiology is mostly unknown. Pulmonary hypertension is defined when mean pulmonary artery pressure exceeded 30 mmHg at rest and was taken as diagnostic of Pulmonary Arterial Hypertension.PH was further categorized as mild (>30 to <35 mmHg), moderate (35 to 50 mmHg), and severe (>50 mmHg) in patients with CKD stages 4 and 5 and Aged≥18 years. Pulmonary hypertension is common in patients with chronic kidney disease (CKD) and is associated with increased mortality but the hemodynamic profiles, clinical risk factors, and outcomes have not been well characterized. This study sought to estimate the prevalence and consequences of Pulmonary hypertension in the setting of chronic kidney disease. **Method:** It is a cross-sectional study was conducted on 100 patients of CKD stages 4 and 5 at SriNijalingappa Medical College and Hengal Shri Kumareshwar Hospital Bagalkot, A detailed history and all the necessary investigations were done. **Results:** Pulmonary Arterial Hypertension is a common disorder in the patient with chronic kidney disease. Out of 100 CKD Patients, PAH was found in 58 of them. Out of 58 patients, 25 had mild PAH, 28 had moderate PAH, and 5 had severe PAH. A significant association was found in patients with Diabetes Mellitus, AV fistula, and BMI. Blood Parameters like Haemoglobin, Creatinine and Serum Calcium were also significantly associated with PAH.

KEYWORDS :

INTRODUCTION:-

Chronic kidney disease (CKD) is a serious public health concern, both because of the enormous number of individuals who are affected and because of the expensive expense of medical treatment and care. Because people with CKD are more likely to die from heart disease than from renal failure, the severity of the condition was probably overstated in this case.[1] Patients with CKD are more likely to develop pulmonary hypertension, which is only rarely life-threatening in its severity.[3] CKD patients before the start of dialysis or while on dialysis patients are more likely to develop PAH, which can cause ventricular dysfunction, which in turn can affect other organs and lead to higher mortality and morbidity.[1,2] Right-heart catheterization is the gold standard for identifying if a patient has PAH.[4-6] Because right-heart catheterization is both expensive and difficult to execute, echocardiography has been suggested as a potential approach for the identification of PAH. Specifically, the purpose of this study is to investigate the prevalence of PAH in patients with CKD who are undergoing haemodialysis. To prevent PAH in dialysis patients, it is critical to recognise and manage this potentially life-threatening illness in these patients. In this study, we determined the frequency of PAH in patients with CKD undergoing haemodialysis.[7]

Pathophysiology

Pulmonary Arterial Hypertension in CKD patients' pathophysiology is still complex and not completely clear. We usually observe pulmonary circulation impairment together with chronic volume overload, connective tissue diseases, acquired and congenital cardiopathies, HIV infection, hepatic cirrhosis with portal hypertension, and all chronic comorbidities with increased pressures in the left heart side.[8] CKD patients have two distant clinical features which are the presence of anaemia and arteriovenous fistula; both factors lead to an increased preload on the right heart chambers.[9] Pulmonary hypertension can lead to increased levels of cytokines and growth factors, such as FGF, PDGF, and TGF- , with concomitant pulmonary angiotensin-converting enzyme (ACE) activation.[10,11] Endothelial dysfunction, together with lower activation of nitric oxide synthase (NOS), and increased levels of serum endothelin and fibrin storages, could involve an extensive growth of endothelial cells until complete obliteration of pulmonary vessels. Myointimal proliferation, intimal laminated (both concentric and eccentric) fibrosis, thrombosis, and arterial obliteration are typical pathological features of disease progression.[9] The right ventricle has thin muscle equipment because it usually works with low blood pressure and is unable to force high vascular resistance.

Together with pulmonary hypertension due to pressure overload, once the right heart chambers lose their distensibility, this leads to tricuspid regurgitation and further right heart volume overload.[12] Therefore it is crucial to provide an early and careful diagnosis based upon a multidisciplinary approach involving any therapeutic method able to delay pathophysiological events leading to pulmonary hypertension.

METHODS AND MATERIALS:

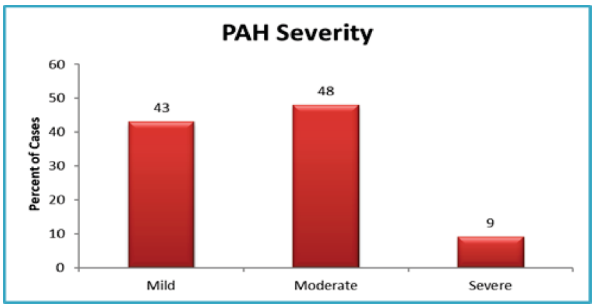
It is a Hospital based Cross-sectional study conducted in the Department of General Medicine at Sri Nijalingappa Medical College and Hengal Shri Kumareshwar Hospital Bagalkote. A detailed history and all the necessary investigations were done for a total Sample size of 100. On admission patient detailed history and clinical examination and relevant investigations were done including CBC, Kidney function test, Random blood sugar, Serum Electrolytes, Urine Routine and Microscopy, USG abdomen and Pelvis, ECG, and Echocardiography was done. PAH was diagnosed based on echocardiography and was defined when mean pulmonary artery pressure exceeded 30 mmHg at rest and was taken as diagnostic of Pulmonary Arterial Hypertension.PH was further categorized as mild (>30 to <35 mmHg), moderate(35 to 50 mmHg), and severe (>50 mmHg) in patients with CKD stages 4 and 5 and Aged≥18 years.

Statistical analysis was done using SPSS software 19.0. The data obtained were tabulated in the Excel sheet and analysed. Quantitative data will be expressed as mean + standard deviation and nonparametric data will be expressed as median and min-max values. Percentages are used for representing qualitative data. Chi-square test for proportions in qualitative data.Student's unpaired t–test for Quantitative data. Other appropriate statistical tests will be applied. P< 0.05 will be considered statistically significant.

Inclusion criteria:-
Patients of CKD in stages 4 and 5.
Age ≥ 18 years.

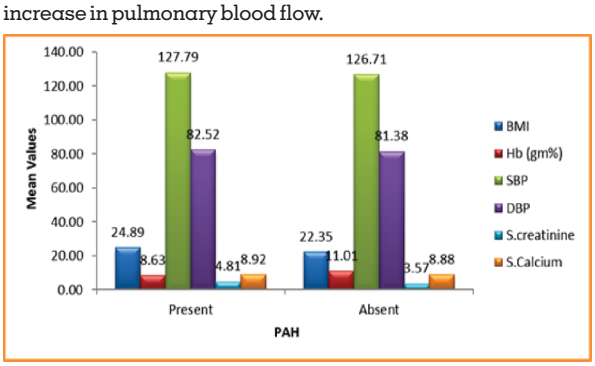
Exclusion criteria:-
Valvular heart disease
Congenital heart disease
Chronic Obstructive pulmonary disease
Chronic parenchymal lung disease
HIV-infected disease
Connective tissue diseases
Hypothyroidism and hyperthyroidism
Pregnancy
Chronic thromboembolic states.

RESULTS:-
Pulmonary Arterial Hypertension is a common disorder in the patient with chronic kidney disease. In Total 100 CKD patients were evaluated, among them 65 were males and 35 were females. 58 (58%) of patients had Pulmonary arterial hypertension assessed by 2D Echo. Out of 58 patients, 25 (43%) had mild PAH, 28 (48%) had moderate PAH, and 5 (9%) had severe PAH.



Graph 1:- Pulmonary Arterial Hypertension Severity in Chronic Kidney disease patients

A significant association was found in patients with Diabetes, BMI, presence of AV fistula and Severity of CKD, and Blood parameters like Serum Creatinine, Mean value among patients with Pulmonary Arterial hypertension was 4.81 whereas the value was 3.57 in Patients with No Pulmonary arterial hypertension. The mean value of serum calcium among patients with pulmonary hypertension is 8.92 and CKD patients without pulmonary hypertension is 8.88. There is a Positive correlation between serum calcium and pulmonary hypertension seen. The mean value of haemoglobin among patients with pulmonary hypertension is 8.63 and for CKD patients without pulmonary hypertension is 11.01. There is a positive correlation seen as a decrease in haemoglobin seen in patients with pulmonary hypertension, this may be due to an anaemia-related increase in cardiac output and an increase in pulmonary blood flow.



Graph 2: - Parameters and their Mean Values

DISCUSSION:-
PAH is a common but often underrecognized driver of morbidity and mortality in patients with CKD. PAH, a disorder characterized by elevated pulmonary artery pressure, is a progressive disorder complicating heart, lung, or systemic disease's increased morbidity and mortality regardless of its aetiology. Although the exact mechanisms underlying the high prevalence of PH in CKD are mostly unknown, factors related to decreased GFR and the management of kidney failure have been implicated. Volume overload dominates the current paradigm of PH progression and remains the predominant modifiable factor. Chronic volume overload may accelerate pulmonary vascular remodelling and lead to combined pre- and postcapillary PH in certain susceptible subpopulations of patients with CKD.[13]

In our study, a significant increase in BMI (kg/m^2) with severity of pulmonary hypertension was seen. Similar results were observed in many studies where patients with higher BMI had severe PH. Although obesity is a risk factor for the development of cardiovascular disease, diabetes mellitus, hypertension, renal disease and metabolic abnormalities, the results of the association of BMI with the severity of PH are conflicting.

Hypertension and diabetes mellitus, 2 dominant causes of kidney disease, trigger LV diastolic dysfunction, an alteration bound to increase pulmonary venous and arterial pressure. Chronic volume overload, a factor implicated in LV disorders and the high venous return in patients with CKD, may induce pulmonary venous hypertension by both increasing pulmonary blood flow and adversely affecting LV function. In addition, myocardial stiffness secondary to myocardial infarction, another frequent complication of CKD, may contribute to pulmonary hypertension.[14]

In our study, a significant association was seen in the distribution of the presence of AVF with the stage of pulmonary hypertension. Although heart failure will aggravate due to the higher output imposed by the AVF, a 25%-30% increase in basal cardiac output over a relatively short period is not enough to predispose to high flow-induced changes in the pulmonary vascular bed leading to PH. In our study, haemoglobin in mild pulmonary hypertension was significantly higher as compared to moderate and severe pulmonary hypertension and a significant association was seen in the decrease of haemoglobin with the stage of pulmonary hypertension. Our study also showed a significant association between Calcium levels and Serum Creatinine levels.

As part of a systemic phenomenon, arterial rigidity is increased in patients with CKD and calcium deposits can be demonstrated in the pulmonary artery in patients with kidney disease, thus implicating arterial stiffness in pulmonary hypertension in this population.[15] Stiffness aside, experimental studies in dogs show that parathyroid hormone levels may increase pulmonary resistances.[16] However, 2 independent studies in patients with kidney disease failed to show an association between the severity of pulmonary calcifications and parathyroid hormone levels. Furthermore, parathyroid hormone levels do not differ between patients with and without pulmonary hypertension.[17] Severe anaemia is an established cardiovascular risk factor in CKD and its impact on the cardiovascular system extends to pulmonary circulation because low haemoglobin levels can contribute to pulmonary hypertension by aggravating hypoxia triggered by concomitant conditions.[18]

In symptomatic HD patients, repeated exposure to dialysis membranes may adversely affect lung microcirculation and the high frequency of pulmonary artery hypertension in symptomatic dialysis patients further support this possibility. In dialysis patients with persisting pulmonary hypertension, after volume overload has been corrected and LV disorders have been treated adequately, right-sided cardiac

catheterization and measurement of pulmonary wedge pressure will determine whether the clinical assessment is accurate and can distinguish whether further treatment for volume overload and/or LV dysfunction is needed or if treatment directed at pulmonary artery hypertension is indicated.

Patients with a diagnosis of pulmonary hypertension benefit from lifestyle changes such as cessation of smoking and starting mild physical practice. Care of blood pressure control, optimal and stable haemoglobin levels, and proper management of dry weight. Concerning pharmacological treatment, scientific evidence and references in the literature have focused on digoxin, diuretics, and calcium channel blockers.

In summary, Pulmonary Arterial Hypertension was widely prevalent in those patients with Chronic kidney disease, and lower levels of kidney function are associated with an increased risk of death. Future studies should explore the mechanisms that might underlie these associations because they will eventually help us identify some potential therapeutic interventions for this high-risk population.

CONCLUSIONS:-

Pulmonary hypertension remains an underrecognized yet significant cardiovascular complication for patients with CKD, particularly in patients with stage 5 maintained on HD. Pulmonary hypertension in patients with CKD potentially is a reversible process because, along with associated LV disorders, it may regress after kidney transplantation. Several risk factors, including LV dysfunction, sleep apnoea, AVFs, and an imbalance between endogenous vasoconstrictor and vasodilator substances, are implicated in pulmonary hypertension in patients with CKD. Pulmonary hypertension has been associated with a higher risk of death in Patients with CKD. In dialysis patients with established pulmonary hypertension, the excess risk of death may persist after kidney transplantation.

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