PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN PATIENTS WITH CHRONIC RENAL DISEASE IN AL-NASSIRYAH CITY

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ABSTRACT

Background : Subclinical hypothyroidism is highly prevalent in the general populations especially in elderly, however ,the prevalence of subclinical hypothyroidism in persons with chronic kidney disease is not well studied .

Design : Cross sectional data from (245) persons , 110 persons of them considered as a control group and other persons (135)with chronic kidney disease , all of them were collected from (1-9-2010 to 1-7-2011) in Al – Hussein teaching hospital (out patient and inpatient). All patients and control group were routinely referred for thyroid function tests , renal function test (in form of plasma creatinine) and estimation of glomerular filtration rate (GFR). Multivariable logistic study was used to evaluate the independent association between prevalent subclinical hypothyroidism and estimated GFR .

Results : Among (245) adult participants with serum creatinine , GFR and thyroid function test results , the mean age for both groups were (58 ± 4) year , 148 male while 97 of those were female. The prevelance of subclinical hypothyroidism increased specially with lower GFR (in unit of ml / min. / 1.73 m2) , occurring in 7.5 % of subject with GFR (60 – 90 ml /min.) while those patients with GFR less than (60 ml / min.) the prevalence were increased to 16.5 % ($P < 0.001$). The control group were 110 persons , only 3 participant with subclinincal hypothyroidism (2 %). A significant difference when we compared patient with chronic kidney disease and control group ($P < 0.001$).

INTRODUCTION :

The kidney normally play an important role in the metabolism , degredation and excretion of thyroid hormone. It is not surprising therefore that impairement in kidney function lead to disturbed thyroid physiology . All levels of hypothalamic – pituitary - thyroid axis may involved , including alteration in hormone production, distribution and excretion . (1-2) As a result , abnormalties in thyroid function test are frequently occurred in uremia nevertheless , it is ordinarily possible in the uraemic patient to asses the thyroid status accurately by physical diagnosis and thyroid function testing . Epidemiological data suggest that predialysis patients with chronic kidney disease have an increase risk of hypothyroidism (1-2). The kidney normally contributed to clearance of iodide, primarily by glomerular filtration (3). Thus iodide excretion is diminished in advanced renal failure leading to an increase in plasma inorganic iodide concentration and an initial increment in thyroid iodide uptake (3). The marked increment in intrathyroidal iodide pole result in diminished uptake of radiolabeled iodide by thyroid in ureamic patient .(3) Increases in total body inorganic iodide can potentially blocked thyroid hormone production (the wolff – chaikoff effect). Such a change may explain the slightly higher frequency of goiter and

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hypothyroidism in patient with chronic kidney disease (4). Most patient with renal failure have decreased plasma level of free triiodothyronine (T3) which reflect diminished conversion of T4 to T3 .(5-7)
This abnormality is not associated with increase conversion of T4 to the metabolically inactive reversed (rT3).(5-6) , since plasma (r T3) level are typically normal , this finding differentiate the uraemic patient from patient with chronic illness (6-7). In the latter setting , the conversion of T4 to T3 is reduced but the generation of (rT3) from T4 is enhanced .(6-7). The circulating level of T3 sulfate may be increase in patient with end stage renal failure possibly due to decrease renal clearance (8). Low level of total T3 may also be reflect metabolic acidosis, and reduced protein –binding (9), with respect to the latter , circulation thyroid hormone are normally bound to thyroid binding globulin (TBG) and to a lesser extent , to prealbumine and albumin , although circulating TBG and albumin level are typically normal in uremia (9). Retained substances in renal failure may inhibit hormone binding to these protein as example urea , creatinine , indols and phenols all strongly inhibit protein binding (10-11) , this inhibition may explain why some patient with chronic renal disease have low serum T4 level. Free fatty acid and heparin also interfere with T4 binding to TBG , thus , routine use of heparin to prevent clotting in dialysis tubing may explain the transient increment in serum T4 in haemodialysis (12). Low plasma free T3 may be associated with decrease survival and presence of malnutrition and inflammation (13-14). The plasma concentration of TSH is usually normal in chronic kidney disease (15), However , TSH response to exogenous thyroid releasing hormone (TRH) is often blunted and delayed , with prolong time required to return to basal line (16-17). Reduced renal clearance may contributed to delayed recovery (17).when compared to normal, patient with chronic kidney disease have an increase in TSH during evening hours and the normally pulsatile secretion of TSH is smaller in amplitude (18-19-20).

PATIENTS & METHODS :

1- patient selection : One hundred thirty eight (135) participates whose age were (58 ± 4) year with chronic kidney disease at different levels of GFR diagnosed depending on history , clinical examination and investigations in form of (renal function tests and thyroid function tests) . All those were collected from al- Hussein teaching hospital in Al- Nassiriah city from (10-8-2009 to 15-7-2010). One hundred ten participates as a control group , collected routinely from outpatient clinic .

2- laboratory data : Blood samples were obtained from patients and control groups and measurement of plasma creatinine (colorimetric method) by which the creatinine in alkaline solution reacts with picric acid to form a coloured complex , the amount of the complex formed is directly proportional to the plasma creatinine concentration . (21) thyroid function test which measured by using an automated quantitative test for use on the VIDAS instruments by the assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA) by the assay principle for measurement of thyroid hormone test .(22) these subjects were matched on the basis of thyroid function test TSH (0.25 – 5.0 μ U/L) , free T3 (0.92- 2.33 nmol/L) and free T4 (60-120 nmol/L). (22) And the GFR which is measured depending on the formula : Urinary (creatinine) / plasma creatinine X urine volume (normal value of GFR = 80-120 ml/min.). (23)

3- Statistical analysis : The statistical analysis was done by using (t- test) , all are significant if (P. value < 0.005).

RESULTS :

All participates were (245) were collected from Al- Hussein teaching hospital in Al – Nassiriah city , among those persons (110

) participates consider as control groups collected routinely from outpatient clinic without history of chronic renal impairment (group I) , three participates of this group were with subclinical hypothyroidism (2.7 %) i.e (low TSH but T3 and T4 within normal values) as shown in Table I, The other group (group II) were those patients with chronic renal impairment with GFR (60 – 90) ml/min. /1.73 m2 , the number of this group were 85 patients, Six (6) of those patients were with abnormal thyroid function test i.e subclinical hypothyroidism (7 %) , while (79) patients were with normal thyroid function test as shown in table II. The last group (group III) those are 50 patients with advanced chronic renal impairment with (GFR < 60 ml/min./ 1.73 m2) , eight (8) patients of them were with subclinical hypothyroidism (16 %) , while 42 patients of those with normal thyroid function test as shown in Table 3. The characteristic of this study was shown in Table 4.There is significant difference with P . value (P < 0.01) when we compared group II and III with control group (group I) as shown in table 5

DISCUSSION :

There is subclinical overlap between chronic kidney disease and hypothyroidism , in addition to low total and plasma free T3 level , there are number of symptoms that are common to both conditions including cold intolerance , puffiness appearance , dry and rough skin with non piting edema (Myxedema), lethargy , fatigability and constipation .(24) , further more the frequency of goiter markedly increases in end stage of renal disease (5), despite these findings , most uraemic patients are consider to be euthyroid as evidenced by normal plasma concentration of TSH and free T4 and normal basal metabolic rate and tendon relaxation (5,6,15). So , hypothyroidism can occur in patient with renal disease (specially those on hemodialysis and peritoneal dialysis .(4) Despite the euthyroid status of most uraemic patients , there is some evidence for blunted tissue responsiveness of T3 (15). It had also been suggest that the decresed T3 production may have a protective effect by minimizing protein catabolism . (20) As we know many studies suggest a higher prevelance of thyroid abnormalities in chronic renal failure specially end stage renal failure (7), but little is known regarding this epidemioliogy i.e, of subclinical hypothyroidism in chronic renal failure .

In one study by Chonchol etal (25) , showed higher prevalence of subclinical hypothyroidism in patient with chronic kidney disease , but not requiring chronic dialysis with significance (P .value < 0.001). In our study , we collect all 3 groups , control and patients with chronic renal diseases but with different stages of renal impairment and different level of GFR , there was low TSH with normal limit of T3 and T4 in group of patient i.e, patients with subclinical hypothyroidism with significant difference (P .value < 0.01) when compared with group I (control group).

CONCLUSION :

Our study suggest that subclinical hypothyroidism is a relatively common condition among patients with chronic kidney diseases and these finding is independently associated with lower GFR more than higher GFR .

TABLES

Table I

Parameters	Control	Case
	No. 107	**No.3**
T3	0.7 ± 0.05	0.8 ± 0.08
T4	59.4 ± 22.8	64 ± 2.8
TSH	2.9 ± 1.1	0.03 ± 0.02

Table II

Parameters	**Control**	**Case**
	No. 79	**No. 6**
T3	0.6 ± 0.05	0.7 ± 0.08
T4	60.1 ± 2.8	62 ± 1.01
TSH	2.9 ± 1.2	0.01 ± 0.02

Table 3

Parameters	**Control**	**Case**
	No. 42	**No. 8**
T3	0.7 ± 0.05	0.6 ± 0.08
T4	58.1 ± 2.08	60 ± 2.01
TSH	2.8 ± 1.08	0.01 ± 0.01

Table 4

Parameters		**Control**		**Patients**	
		No. 228	**%**	**No. 17**	**%**
Age		**58 ± 4**		**58 ± 4**	
sex	**male**	138	60.5	١0	58.8
	femal	90	39.5	7	41.2

Table 5

patients	Subclinical hypothyroidism	Normal TSH	total
control	3 (2.7 %)	107 (97.3 %)	110 (100%)
GFR(60-90) ml/min.	6 (7 %)	79 (93 %)	85 (100%)
GFR less than 60 ml/min.	8 (16 %)	42 (84 %)	50 (100%)
TOTAL	17 (6.4%)	228 (93.6%)	245 (100 %)

REFERENCES :

1- Ramirez , Jubiz , W , Gutch , CF, etal . thyroid abnormalities in renal disease .

2-Castellano M, Turconi A , chaler E , Maceives M , Rivavda MA , Belgorosky A. thyroid function and thyroid binding protein with chronic renal failure S.pediatr 1996 Jun, 128 (6) : 784-90 .

3- Thyroid hormone in end stage renal diseases Kapton EM , Quion verde …….

4- Lin CC , chen TW , Ng YY , Chon YH , Yong thyroid dysfunctions and nodular goiter in hemodialysis and peritoneal dialysis . perit dial int 1998 sep-oct. , 18(5), 516-21

5- Kaptein EM , Quion – verde H , chooljian CJ , Tang ww , ..etal . the thyroid in end stage renal failure , medicine (Baltimove) 1988 May , 67 (3) : 187-97 .

6- Spaulding , SW, Gregerman , RI , free thyroxin in serum by equal dialysis 1989 Jun., 99 (6) : 224- 64 .

7- Medri G, Carella C , Padmano V ,… etal pituitary glycoprotein hormone in chronic renal failure 1993 Nov. , 16 (3) : 169-74 .

8- Santini f, chiovotol , Bartalena L, …etal , study of serum triiodothyronin sulfate concentration in patient with non thyroidal illness . Eur. J endocrinal 1996 Jan. 134 (1) : 45-9

9-Wiederkehr MR , Kalogiros J , Krapf R correct of metabolic acidosis improves thyroid and growth hormone axes in hemodialysis patient Nephrol Dial transplant 2004 may 19 (5) , 190-7 . Epub 2004 feb. 19.

10-Spaulding , SW, Gregerman , RI , free thyroxin in serum by equilibrium dialysis , effect of dilution . J. clin endocrinal metabolism 1972 , 34: 974 .

11- Hochstetler , LA , flanigon MJ , Lim VS abnormal endocrine test in hemodialysis patient Jam sac nephrol 1994 April , 4 (10) , 1754 – 9 .

12- Herschman , JM , Jones , CM, Bailay ,Al . Reciprocal changes in serum thyrotropin produced by heparin. J clin.endocrine metab. 1972 , 34 : 574

13- Zoccoli C, Tripepig , low triiodothyronin a new focet of inflammation in end stage renal diseases. JAM soc Nephrel 2005 sep. , 16 (9) , 2789-95 , Epub 2005 Jul.20

14- Zocolic , Mollamacif. Low triiodothyronine and survival in end stage renal disease. Kidney int. 2006 Aug. 70 (3) , 523-8 , Equb 2006 Jul. 14.

15- Lim Vs , Flanigon MJ Zavala DC , Freeman RM . protective adaptation of low T3 in patient with chronic renal failure . Kidney int 1985 sep. , 28 (3) , 541-9 .

16- Czernichew P, Dauzet MC, Broyer M. abnormal TSH , prolactine and growth hormone response to TSH in chronic renal failure . J. Clin. Endocr. Metabo. 1976 sep. 43 (3) 1630-7

17- Duntash , Wolf Sf , Keck FS . TRH , pharmacokinetic and pharmacodynamic properties in chronic renal failure clin. Nephrology 1992 oct , 38 (4) 214-8.
18- posqualini T, Zantleifer D , Balzoretti M. evidence of hypothalamic -pituitary thyroid abnormalities in children with end stage renal failure . J.pediatic 1991 , June , 118 (6) : 873-8.
19-Wheatley T, Clerk PM , Clerk JD , Holde R, abnormality of TSH evening raise and pulsatile release in hemodialysis patients . clin. Endocrinal (oxf.) 1989 Jul, 31 (1) , 39-50 .
20- Spector DA , Dovis PJ , Heldeman JH . thyroid function and metabolic rate in chronic renal failure . Ann intern. Med. 1976 Dec. , 85 (6) : 724-30 .
21- Randox . Bartels , H. Bohmer , M. (1972) clin.chem. Acta 37 : 193 .
22- Beirsack H.J. Hotze A. the clinician and the thyroid . Eur. J. Nucl .Med. 1991 ,18 : 761-778.
23- Formerly Zilva . Pannall . Mayne . Clin. Chem. In diagnosis and treatment 6 th edition 1994 , 18 (1) .
24- Drazen , Gill , Griggs, …etal . Cecil textbook of Med. , Clin.manefes. of hypothyroidism , 21 th. Edition 2004 , 239 : 1401-3.
25- Chonchol M. , Litti G. , Salvgno G., ..etal , prevelance of subclinical hypothyroidism in patient with chronic kidney disese , Clin. , J . Am. Soc. Nephrol. 2008 , sep. , 3 (5) : 1296-300.

معدلات هبوط افراز الغده الدرقيه غير السريري عند مرضى عجز الكليتين المزمن في مدينة الناصريه.

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الخلاصه :

الهدف : ان الهدف لهذه الدراسه هو للتعرف على معدلات هبوط افراز الغده الدرقيه غير السريري عند مرضى عجز الكليتين المزمن .

نمط الدراسه : صممت هذه الدراسه في مستشفى الحسين التعليمي في مدينة الناصريه ، و امتدت على نحو عشرة اشهر من ايلول ٢٠١٠ الى شهر تموز ٢٠١١ . جمعت عينات الدم والادرارمن جميع المرضى الداخلين في الدراسة(سواء كانوا من المرضى او المجموعة الضابطة) لتعيين مستويات هرمونات الغدة الدرقية والكرياتنين ولمعرفة علاقة معدل الترشح الكلوي الكبيبي وافراز الغدة الدرقية عند مرضى القصور الكلوي .تم اخذ ٢٤٥ مشترك (١١٠ هم من المجموعة الضابطة و ١٣٥ من مرضى القصور الكلوي) والذين يتراوح معدل اعمارهم بين (4 ± 58)) ، منهم ١٤٨ رجل و ٩٧ امرأه.

النتائج : اظهرت نتائج الدراسه الحاليه انخفاض افراز الغده الدرقيه غير السريري عند مرضى القصور الكلوي بنسبة ٧% عند مرضى القصور الذين تتراوح عندهم معدل الترشح الكلوي الكبيبي من (٦٠-٩٠ مل –الدقيقه) ، بينما كانت النسبه ١٦ % عند المرضى الذين كان معدل الترشح الكلوي الكبيبي عندهم اقل من (٦٠ مل – الدقيقه) ، حيث تم ملاحظة ارتفاعاً معنوياً ((P < 0.001) وقد تم ملاحظة نسبة 2.7 % عند المجموعه الضابطه ، حيث تم ملاحظة ارتفاعاً معنوياً عند مقارنة المرضى بالمجموعه الضابطه ((P < 0.01) .

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