INVESTIGATION OF THE RELATIONSHIP BETWEEN ANEMIA AND PARATHYROID HORMONE AMONG PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS

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Abstract:

Objective: This research looked at the link between hemoglobin (Hb) levels and intact parathyroid hormone (iPTH) levels in patients with end-stage renal disease (ESRD) receiving hemodialysis.

Methods: The Study was conducted in Lady Reading Hospital Peshawar during February 2020 to March 2021. Observational cross-sectional research was undertaken at Mayo Hospital in Lahore, Pakistan. The research only included participants who gave their informed permission and had received institutional review board clearance. Measurements of Hb, ferritin, iPTH, creatinine and urea, vitamin D, and transferrin saturation were made using serum samples.

Results: The most frequent cause of ESRD was shown to be diabetes mellitus in the research, which had 94 individuals, 66.0% of whom were males. The majority of patients had been receiving hemodialysis twice a week for more than 5 years. The average levels of Hb, iPTH, and vitamin D were 9.29 g/dl, 576.59 ng/dl, and 25.47 ng/ml, respectively. The findings showed a substantial negative connection between iPTH levels and anemia.

Conclusions: This research concludes that hyperparathyroidism is a significant cause of anemia in those on maintenance hemodialysis.

Keywords: hemodialysis, kidney, anemia

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Introduction:

One of the most common side effects of chronic renal failure is anemia, particularly in those undergoing hemodialysis as a type of therapy. [1] Erythropoietin (EPO) production is diminished, which is the main factor contributing to anemia in individuals with end-stage renal disease (ESRD), although there are other contributing factors as well. [2]

Recombinant EPO is used as the main therapy for the treatment of anemia brought on by renal insufficiency.[3] As a result, the expense of the course of therapy rises significantly.[4] Several studies showed that inflammation, deficiencies of iron, infections, and persistent loss of blood are the primary causes of erythropoietin's incapacity to treat secondary anemia in ESRD patients.[5-8] Secondary hyperparathyroidism co-occurring with ESRD in individuals is another crucial aspect.[9] Due to phosphate preservation, low calcium levels, and low levels of calcitriol, the active component of vitamin D, this is yet another serious side effect of ESRD.10 Thyroid glands are situated in front of the parathyroid glands. The hormonal system of the human body includes them and they are mostly in charge of controlling calcium. Parathyroidectomy has been shown to improve hemoglobin and lessen the need for EPO.[10]

As a putative inhibitor of EPO synthesis, initiator of myelofibrosis, and shortener of red blood cell survival, the hormone parathyroid has been regarded as a uremic toxin, reducing hematopoiesis in the long run.[11] The relationship between parathyroid hormone and anemia in ESRD patients receiving hemodialysis has only been the subject of a small number of research. These relationships were examined in several research, however, the findings were inconsistent. [12,13]

Figure 1: Maintenance Hemodialysis

The hormone fibroblast growth factor 23 (FGF 23), which is similarly released by the bones, may potentially have an impact on erythropoiesis in people with chronic kidney disease. [14] To determine how intact parathyroid hormone levels (i-PTH) and hemoglobin (Hb) levels in ESRD patients receiving hemodialysis relate to one another, this research was carried out.

Methods:

Study Design: The Study was conducted in Lady Reading Hospital Peshawar during February 2020 to March 2021. Pakistan's Department of Nephrology from June 2022 to May 2023. The institutional review board gave its approval to the research to guarantee that all ethical requirements were satisfied. The investigation of patients receiving erythropoietin (EPO) therapy while undergoing maintenance hemodialysis was the goal of the research.
All patients over the age of 18 who were currently undergoing maintenance hemodialysis and receiving EPO treatment were included in the trial. Based on the target hemoglobin levels, which were set between 10 and 11.5 g/dl, the dose of EPO was changed.

To maintain the study's focus and the accuracy of the data, several exclusion criteria were used. Patients with current cancers, hematologic conditions, infections that were still present, and instances of pure red cell aplasia with supporting documentation were disqualified from the research. We attempted to reduce confounding variables and preserve the homogeneity of the research population by omitting these instances.

We gathered pertinent information from the participants throughout the research period. This includes details on the patient's age, sex, age, marital status, comorbidities, ethnicity, notable family history, and any history of smoking or drug usage. To provide a complete picture of the patient's features, all of these specifics were noted.

We also took serum samples from the participants in addition to the patient-related data. These samples were taken just before the week's first hemodialysis session. Hemoglobin levels, serum intact parathyroid hormone (i-PTH) levels, vitamin D levels, ferritin levels, creatinine and urea levels, and transferrin saturation were all determined in the collected blood samples. To ensure reliable data collection, these measurements were made using a predetermined proforma.

We wanted to learn more about the patients at Mayo Hospital who were getting EPO therapy and maintenance hemodialysis by performing this observational, cross-sectional research.

Statistical Analysis: The program SPSS version 27 was used to analyze the data. The mean values of the continuous variables, such as the mean age of the patients, and other continuous variables were provided together with the accompanying standard deviations. An independent t-test and Pearson correlation were used to compare the main outcome, which was the connection between hemoglobin and parathyroid hormone. The study group and control group were compared using these statistical tests. We used the chi-square test for categorical variables. Statistical significance was defined as a p-value less than 0.05 showing a meaningful difference between the groups being compared.

Results:

The research included 94 individuals with end-stage renal disease (ESRD), and it was shown that hypertension and diabetic nephropathy were the main causes of ESRD in the majority of these patients. There were 66% males and 34% women among the patients. The patient's test results are included in Table 1 for reference. The research discovered that anemia was more prevalent in women than in men, with a mean serum hemoglobin (Hb) level of 9.48 ± 1.4 g/dL for women and 10.03 ± 1.2 g/dL for males. Similar to this, women exhibited average integral parathyroid hormone (iPTH) levels that were higher (662.46 pg/dL) than those of males (554.05 pg/dL). In patients with ESRD brought on by diabetes and hypertension, anemia and hyperparathyroidism were shown to be more severe, as indicated in Table 3.

Table 1: Demographic information of the study population

Variables	**Mean(SD)**
Age	45.2 ± 12.6
Uric Acid	8.16 ± 15.41
Ferritin	592.92 ± 399.78
i-PTH	646.22 ± 587.42
Hemoglobin	9.02 ±1.32
Session/week	1.54 ±.50
Dialysis duration	4.09 ± 1.14
Albumen	3.33 ±.538
Creatinine	7.95 ± 2.50
Phosphate	5.67 ± 1.70
Calcium	8.11 ±.82
T-Stat	37.85 ± 16.69

Iron	100.01 ± 73.69
Vit-D	22.43 ± 11.98

In the study's analysis of hemodialysis frequency, it was discovered that 54.3 percent of patients got hemodialysis twice a week and that around half of them had been receiving it for over five years. Figure 2 and Table 4 show the results of a Pearson correlation study that demonstrated a substantial association between iPTH and Hb levels.

Table 2: Etiology of individuals' end-stage renal illness in the population under study

Cause	**n (%)**
Myeloma	2(2.1%)
Kidney Stone	6(6.4%)
DM	45(47.9%)
Nephropathy Induced by Contrast	2(2.1%)
Glomerulonephritis	10(10.6%)
Small size bilateral kidneys	10(10.6%)
Pregnancy	3(3.2%)
Hypertension	16(17%)

Table 3: Association between i-PTH and Hemoglobin

Cause	**Hemoglobin**		**i-PTH**		**p**
	Mean	**SD**	**Mean**	**SD**	
Myeloma	10.9	0.98	195.3	96.73	
Kidney Stone	9.81	1.55	428.51	297.35	
Diabetes Mellitus	9.58	1.33	538.07	593.1	
Nephropathy Induced by Contrast	9.7	1.27	452.75	90.15	**0.0001**
Chronic GN	8.78	1.1	546.3	309.58	
Small size bilateral kidneys	9.11	1.51	613.9	712.98	
Pregnancy	9.73	1.53	602.06	540.04	
Hypertension	8.38	1.29	794.45	752.15	

Table 4: Analysis of the mean hemoglobin's significant association with several factors.

Variables	**t-stat**	**df**	**Significance**
Ferritin	-1.441	21.1	0.16
Iron	-0.579	15.3	0.57
Vit-D	0.053	10.08	0.96
Albumen	-0.815	13.3	0.43
Calcium	-1.088	14.79	0.29
Phosphate	-0.546	14.27	0.59
Session-week	-0.927	11.1	0.37

Hemodialysis duration	-2.988	10.26	0.01
Cause	2.028	11.95	0.06
Creatinine	0.42	11.25	0.68
PTH	-8.214	91.99	0

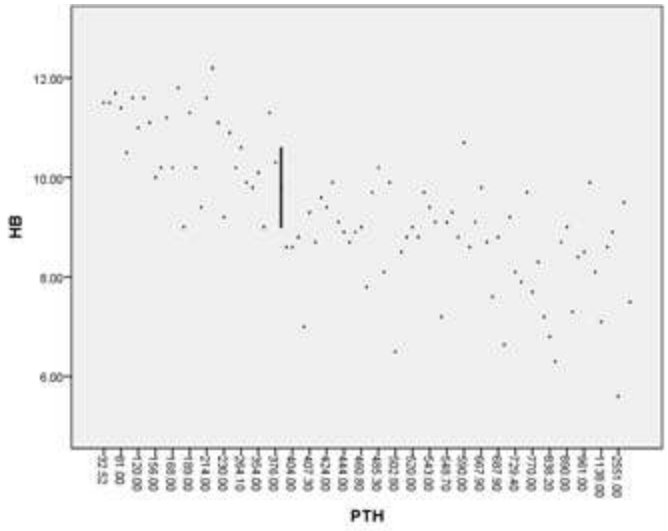

Figure 2: Association between i-PTH and Hemoglobin

In general, this research sheds light on the features of ESRD patients in terms of their gender, etiology, laboratory results, and course of therapy. According to the research, diabetes mellitus, and hypertension cause anemia and hyperparathyroidism to be more prevalent and severe in ESRD patients, and women may be more prone to developing these illnesses than males. The research also emphasizes how crucial it is to keep an eye on patients with ESRD's iPTH and Hb levels since they are linked and may have an impact on how they respond to treatment.

Discussions:

In patients receiving continuous EPO therapy while on maintenance hemodialysis, our research unequivocally shows that secondary hyperparathyroidism might contribute to chronic anemia. The major cause of anemia in hemodialysis patients is a lack of erythropoietin, which may be either caused by a decrease in erythropoietin production or by the body's resistance to the hormone. Anemia worsens outcomes and lowers prognosis. [15,16] In addition, high FGF23 values and low levels of iron are often found. Hyperparathyroidism also contributes to anemia by inducing stiffness of the bone marrow. [17-22]

Despite having a sufficient iron status, our patients developed hyperparathyroidism. Chronic anemia (hemoglobin 10–12 g/dL) or the need for very high erythropoietin dosages of epoetin alfa (300 IU/kg/week subcutaneously or 450 IU/kg/week intravenously) are considered to be EPO resistance.[23] Neither of the people we treated was using EPO dosages that may indicate EPO resistance. Anemia was shown to be prevalent (68.5%) in recent research with sufficient iron reserves.[24] They hypothesized that insufficient EPO dose and inadequate dialysis were the primary causes of anemia. Even though they did not specify the anemia incidence in their group, a different study found that elevated turnover osteoporosis was prevalent among 61 individuals on maintenance dialysis.[25] A comparable high incidence of anemia and hyperparathyroidism was found in different research, but no correlations were made to determine the

significance of the effect.[26] Our research fills up these gaps in the local literature by conclusively demonstrating a link between anemia prevalence and hyperparathyroidism in maintenance hemodialysis patients. Our findings agreed with those from other countries that had been published. [27,28]

A compelling theory about the treatment of secondary hyperparathyroidism in maintenance dialysis patients with vitamin D therapy has recently been put up by another study.[29,30] Our patients had relatively low average vitamin D levels (23.5ng/mL). It would be interesting to observe whether secondary hyperparathyroidism can be managed with vitamin D supplementation. whether so, the anemia status might improve, and potentially the need for EPO could decline. Therefore, research is required to investigate this component of therapy for maintenance hemodialysis patients who have secondary hyperparathyroidism and anemia.

Conclusions:

Erythropoietin and low levels of iron are the most typical causes of anemia in ESRD patients. Our research unequivocally shows that hyperparathyroidism is a substantial contributor to anemia, most likely as a result of EPO resistance. To avoid anemia and EPO resistance, hyperparathyroidism must be strictly monitored and controlled.

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