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Mild Hyperhomocysteinemia in Children and Young Adults on Dialysis: A Single Center Study

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Introduction: Hyperhomocysteinemia is common in end stage renal diseases. We aimed to determine the prevalence of hyperhomocysteinemia in dialysis cases and define independent risk factors of the development of hyperhomocysteinemia.
Materials and Methods: The total plasma homocysteine values were measured in 46 dialysis patients including 20[43.4 %] girls and 26[56.6 %] boys aged 1.6-25 [19.9±6.5] years based on two different reference values for children [age dependent] and adults [cut off point of 15 µmol/L].
Results: Using the reference values for children, 26 cases [56.2 %] had hyperhomocysteinemia including 41.6% of CAPD and 2/3 of hemodialysis patients with no significant difference based on age, gender, duration and modality of dialysis, and dosage of folate supplement [p>0.05 for all]. Using a cut-off point of 15 µmol/L, hyperhomocysteinemia was reported in 30.4% of the patients including 11 hemodialysis and one CAPD [P=0.022], 10 out of 19 girls [52.6%%] and 4 out of 26 boys [15.4%] [p=0.063], but logistic regression analysis did not show any significant differences in the incidence rate of hyperhomocysteinemia according to the modality of dialysis and gender [P=0.998 and 0.137 respectively].
Conclusions: We found mild hyperhomocysteinemia as a common finding in dialysis patients; also, the prevalence of hyperhomocysteinemia was comparable in children and young adults. However, we noted that hemodialysis patients and females were more prone to more intense elevations of plasma homocysteine levels. We found that neither gender nor modality of dialysis played a role as risk factors for development of hyperhomocysteinemia in children and young adults.

Keywords: Hyperhomocysteinemia; Child; Hemodialysis; Peritoneal dialysis; Adults.

Running Title: Hyperhomocysteinemia in Children and Young Adults on Dialysis

Introduction

Homocysteine (Hcy) is a metabolite of methionine, an essential amino acid derived from the dietary protein. It is metabolized by one of two pathways: remethylation into methionine, catalyzed by the vitamin B12-dependent enzyme methionine synthase; or trans-sulfuration to cysteine and glutathione [1].

As early as 1969, homocysteine was postulated to affect atherosclerotic processes. Since then, evidence has shown a relationship between hyperhomocysteinemia and the risk of cardiovascular disease. This metabolic abnormality has been suggested as a modifiable independent risk factor for coronary artery

disease, stroke, and deep vein thrombosis [2]. Hcy is normally produced by demethylation of methionine. Folate and cyanocobalamin [vitamin B12] are important regulators of the metabolism of homocysteine, and an inverse relationship has been reported between the levels of these factors and the levels of homocysteine in the blood by different studies [3] while a few studies have reported no correlation between serum folate and vitamin B12 with plasma Hcy concentrations [4] Hyperhomocysteinemia can be caused by nutritional deficiencies in vitamins required for its metabolism (folate, vitamin B12, and vitamin B6), genetic defects in the enzymes involved in homocysteine metabolism, or drugs and toxins [1]. Alcohol increases serum Hcy possibly due to interference with folate metabolism. Several drugs such as cyclosporine, methotrexate, fibrates, and L-dopa elevate the plasma Hcy concentration [5]. Serum Hcy is directly associated with the renal function and glomerular filtration rate; patients with end-stage renal disease (ESRD) present with significant hyperhomocysteinemia [5,6]. Other causes of hyperhomocysteinemia include leukemia, psoriasis, sickle-cell anemia, polycythemia vera, and idiopathic thrombocytosis [5]. Hyperhomocysteinemia has been reported frequently in end stage renal diseases (ESRD) [7]. We aimed to first define the prevalence of hyperhomocysteinemia in dialysis patients with regards to the age (age group ≤18 years and those aged >18yr). The Second purpose of study was to determine possible factors which might play a role as independent risk factors in the development of hyperhomocysteinemia.

Materials and Methods

Forty-five patients with chronic kidney diseases (CKD) stage 5 who were supervised by hemodialysis (HD) and peritoneal dialysis (PD) sections of an academic children hospital and consented to participation in the study were enrolled. Those who were taking drugs that might show falsely elevated Hcy levels (such as carbamazepine, phenytoin) were excluded from the study. None of our patients were taking these drugs. Written consent was taken from patients or their parents. The study was funded by a research grant from the research and development section of our local academic center and was approved by a local ethics committee. Based on age, the patients were categorized in to 2 groups:

1- Cases ≤ 18years 2- patients>18 years.

Table I shows the characteristics of cases in each age subgroup. Folate supplement was recommended routinely before or immediately after dialysis (0.125-0.25 mg/daily for infants, 0.25-0.5 mg/daily for small children and 0.5-1 mg /day for school aged children and adolescence). Patients took folate supplement in the form Nephrovite tablet (mixture of hydro soluble vitamins containing 0.5 mg folic acid,10 mg vitamin B6, and 6 µg vitamin B12) or as folate tablet. The dose of nephrovite was adjusted according to the dose of the required folate. Nine cases were not sure about regular consumption of folate and 36 subjects received folate 0.25-1 (0.49±0.2) mg/day, 42 subjects were supplemented by vitamin B6 1-52 (20.42±19.57) mg/day [they did not receive vitamin B6 supplement by using vitamin B complex syrup or tablet, vitamin B6 tablet (40mg) or nephrovite tablet or a combination of them], and 39 patients received vitamin B12 3-6 (4.42± 2.3) µg/day.

In HD cases, the type of the dialysis machine was Fresenius 4008 (Germany) or AK95 and AK96 (Switzerland) and the type of the dialyzer was low flux dialyzer (R3-R5 and low flux Poly Sulfone membranes). The blood flow rate was regulated on 100-300 cc/min. Thirteen (48.1%) patients underwent standard HD (12 hours per week) whereas a dialysis duration <12 hours per week was prescribed in 14 (51.9%) subjects (patients or their parents did not accept or had problems for 3 sessions of dialysis /week). The calculated Kt/v in HD patients was 0.79-3.06 (1.86±0.55). The wide range of calculated Kt/v in our cases may be due to using different types of dialyzer membranes and differences in the duration of dialysis in each session (some cases underwent HD for 2-3 hours in each session instead of 4 hours). In addition, the short distance between arterial and venous lines of the fistula might have affected the quality of dialysis and the amounts of Kt/v. In cases that received continuous ambulatory peritoneal dialysis (CAPD), dialysis solution number 1 was routinely administrated. The number of dialysis cycle per day was 4-6 (4.82±0.52) with a dwelling time of 2-4 (3.4 ±0.92) and dialysis solution volume of 27-77 (40.26±15.83) cc/kg. We used a short dwelling time and more dialysis cycles in our patients because of some local problems in access to dialysis solution. Total fasting plasma homocysteine (tHcy) was measured using blood samples drawn at regular monthly visits and prior to hemodialysis in HD cases.

Laboratory method for plasma Hcy measurement: The kit FHRWA100/200/1000 was used for the

measurement of the plasma homocysteine level. The calibrators were prepared gravimetrically and were traceable to NITS SRM 1955, confirmed by a designated measurement procedure (HPLC). Quality control procedures included assayed control materials with values for homocysteine in both normal and abnormal ranges to validate the reagent performance.

Definitions:

There is no systematic description for the effect of age and sex on fasting homocysteine concentrations during childhood; the reported reference values for tHcy are different and no standard definition and cut off point exist for tHcy in children according to the age [8-10]. The reference data for homocysteine levels in the pediatric age groups is lacking or sparse and inconsistent. [11,12] There is no extended study in the Iranian pediatric population for defining the normal value of Hcy. In addition, because of some limitations, we had no control group in our study; therefore, we used the established reference values for children for subjects <18yr and defined abnormal tHcy as plasma levels >8.3 µ mol/L**, >**10.3 µ mol/L**, >**11.3 µ mol/L in age groups 2-120 months [2 months -10 years], 121-180 months [10-15 years], and 181-216 months [15- 18 years], respectively [11]. In age group >18 years the laboratory normal reference values for Hcy considered 5-15 µ mol/L and levels >15 µ mol/L was defined abnormal [13]. In the age group <18 years, we performed data analysis in 2 stages. In addition to data analysis based on age-matched normal values, in the second stage of the analysis, Hcy levels >15 µ mol/L were considered abnormal and data analysis was repeated.

Statistical analysis: Descriptive statistics included mean ± SD for continuous and percentage for categorical data. Chi square and independent T tests were used for data analysis. According to these definitions, the patients were categorized into 2 groups: case with normal and those with high plasma Hcy concentrations. Univariate analysis was performed using a model with plasma Hcy as the dependent variable and age, gender, duration and modality of dialysis, hours of dialysis per week in HD subjects, mean±SD serum creatinine concentration, mean±SD Kt/v measurement, and amount of folate supplement as independent variables. Logistic regression was used for multivariate analysis and P-values ≤0.05 were considered statistically significant. In logistic regression analysis, P-value <0.05 were defined as significant independent risk factors of the development of hyperhomocysteinemia. Plasma Hcy Levels of 15-30 µmol/L, 30-100 µmol/L, and >100 µmol/L were defined as mild, moderate, and severe hyperhomocysteinemia, respectively [14].

Results

Characteristics of the study groups are shown in table 1. Total plasma Hcy levels ranged from 5 to 24 (12.4±5.2) µmol/L. Using a cutoff point of 15 µmol/L [for both age groups], the plasma tHcy levels were normal in 32 (71%) and high in 13 (29%) subjects, including 6 out of 13 (46.2%) young adults and 7 out of 32 (21.9%) children enrolled in the study. Using age- based values for Hcy concentrations in children (≤18), 19 out of 32 cases (59.4%) had hyperhomocysteinemia. Plasma Hcy levels were 5-24 (11.05±4.68) µmol/L in cases ≤18 yr and 5-22.2 (14.82±5.28) µmol/L in the adult age group (>18yr). The highest level of plasma Hcy was reported in a sixteen-year-old girl that received HD since 28 months before the study. The etiology of CKD in the patient was idiopathic. HD and CAPD patients were 72-300 (227.75) months and 19-183 (77) months, respectively**.** The only CAPD patient with a plasma tHcy level>15 µmol/L was a 27-month girl who was placed on dialysis since 2 years ago. The etiology of CKD in this patient was infantile polycystic kidney disease. Hyperhomocysteinemia (Hcy levels>15 µmol/L) was reported in about 60% of HD patients, and more than 70% of the subjects with high homocysteine levels were girls (Table 2). All cases of hyperhomocysteinemia showed mild elevation of plasma tHcy (≤30µmol/L). Age, duration of dialysis, hours of dialysis per week in hemodialysis subjects, mean serum creatinine concentration, and the dose of folate supplement were comparable between the 2 groups, and no significant differences were found (P>0.05 for all) whereas there were significant differences in the incidence rate of hyperhomocysteinemia (plasma Hcy levels >15 µmol/L) in girls compared with boys and HD versus CAPD patients (P-values 0.022 and 0.063, respectively) (Table 2). Figures 1 and 2 show plasma Hcy levels based on gender and modalities of dialysis. The mean plasma levels of tHcy were significantly higher in HD compared with CAPD subjects (P= 0.001). The Mean tHcy plasma levels in CAPD and HD patients were 8.53±4.51 and 14.08±4.88 µmol/L, respectively.

Using logistic regression analysis for univariate and multivariate analysis revealed no significant differences in the incidence rate of hyperhomocysteinemia (Hcy levels < 15 µmol/L)

Table I. Characteristics of enrolled cases

Characteristic	Age group ≤18yr (32, 71%)	Age group >18yr (13, 29%)	Total Number
Age (month)	132.6±64.1	248.9±21.5	45
Gender			
Female	13	6	19
Male	19	7	26
Modality of dialysis			
CAPD	12	0	12
HD	17	10	27
Both modalities	3	3	6
Duration from onset of dialysis (month)	32.3 ±15.6	76.8±36.3	45
Hours of dialysis per week (HD cases)	9.3±3	10.9±2.6	27
History of renal transplantation			
Yes	3	5	45
No	29	8	
Characteristics of dialysis in CAPD cases			
Cycle per day	4.8±0.58	5	12
Volume of each cycles(cc/kg)	40.34±17.3	36.6±11.5	
Dwelling time (hour)	3.5±0.75	4	
Etiologies of CKD			
Urological anomalies /renal	15	6	21
dysplasia	7	2	9
Glomerular diseases	4	1	6
Idiopathic	4	0	5
Neurogenic bladder	2	2	2
Tubolointerestitial disorders	0	2	2
Stone diseases			

according to modality of dialysis and gender (P=0.998 and 0.137, respectively) (Table 3). Hyperhomocysteinemia in enrolled children based on age –matched established Hcy levels: In the second step of study, the reference values for children [11] were used to interpret the results of tHcy plasma levels in cases ≤ 18yr (Table 4). As the Table presents, 6 cases ≤18 yr had plasma Hcy concentrations>15µmol/L. Table 5 shows the distribution of hyperhomocysteinemia in patients based on age and gender with considering the modality of dialysis. 1/3 of CAPD and 2/3 of HD patients had Hcy concentrations higher than their age–matched levels.

Table 2. Epidemiological and clinical characteristics of patients with high plasma Hcy concentration compared with those with normal Hcy levels.

Characteristic	Normal serum Hcy levels (≤15µmol/L) (32; 71.1%)	High serum Hcy levels (>15µmol/L) (13;28.9%)	P- value measures
Age a	152.2±75 months	187.64±81.85months	0.159
Gender b **Female** **Male**	 10(52.73 %) 22(84.5%)	 9(47.3%) 4(15.5%)	 0.019
Duration of dialysis a	42±29.6 months	47.9±35.11 months	0.574
Modality of dialysis b **CAPD** **HD**	 11 (91.6%) 16(59.2%)	 1(8.4%) 11(40.8 %%)	 0.063
Hours of dialysis per week (HD cases)a **<12 hours** **≥12 hours**	 9(33.4 %) 7(25.9%)	 4(14.8%) 7(25.9%)	 0.44
Mean ±SD dosage of folate a supplement (mg/day)	0.48±0.19	0.52±0.17	0.529
Serum creatinine concentration a (mg/dl)	7.24±2.9	9.1±2.6	0.076
Kt/V a	1.86±0.61	1.84±0.49	0.927

Values are presented as number (%) or mean standard deviation. a: Student's t-test, b: Fisher's exact test.

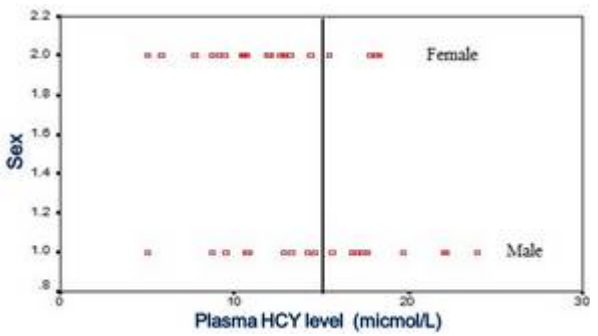

Fig 1. Plasma Hcy levels according to gender

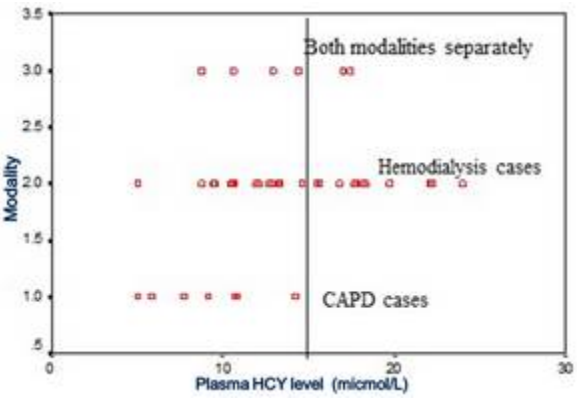

Fig 2. Plasma Hcy levels according to modalities of dialysis

Table 3. Multivariate analysis of risk factors for hyperhomocysteinemia

Variables	Normal serum Hcy levels (≤15µmol/L) (32; 71.1%)	High serum Hcy levels (>15µmol/L) (13;28.9%)	Odds ratio	p-value
Gender				
Female	10(31.3 %)	9 (69.2%)	0.14	0.137
Male	22(68.7 %)	4(30.8%)		
Modality of dialysis				
CAPD	12(100%)	1(8.4%)	0.998	8.23E
HD	16(59.2%)	11(91.6%)		

Table 4. prevalence of hyperhomocysteinemia based on age in our series (11)

Age group	(N/%)	Reference values of plasma tHcy concentration for children (µmol/L)	Plasma tHcy concentration (µmol/L) in our cases	Prevalence of Hyperhomocysteinemia in age group
2 months to 10 yr	13 (28.3)	3.3-8.3(5.8)	5-18.3(9.3)	Hyperhomocysteinemia based on age reference values: 6 (46.2%)[1] tHcy >15 µmol/L: 2 (16.7%)
11-15 years	9 (19.6)	4.7-10.3(6.6)	5.8-17(11.62)	Hyperhomocysteinemia based on age reference value: 5(55.5%)[2] tHcy >15 µmol/L: 2(22.2%)
16-18 yr	10 (21.7)	4.7-11.3(8.1)	9.4-24(13)	Hyperhomocysteinemia based on age reference value: 8 (80%)[3] tHcy >15 µmol/L : 2(20%)
>18 yr	13 (29)	5-15	5-22.2(14.7)	tHcy >15 µmol/L: 6 (46.2%)[4]

1) Three of 4 girls and 4 of 9 boys had tHcy levels >8.3 µmol/L
2) Five of 6 girls and 1 of 3 boys had had tHcy levels >10.3µmol/L
3) Three of 4 girls and 5 of 7 boys had tHcy levels >11.3µmol/L
4) Four of 6 girls and 2 of 8 boys had tHcy levels >15µmol/L

Considering the normal values of Hcy in children (≤18yr), there were no significant differences in the incidence rate of hyperhomocysteinemia between HD and CAPD cases, girls and boys, and the mean dose of folate supplement (P=0.053, 0.138, and 0.529, respectively). The total plasma Hcy levels were normal in all 9 children aged < 6 years except for one CAPD subject. The duration of

dialysis in this age group (<6 years) was 12-60 (30.3) months [1-5 (2.5) years].

Discussion

Different plasma Hcy levels in healthy people have been reported in various countries ranging from 6 µmol/L in Japan to 13µmol/L in South Africa [15]. An extended study in different age groups of Iranian people by Golbahar et al. [16] showed that Hcy concentrations in the Iranian population were comparable with levels reported in Japan, France, and Spain; countries with the lowest Hcy levels in their healthy people. The mean ±SD of Hcy concentration in their studied population aged 15-25 years was 6.7±3.9 µmol/L while it was 14±5.2 µmol/L in our cases, a concentration about 2 times greater than the levels found in normal Iranian population in the same age group

Limited studies have been done about normal values of plasma Hcy in healthy children [11, 12]. The results of the third national health and nutrition examination survey (NHANES III) in participants aged 4–19 in the USA showed normal values of Hcy in the healthy pediatric population [17]. The reported normal values based on this study were <5 µmol/L, <5.8µ mol/L, <8µmol/L, and <9.5 µmol/L in the age groups 4-5, 6-1, 12-15, and 16-19 years, respectively. The lower limit of normal reference for plasma tHcy is 5 µmol/L, but the upper limit varies considerably among clinical laboratories [14]. Depending on age, sex,, ethnic group, and dietary intake of folate, the upper limit may vary between 10 and 20 µmol/L [18]. A recently published paper considered normal values of plasma tHcy levels as 3.3-8.3 (median 5.8) µmol/L for the age group 2 months -10 years, 4.7-10.3 [median 6.6] µmol/L for the age group 11-15 years, and 4.7-11.3 (median 8.1) µmol/L for the age group 16-18 years. [9].

Dialysis patients are at a greater risk of the deficiency of water soluble vitamins and hyperhomocysteinemia. The 2005 KDOQI guidelines do not provide specific recommendations for vitamin supplements to patients on maintenance hemodialysis, but indicate that routine B-vitamin supplementation is required to replace the loss from dialysis and to prevent rises in serum homocysteine concentrations that result from deficiency in folate, riboflavin, vitamin B6, or B12 [19]. Folate 250 µg/day to a maximum of 2.5 mg daily for infants, 2.5 mg daily in children aged 1–5 years, and 5 mg daily for children >5 years is recommended [20]. It has been reported that the use of the recommended doses of folic acid supplement results in normal or mildly higher-than-normal blood concentrations; therefore, lower doses of folic acid supplement, i.e. 60 µg daily for infants and 400 µg daily for children, are recommended (21). An age-related increase in tHcy in adolescents reflects decreased levels of folate and vitamin B 12 [22]. The plasma Hcy concentration increased with an increase in age and is normally higher in boys than in girls [8-10], In contrast to the reported higher tHcy plasma concentrations in healthy boys than girls [23], the majority of the cases with Hcy plasma levels >15µmol/L were girls (P<0.05) in our series. The girls and boys with hyperhomocysteinemia were 108-300 [186] months (15.5 years) and 72-252 (168) months (14 years), respectively. Four out of 6 (2/3) girls and 2 out of 7 boys (28.5%) with Hcy >15 µmol/L were older than 18 years. The plasma Hcy concentration was 5-24 (11.9) and 5-18.3 (10) µmol/L in pediatric females and males and 12.8-22.2 (17.9) and 5-18.2 (12.2) µmol/L in adult females and males, respectively.

In our series including children and young adults, hyperhomocysteinemia was significantly more intense in girls than in boys (14.6±5.4 µmol/L versus 10.6± 4.17 µmol/L, P=0.008). The Hcy concentrations were 10.7-24 (15.2) and 9.1-18.3 (12.9) µmol/L in girls and boys ≤18 years with hyperhomocysteinemia and 17.6-22.2 (20.4) and 17.8-18.2 (18) µmol/L in girls and boys aged >18 years, respectively. In addition, hyperhomocysteinemia was more intense in HD versus CAPD cases (14.08±4.9 and 7.6±3.05 respectively, P=0.0001). Although cases who were placed on HD were significantly older than CAPD patients (202.44±53.1 months versus 81.16 ±49.3 months respectively, P=0.0001), patients with hyperhomocysteinemia were not significantly older than those with normal Hcy levels (172.8±75.1months versus 157.5±78.4 months respectively, P=0.51); thus, the greater increase in plasma Hcy did not seem related to age.

The Hcy levels in CAPD and HD cases ≤ 18 years were 9.1-14.2 (11.2) and 5-24 (14.8) µmol/L, respectively. In HD cases >18 years, the Hcy level was 17.6-24 (20.2) µmol/L, and there was no case >18 years who only received CAPD modality. In our cases, despite supplementation with folate, vitamin B12, and vitamin B6, hyperhomocysteinemia was a common finding especially in HD cases. Moreover, the incidence of hyperhomocysteinemia was comparable in children and young adults who participated in the study (P= 0.103).

In contrast to various published studies about hyperhomocysteinemia in adults, limited studies have been performed in pediatric dialysis cases [11,24,25]. The Hcy concentration in children [<18 years] in a study by Schröder et al [26] was 13.7–26 [20] μmol/l, and about 1/3 of the cases had Hcy levels >15μmol/L while in our series, the Hcy concentration was 5-24 (12.4) μmol/L and 12 out of 45 (26.5%) cases had Hcy concentration >15μmol/L. Differences in incidence of high plasma Hcy in our study compared with other studies in children may be due to differences in the age of the enrolled cases [11,24,25], and more important differences in the lifestyle including diet. In fact, as our study and similar studies could not find the main risk factors for hyperhomocysteinemia in dialysis subjects, it is very difficult to explain the reason for the difference in the mean plasma Hcy levels and the incidence rates of hyperhomocysteinemia reported by various studies.

A cases-control study by Lilien et al. [27] in children younger than 18 years showed significantly higher plasma Hcy levels in HD cases versus healthy children (22.2±13.5 μmol/L in HD and 9.6±2.7 μmol/L in normal children; P=0.002). The mean ±SD concentration of HCy in our pediatric [≤ 18 years] HD cases was 13.03±4.47 μmol/L. In our series, the mean±SD Hcy concentration was significantly higher in HD compared with CAPD cases (13.03±4.47 μmol/L versus 7.6 ± 3, P=0.001).

Feinstein et al. [28] evaluated 29 dialysis children and young adults (21 HD and 8 CCPD cases) aged 1.5–20 (9.7±1.0) years. In contrast to our findings, the mean plasma Hcy level in their HD patients was comparable with CCPD cases (4.2±0.7 compared with 4.7±2.8, respectively). Farid et al. [24] evaluated 40 patients with chronic renal failure, 30 on regular hemodialysis treatment (group I) and 10 who did not require dialysis and were on conservative treatment (group II), and 20 healthy age- and sex-matched controls (group III) for hyperhomocysteinemia. The mean serum Hcy was significantly higher in those on regular HD compared with the other 2 groups. In contrast to our results, Ertek et al. [29] reported that the incidence hyperhomocysteinemia was high in PD patients. In their series that included 60 PD subjects with a mean age of 46.2 ± 13.2 years (range: 20–69 years), 88.3% of the patients had hyperhomocysteinemia. In a case control study including 19 healthy subjects, 20 HD, and 18 CAPD patients, the mean plasma Hcy level in dialysis patients was higher than the reference values [30] with no significant difference based on the modality of dialysis. Borazan and colleagues [31] found high serum Hcy levels in 73.1% of HD cases, 65.4% of CAPD cases, and 9% of the healthy control group.

Nair et al. reported high plasma Hcy levels in 82% of their HD patients with no differences in pre- and post-dialysis time [32]. Bostom and colleagues found that the mean plasma HCY levels were markedly higher in the dialysis patients versus controls [33] and that they were 33 times more likely than controls to have hyperhomocysteinemia. Kharlamova et al. found mild and moderate hyperhomocysteinemia in 49.5% and 43.1% of their HD patients, respectively [34].

Cetin et al. [35] reported different tHcy values in HD, PD, early stage chronic renal failure (CRF) and control groups. Despite supplementation with multivitamin, Hcy levels in the first 3 groups were significantly higher than the normal levels, and PD patients had the highest t-Hcy values. In contrast to our study, a similar study in children and adolescents on chronic renal replacement therapy (HD or CCPD) failed to show any significant differences in the mean plasma Hcy level between HD and CCPD subjects [34]. Cetin et al. [35] reported that oral folate supplementation normalized the increased plasma Hcy levels and recommended folate supplements in all children with impaired renal function. The majority of our patients were supplemented by folate before undergoing dialysis, but there were no significant relationships between the dose of folate (<0.5 mg /daily versus≥ 0.5 mg /daily) supplementation and plasma Hcy levels (P=0.235).

Limitation of our study: The main limitations of our study included the lack of a control group, small number of the patients especially in the CAPD group, lack of CAPD cases in the age group >18 years, and lack of information about dietary intake in patients.

Conclusions

In summary, we concluded that mild hyperhomocysteinemia was common in children and young adults undergoing dialysis. The results of the study showed that HD patients and females were more prone to greater elevations of tHcy plasma levels (levels >15μmol /L); these factors did not seem to play a role as independent risk factors of the development of hyperhomocysteinemia. It is not clear why HD cases and females had more elevated Hcy levels.

Performing similar studies, preferably case-control ones, with considering the effect of diet on plasma Hcy concentration in dialysis cases is very attractive and recommended.

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Conflict of Interest

None declared

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