



## FREQUENCY OF ANEMIA IN PATIENTS WITH INCREASED LEVEL OF PARATHYROID HORMONE AMONG PATIENTS ON MAINTENANCE HEMODIALYSIS.

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**ABSTRACT... Objectives:** One of the most frequently occurring complication of end stage renal disease is anemia. It can be defined as decrease in red blood cells with hemoglobin concentration less than 12 g/dl in women and less than 13 g/dl in men. Parathyroid hormone levels are also raised among patients with end stage renal disease to maintain serum calcium levels. The objective of this study is to evaluate the degree of anemia in patients with end stage renal disease currently on maintenance hemodialysis and have raised PTH levels. **Study Design:** Cross-sectional study. **Setting:** Kidney Center, Karachi. **Period:** November 2015 to July 2016. **Material & Method:** Patients undergoing maintenance hemodialysis during the study duration with PTH levels greater than 300 ng/L were included in the study. Patients with other co-morbid conditions like chronic liver disease and hypersplenism were excluded from the study. **Results:** The total number of patients on maintenance hemodialysis in the kidney center that matched our inclusion criteria was 110. Amongst them there were 47.3% (n=52) males and 52.7% (n=58) females. The mean age of patients in our study is  $50.15 \pm 12.92$  years. The mean PTH level of patients was found to be  $642 \pm 405.9U$ . Since all the participants of the study are on maintenance dialysis, the mean duration of hemodialysis was found to be  $4.2 \pm 3.19$  months. The mean hemoglobin level of patients was found to be  $9.75 \pm 1.47$  g/dl. **Conclusion:** Patients with hyperparathyroidism and undergoing maintenance hemodialysis frequently develops anemia. Many factors account for this including raised PTH levels causing bone marrow fibrosis, decreased production of erythropoietin and resistance of produced erythropoietin are some factors responsible for the anemia.

**Key words:** Anaemia, Parathyroid Hormone, Maintenance Hemodialysis, Erythropoietin.

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### INTRODUCTION

One of the most common complication of end stage renal disease is anemia, primarily due to decreased erythropoietin production by the kidneys leading to decrease in red blood cell count. Anemia can be defined as decreased hemoglobin levels i.e less than 12 g/dl in women and less than 13 g/dl in men.<sup>1</sup> There are multiple studies conducted to evaluate the severity and multiple mechanisms related to anemia. It has been recommended internationally to use supplements of iron, folate and synthetic erythropoietin to manage the associated anemia.<sup>2</sup> The NHANES survey showed that the levels of hemoglobin decreases directly in proportion to the decrease in glomerular filtration rate (GFR).

It concluded that the prevalence of anemia in these patients can range anywhere from 1% to 67%. The prevalence of anemia was reported to be 67% at GFR of 15 ml/min.<sup>3</sup> Anemia among these patients can further lead to altered cardiac output and cardiac complications.<sup>4</sup> Another mechanism suggested by researchers is the role of the parathyroid hormone in anemia.<sup>5,6</sup> Along with inflammation and iron deficiency, the raised parathyroid hormone level also contributes in causing anemia by causing bone marrow fibrosis. There are multiple mechanisms suggested by researchers by which raised PTH levels can further decrease hemoglobin and one of the most commonly suggested mechanism is bone marrow fibrosis.<sup>7,8</sup> Researchers have

proved their hypothesis by concluding that parathyroidectomy led to elevation in hemoglobin levels and decreased requirement for synthetic erythropoietin.<sup>9</sup>

The objective of this study is to evaluate the frequency of anemia in patients with end stage renal disease undergoing maintenance hemodialysis and have raised PTH levels.

## MATERIAL & METHODS

This is a cross-sectional study performed at the Kidney Center, Karachi. The study duration was starting from November 2015 to July 2016. Patients undergoing maintenance hemodialysis for more than 3 months for end stage renal disease with PTH levels greater than 300 ng/ml were included in the study. The age range of patients was 18 to 65 years. Patients with other co-morbid conditions such as chronic liver disease, hypersplenism, auto-immune diseases, gastrointestinal and genitourinary pathologies were excluded from study. Patients had PTH levels measured and CBC were performed. Data was analyzed using SPSS v.20. T-test and Chi square were used to analyze p-value and the association between hemoglobin and PTH levels among patients on maintenance hemodialysis were analyzed.

## RESULTS

The total number of patients on maintenance hemodialysis in the kidney center that matched our inclusion criteria was 110. Amongst them there were 47.3% (n=52) males and 52.7% (n=58) females. The mean age of patients in our study was 50.15 + 12.92 years. The mean PTH level of patients was found to be 642 + 405.9 units. The mean duration of hemodialysis was found to be 4.2 ± 3.19 months. The mean hemoglobin level of patients was found to be 9.75 ± 1.47 g/dl. The range of hemoglobin level was found between 8.5 to 11 g/dl. Table-I shows associated co-morbid of the patients in the study. Table-II shows the correlation of anemia to different factors like age and co-morbid. Figure-1 shows the correlation of anemia to Hepatitis B&C.”

Variable	No. of Patients	Percentage
Hepatitis B	12	11%
Hepatitis C	18	16.3%
Diabetes Mellitus	56	51%
Hypertension	108	98.2%
Anemia		
Yes	85	77.27%
NO	25	22.72%

Table-I

Variable	Anemia		P-Value
	Yes	No	
<b>Age</b>			
20-45 years	27	12	0.296
46-70 years	42	26	
<b>Gender</b>			
Male	29	23	0.153
Female	40	18	
<b>Duration of Hemodialysis</b>			
0.5-8 years	72	21	<0.001
9-16 years	13	4	

Table-II. Stratification of anemia with different variables n=110

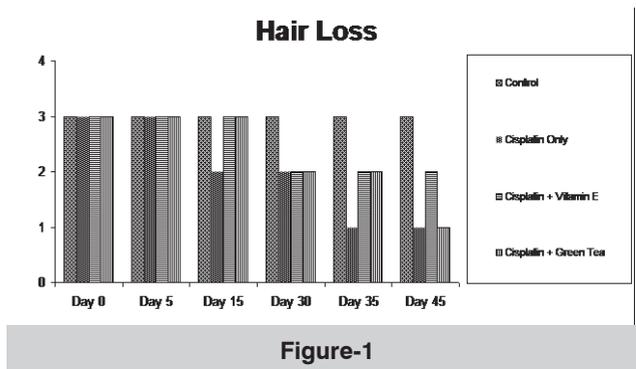


Figure-1

## DISCUSSION

Subjects in our study had anemia and raised PTH levels. The mean hemoglobin level in our study was 9.75 ± 1.47 g/dl which is less than normal. It can be concluded that raised PTH levels inhibit the production of red blood cells and alleviate the degree of anemia. Other studies have also concluded this finding.<sup>10</sup> Bone marrow fibrosis decreased production of erythropoietin and resistance of produced erythropoietin are some factors responsible for the anemia.<sup>11</sup> Patients with high levels of PTH require greater

levels of synthetic erythropoietin. Yasunaga has concluded in his study that even after a year of parathyroidectomy the requirement for synthetic erythropoietin was not raised.<sup>12</sup>

Chutia and roram conducted a study to evaluate the role of PTH levels and anemia among patients with end stage renal disease. His study results conclude that there is an inverse relation between serum PTH and hemoglobin levels.<sup>13</sup> Baradran and Nasri have also concluded in their study that raised PTH levels can be correlated directly with the degree of anemia and inversely with hemoglobin levels.<sup>14</sup> Trovato et al has also concluded the same findings and he has also suggested that the levels of recombinant erythropoietin should be increased among patients with raised levels of PTH.<sup>15</sup>

Zingraff et al performed parathyroidectomy and observed an increase in hemoglobin levels from 6g/dl to 9g/dl among 8 patients. This study proved significant association between hyperparathyroidism and anemia. This study was conducted in 1978 and it was the first study showing association between hyperparathyroidism and anemia.<sup>16</sup> Goicoechea et al conducted a similar study and showed a significant improvement in anemia and decreased requirement for erythropoietin. He concluded that the erythropoietin requirements decreased from 194 to 94 units per kg body weight per week.<sup>17</sup>

Researchers have suggested that the raised PTH levels contribute to decreased osmotic fragility and hence account for decreased hemoglobin.<sup>18</sup> Another mechanism suggested by researchers is the resistance of produced erythropoietin which hinders erythropoiesis.<sup>18,19</sup>

The limitation of our study includes small sample size and inability to evaluate the improvement in hemoglobin levels after the correction of hyperparathyroidism.

## CONCLUSION

It can be concluded that patients with hyperparathyroidism undergoing maintenance hemodialysis frequently develops anemia. This

could be due to decreased osmotic fragility and resistance of produced erythropoietin leading to increased breakdown and decreased production of red blood cells respectively that accounts for increase in the need of erythropoietin dose and also put extra financial burden to the patients. Further studies are required to investigate the underlying mechanism and its management.

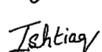
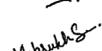
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## REFERENCES

1. Guinn NR, Guercio JR, Hopkins TJ, Grimsley A, Kurian DJ, Jimenez MI, Bolognesi MP, Schroeder R, Aronson S, **Duke Perioperative Enhancement Team (POET). How do we develop and implement a preoperative anemia clinic designed to improve perioperative outcomes and reduce cost?**. *Transfusion*. 2016 Feb; 56(2):297-303.
2. Bellasi A, Mangano S, Minoretti C, Campana C, Di Iorio B, Di Lullo L, Ratti C, Cozzolino M. **Single-center open-label randomized study of anemia management improvement in ESRD patients with secondary hyperparathyroidism**. *Nephrology@ Point of Care*. 2016; 2(1):pocj-5000196.
3. Astor BC, Muntner P, Levin A, et al. **Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988-1994)**. *Arch Intern Med*. 2002; 162:1401.
4. **KDIGO clinical practice guidelines for anemia in chronic kidney disease**. *Kidney Int Suppl*. 2012;2:288
5. Yohay DA, Quarles LD. **Clinical applications of parathyroid hormone immunoassays in patients with end stage renal disease**. In *Seminars in Dialysis* 1993 Sep (Vol. 6, No. 5, pp. 305-311). Oxford, UK: Blackwell Publishing Ltd.
6. Block GA. **The impact of calcimimetics on mineral metabolism and secondary hyperparathyroidism in end-stage renal disease: Management of comorbidities in kidney disease in the 21st century: Anemia and bone disease**. *Kidney international*. 2003 Nov 1; 64:S131-6.
7. Fishbane S, Berns JS. **Hemoglobin cycling in hemodialysis patients treated with recombinant human erythropoietin**. *Kidney international*. 2005 Sep 1; 68(3):1337-43.

8. Grützmacher P, Radtke HW, Fassbinder W, Koch KM, Schoeppe W. **Effect of secondary hyperparathyroidism on the anaemia of end-stage renal failure: In vivo and in vitro studies.** Proceedings of the European Dialysis and Transplant Association. European Dialysis and Transplant Association. 1983; 20:739-45.
9. Bhadada SK, Bhansali A, Shah VN, Behera A, Ravikiran M, Santosh R. **2011 High prevalence of cholelithiasis in primary hyperparathyroidism: Retrospective analysis of 120 cases.** Indian J Gastroenterol 30:100-101.
10. Rao DSS, Shih MSM, Mohini R. **Effect of serum parathyroid hormone and bone marrow fibrosis on the response to erythropoietin in uremia.** N Engl J Med 1993; 328 (3): 171-175.
11. Mandolfo S, Malberti F, Farina M, Villa G, Scanziani R, Imbasciati E. **Parathyroidectomy and response to erythropoietin therapy in anaemic patients with chronic renal failure.** Nephrol Dial Transplant 1998; 13 (10): 2708-2709.
12. Yasunaga C, Matsuo K, Yanagida T, Matsuo S, Nakamoto M, Goya T. **Early effects of parathyroidectomy on erythropoietin production in secondary hyperparathyroidism.** Am J Surg 2002; 183 (2): 199-204.
13. Chutia H, Ruram AA, Bhattacharyya H, Boruah P, Nath C. **Association of secondary hyperparathyroidism with hemoglobin level in patients with chronic kidney disease.** J Lab Physicians 2013; 5(1): 51-4.
14. Baradaran A, Nasri H. **Intensification of anaemia by secondary hyperparathyroidism in hemodialysis patients.** Med J Islam Acad Sci 2001; 14(4): 161-6.
15. Trovato GM, Carpinteri G, Spina S, Squatrito G, Catalano D, Iannetti E. **Hyperparathyroidism, anaemia and erythropoietin: Effects on systolic function of dialysis patients. Abstracts of 31st Congress of European Renal Association/European Dialysis and Transplantation Association, September 5-8, 1999.** Madrid in Nephrol Dial Transpl. 1999; 14:190.
16. Zingraff J, Drueke T, Marie P, Man NK, Jungers P, Bordier P. **Anemia and secondary hyperparathyroidism.** Arch Intern Med 1978; 138: 1650-2.
17. Goicoechea M, Gomez-Campdera F, Polo JR, Tejedor A, Ruiz MA, Vazquez MI, et al. **Secondary hyperparathyroidism as cause of resistance to treatment with erythropoietin: Effect of parathyroidectomy.** Clin Nephrol 1996; 45: 420-1.
18. Wu SG, Jeng FR, Wei SY, Su CZ, Chung TC, Chang WJ, et al. **Red blood cell osmotic fragility in chronically hemodialyzed patients.** Nephron 1998; 78: 28-32.
19. Sikole A. **Pathogenesis of anemia in hyperparathyroidism.** Med hypotheses 2000; 54(2): 236-8.
20. Cunningham J, Locatelli F, Rodriguez M. **Secondary hyperparathyroidism: Pathogenesis, disease progression and therapeutic options.** Clin J Am Soc Nephrol 2011; 6: 913-21.

### AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Saad Muzaffar Azeem	All authors contributed equally. To the conception or design of the study, in analysis and interpretation of data for the work. In drafting of the work and revising it critically for important intellectual content. All authors contributed in final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.	
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