

Measurement of Folate Levels in Patients of End Stage Renal Disease

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Back Ground: Folate deficiency is an important cause of megaloblastic anaemia in renal failure. Red cell folate is better indicator of body folate status. This study was carried out to find out the serum and red cell folate levels of diagnosed patient of End Stage Renal Disease (ESRD).

Methods: Sixty subjects were selected. These included 30 normal healthy subjects as control and 30 patients with ESRD. Absolute values and Hb were done by haematology auto analyzer and serum and red cell folate were done by commercially available kits using competitive immunoassay.

Results: These were analyzed by using Student's't' test and level of significance was determined. A significant decrease in serum and red cell folate in end stage renal disease patients as compared to control was observed.

Conclusion: Patients of end stage renal disease are deficient in folate levels so they need folate supplement to prevent megaloblastic anemia and minimize the risk of transfusion.

Key Words: Anaemia, End Stage Renal Disease (ESRD), Serum folate, Red cell folate.

Introduction

In chronic renal failure, there is progressive loss of renal functions and characterized signs and symptoms of uremia¹. Erythropoietin deficiency occurs in end stage renal disease patient Erythropoietin therapy improves the quality of life by minimizing the anaemia². Erythropoietin is an acidic single chain polypeptide that has two internal disulfide bonds that are necessary for their biological activity³. Anaemia is one of the more constant Clinical features of chronic renal failure and these patients require dialysis therapy to stay alive⁴. During the dialysis anaemia is exacerbated due to mechanical and thermal injury of blood cells⁵. Pathogenic mechanisms of anaemia development in chronic renal failure patients may be due to low level of erythropoietin and development of ineffective erythropoiesis and having a suppressive effect on haemopoiesis⁶. End stage renal disease patients may develop a water soluble vitamin deficiency which was found to be folic acid, caused by poor intake, interference with absorption of drugs, altered metabolism and conditioned folate deficiency⁷. Folic acid vitamin absorbed from the small intestine plays a vital role in regulating cell proliferation and differentiation and is essential for erythropoiesis⁸. Folate coenzymes participate in biochemical reactions involving the transfer and utilization of single-carbon (C) moieties, a critical system required in intracellular purine and pyrimidine metabolism, nucleic acid synthesis and cell replication⁹. Folate deficiency has been

associated with severally altered hemopoiesis, congenital malformations, impaired neurological functions and atherosclerotic vascular disease¹⁰. Folic acid level is significantly decreased in end stage renal disease, so folate supplementation is necessary for patients of end stage renal disease¹¹. In end stage renal disease total homocysteine levels depend on folate status and folate is significantly lost in uremia and its supplement is necessary to prevent complications¹². The purpose of this study was to measure serum folate level in patients with end stage renal disease so that we can manage anaemia due to folate deficiency.

Patients and Methods

Sixty subjects were selected and were divided into two groups (30 diagnosed patients of end stage renal disease and 30 normal healthy subjects as control). Absolute values and Hb were done by haematology autoanalyzer. Serum and Red cell folate were done by commercially available kits using competitive immunoassay (Diagnostic Product Corporation USA). Results were analyzed by using student's't' test and level of significant was done¹⁴.

Results

Results and level of significance of these groups are given in table No. 1-4 and figures I-II. Hb was found to be lower in patients of ESRD when compared with Control and the difference was highly significant ($p < 0.01$). PCV was found to be decreased in patients of ESRD when compared with control group. MCV was found to be raised in patients of ESRD when

Compared with control group. MCV was found to be raised in patients of ESRD when compared with control group. MCH and MCHC were found to be comparable in all the groups and difference was non-significant ($P>0.05$).

Table 1: Comparison of Hb, PCV, MCV, MCH, MCHC in patients with ESRD & control group.

Tests Value	Control	Patients of ESRD	P
Hb (gm/dl)	12.5±1.33	7.9±1.4	HS
PCV(%)	40.6±0.91	22.2±3.3	HS
MCV(fl)	79.8±11.9	104.2±8.5	HS
MCH (pg)	30.6±0.98	28.8±2.02	NS
MCHC (%)	31.4±1.1	31.2±1.5	NS

NS=non significant ($p<0.01$), **HS**=highly significant ($p>0.05$)

Serum Folate Level (Table 2 - Fig. 1):

In the present study serum folate levels were found to be significantly decreased in patients of end stage renal disease (ESRD) as compared to controls. This decreased serum folate level may be due to toxic effects of uremia, as well as conditioned folate deficiency. This study is consistent with the results Armada et al (2001)¹⁷ and Labelane et al (2001)¹⁹ who also observed decreased serum folate levels in patients of ESRD.

Table 2: Comparison of serum folate levels in patients with ESRD and controls.

Serum folate (ng/ml)	Patients of Control	ESRD
Mean ± SD	10.7 ± 2.9	4.1±1.8
Range	4-14	2.5-5.4
Total Subjects	30	30

Statistical Analysis = $P<0.01$ (Highly significant)

Red Cell Folate Levels (Table 3 - Fig. 2):

Red cells folate levels were significantly decreased in patients of end stage renal disease (ESRD) Red cell folate decreased due to poor intake interference with absorption by drugs, altered metabolism⁹. Conditioning folate deficiency occurs due to micro-angiopathic hemolytic anemia, common in ESRD. The present results are consistent with the student of Jafee et al (1994)²⁰ and Hung et al (2001)^{15,16} who also observed decreased red cell folate levels in

ESRD patients with dialysis.

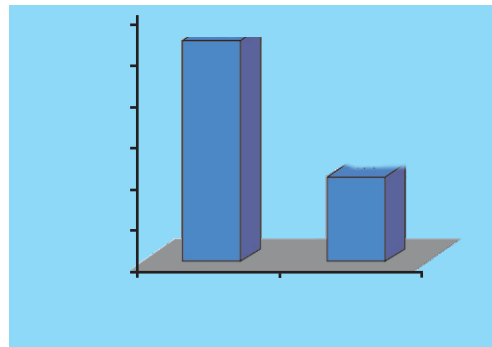


Fig. 1: Comparison of mean levels of serum folate between patients with ESRD and controls.

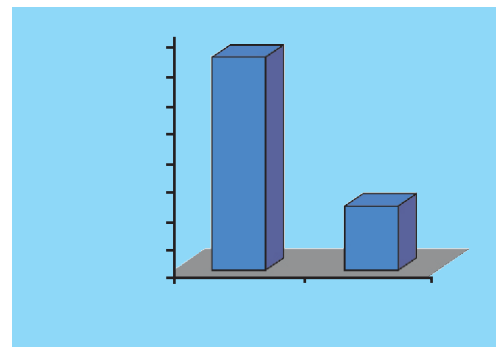


Fig. 2: Comparison of mean Red Cell folate levels between patient with ESRD and controls.

Table 3: Comparison of Red Cell folate levels between patients with ESRD and controls.

Red Cell folate (ng/ml)	Control	Patients of ESRD
Mean ± SD	368.5 ± 119.8	110.7 ± 47.9
Range	181 - 585.6	88.2 160.5
Total Subjects	30	30

Statistical Analysis = $P<0.01$ (Highly significant)

Serum folate level was found to be decreased in 18 patients while Red Cell folate level was found to be decreased in 28 patients (Table 4).

Discussion

Anaemia is one of the more constant clinical features of renal failure; during haemodialysis anaemia is exacerbated due to mechanical and thermal injury (4). Many factors contribute the anaemia of chronic renal failure e.g. Iron deficiency, ineffective erythropoiesis

Table 4: Folate levels in Patients of ESRD

Tests Total	normal folate levels	decreased folate levels	
Serum folate	12 (40%)	18 (60%)	30
Red cell folate	02 (6.7%)	28 (93.3%)	30

Statistical Analysis = P<0.01 (Highly significant)

etc. Identification of the cause underlying anaemia and treating it may improve the quality of life and reduce transfusion demand. Folic acid deficiency is one cause of anaemia. This study was planned observe the float level in end stage renal disease. Serum and red cell folate levels were compared.

The result of our study indicated a significant lower level of Hb, PCV in patients with end stage renal disease as compare to controls.

The present study is in consistent with the result of Jafee et al (1994)²⁰ and Aviles et al (2002)¹⁵ who also Observed decreased Hb levels in ESRD patients. This decreased hemoglobin, because of toxic effects of uremia and may be due to hemolysis. Parathyroid hormone is a uremic toxin, because it produces anemia by inducing fibrosis of the bone marrow cavity and leads to decrease production of red cells.

The present study is in favour of the results of Aviles et al (2002) who also found decreased PCV in ESRD patients under going regular hemodialysis.

MCV was found to be significantly increased as compare to controls. The present study is consistent with the results of Hung et al (2002)¹⁶ who also observed same results. MCV is increased because of folic acid loss in end stage renal disease which leads to megaloblastic anemia.

While MCH, an MCHC were not significantly different.

The patients of end stage renal disease (ESRD) are deficient in folic acid. This deficiency may be due to toxic effect of metabolic products and nutritional deficiency. Increased amount of folic acid may be required due to possible interference with its activity by anions retained in uremic state. These patients have to undergo hemodialysis which further induces folic acid deficiency (4). Red cell folate estimation is considered a better indicator of body folate as compare to serum folate (13). Our study revealed both value to be decreased. But red cell folate was found to be a better indicator as compare to serum folate. (Table-3)

The study reveals that serum folate levels are found to be in lower normal limits in ESRD. Hemodialysis in ESRD further decreases the folate level because folic acid is free and not bound with plasma proteins. So all the patients of ESRD must be supplemented by folic acid to prevent further complications like megaloblastic anemia, atherosclerosis, cerebrovascular disease, peripheral neuropathy, Alzheimer disease and depression. Our study prove that red cell folate is better indicator of body stores than serum folate, so for confirmation of body stores of folate it is necessary to measure the red cell folate levers. In ESRD patients, folate levels are at lower normal limits and lost during dialysis. Anemia in renal disease is multifactorial. However, if folate deficiency can be identified earlier, patient's transfusion requirement may be reduced and quality of life can be improved by folate supplementation.

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