BALIKESİR MEDICAL JOURNAL
e-ISSN: 2564 - 6664

Araştırma Makalesi

BALIKESIR MEDICAL JOURNAL, 2020;4(3): 55-59

DOI: 10.33716 bmedj.821483

Kronik Böbrek Hastalığı Olan Bireylerde Orak Hücreli Anemi Taşıyıcı Sıklığının Belirlenmesi

Determination of the Frequency of Sickle Cell Trait in the Patients with Chronic Kidney Diseases

Serra Sürmeli Döven[1], Selma Ünal[2], Serap Demir[3], Simge Bardak[4], Feryal Karahan[5], Ayşe Jini Güneş[6], Ali Delibaş[7]

[1]Mersin University Faculty of Medicine, Department of Pediatric Nephrology, Mersin, Turkey
e-posta: serrasurmel@yahoo.com
ORCID: 0000-0001-9109-859X

[2]Mersin University Faculty of Medicine, Department of Pediatric Hematology, Mersin, Turkey
e-posta: unalselma@mersin.edu.tr
ORCID: 0000-0002-9951-0291

[3]Mersin University Faculty of Medicine, Department of Nephrology, Mersin, Turkey
e-posta: serapbas@yahoo.com
ORCID: 0000-0002-2189-6825

[4]Mersin University Faculty of Medicine, Department of Nephrology, Mersin, Turkey
e-posta: simgebardak@windowslive.com
ORCID: 0000-0002-6851-4871

[5]Mersin University Faculty of Medicine, Department of Pediatric Hematology, Mersin, Turkey
e-posta: feryalkarahan@mersin.edu.tr
ORCID: 0000-0002-1729-9585

[6]Mersin City Education and Research Hospital, Department of Nephrology, Mersin, Turkey
e-posta: jinigunes@gmail.com
ORCID: 0000-0003-4078-6039

[7]Mersin University Faculty of Medicine, Department of Pediatric Nephrology, Mersin, Turkey
e-posta: delibas@mersin.edu.tr
ORCID: 0000-0002-1469-9276

Atıf İçin: Serra Sürmeli DÖVEN, Kronik Böbrek Hastalığı Olan Bireylerde Orak Hücreli Anemi Taşıyıcı Sıklığının Belirlenmesi, Balıkesir Medical Journal, 2020;4(3):55-59

Başvuru Tarihi: 04.11.2020
Kabul Tarihi: 26.11.2020
Yayınlanma Tarihi: 28.11.2020

Sorumlu Yazar:
Serra Sürmeli DÖVEN, Mersin University Faculty of Medicine, Department of Pediatric Nephrology, Mersin, Turkey
e-posta: serrasurmel@yahoo.com

ÖZ

Amaç: Orak Hücreli Anemi Taşıyıcılığı Türkiye'de özellikle Çukurova Bölgesi'nde yaygın olarak görülmektedir. Orak Hücreli Anemi Taşıyıcısı olan bireylerde en sık görülen böbrek anormallikleri renal konsantrasyon defektleri, renal papiller nekroz ve hematüridir. Orak Hücreli Anemi taşıyıcılığının kronik böbrek yetmezliğine yol açmasıyla ilgili tartışmalı sonuçlar yayınlanmıştır. Türkiye'de Kronik Böbrek Hastalığı olan bireylerde Orak Hücreli Anemi Taşıyıcı sıklığının araştırıldığı herhangi bir çalışma bulunmamaktadır. Bu çalışmada, Türkiye'de tek bir merkezdeki kronik böbrek hastalığı olan bireylerde Orak Hücreli Anemi Taşıyıcılığı' nın sıklığını belirlemek amaçlanmıştır.

Gereç ve Yöntemler: Merkezimizde Erişkin ve Çocuk Nefroloji Polikliniklerinde takip edilen, kronik böbrek yetmezliği, tübülopati, proteinüri ve hematürisi olan 164 hasta çalışmaya dahil edildi. Hastaların tanıları, hemoglobin düzeyleri, glomerüler filtrasyon hızları, idrar dansiteleri, proteinüri, hematüri varlığı ve ailede orak hücreli anemi öyküsünün olup olmaması gibi veriler kayıtlardan elde edildi. Hemoglobin elektroforezi ile HbS ve HbA değerleri elde edildi.

Bulgular: Hastaların yaş ortalaması 33.18±27.33 yıl (min.-maks. 1-92 yıl) idi. Hastaların 92'sinde (%56,1) kronik böbrek yetmezliği, 19'unda (%11,6) tübülopati, 22'sinde (%13,4) proteinüri ve 31'inde (%18,9) hematüri vardı. Orak hücreli anemi taşıyıcılığı kronik böbrek yetmezliği olan üç erişkin bireyde saptandı (%1,8).

Sonuç: Bu çalışmaya göre Kronik Böbrek Hastalığı olan bireylerde Orak Hücreli Anemi Taşıyıcılığı sıklığında artış görülmemiştir. Bu bulguları desteklemek için daha büyük hasta gruplarıyla çalışmalar yapılmalıdır.

Anahtar Kelimeler: Kronik böbrek hastalığı; orak hücreli anemi taşıyıcılığı; orak hücreli anemi hastalığı

ABSTRACT

Aim: Sickle Cell Disease and Sickle Cell Trait (SCT) is commonly seen in Çukurova region in Turkey. Renal manifestations of the sickle cell trait (SCT) include renal concentration defects, renal papillary necrosis, and hematuria. Conflicting results were reported regarding whether the SCT leads to chronic renal failure. Frequency of Sickle Cell Trait in the patients with chronic kidney diseases has yet to be reported in Turkey. This study evaluated the SCT frequency in patients with chronic kidney diseases in a single center in Turkey.

Materials and Methods: A total of 164 patients with chronic kidney disease such as chronic renal failure, tubulopathy, proteinuria, and hematuria who were followed-up in the Pediatric and Adult Nephrology Departments in a center were enrolled in the study. Information regarding diagnosis, hemoglobin levels, glomerular filtration rate, urine density, proteinuria, hematuria, and family history for sickle cell disorder were collected from the records retrospectively. HbS and HbA values were evaluated using hemoglobin electrophoresis.

Results: The mean age of the patients was 33.18±27.33 years (min.-maks. 1-92 years). Ninety-two (56.1%) had chronic renal failure, 19 (11.6%) had tubulopathy, 22 (13.4%) had proteinuria, and 31 (18.9%) had hematuria. SCT was detected in three adult patients (1.8%) with chronic renal failure.

Conclusion: The SCT was not associated with increased frequency of chronic kidney diseases according to this study. Further studies with a larger sample size are needed to support this result.

Keywords: Chronic kidney disease; sickle cell trait; sickle cell disease

INTRODUCTION

Sickle cell disorder (SCD) is a common and serious inherited blood disorder which is due to a substitution of valine for glutamic acid at the sixth aminoacid position of the beta globin gene on the short arm of chromosome 11 (1). Sickle cell trait (SCT) is the heterozygous form of the condition and is seen in 8% of African Americans (2.5 million individuals) and as many as 40% of West Africans (2-4). In Turkey the total number of patients with SCD is approximately 1200 and the frequency of HbS is 0.03% (5). This ratio alters in different regions of Turkey. Çukurova region in Turkey is the most common area for sickle cell anemia patients. The frequency of SCT in Adana 10%, in Antakya 10.5%, in Mersin 13.6%, in Antalya 2.5% (6-9).

Renal manifestations of SCD consist of loss of urinary concentrating ability, papillary necrosis, glomerular lesions, such as focal segmental glomerulosclerosis (FSGS), interstitial scarring and iron deposition (10) due to microvascular obstruction and tissue damage. Studies demonstrate that intrarenal medullary blood vessels are significantly damaged in both SCD and SCT (11). SCT patients present with papillary necrosis, hematuria and urinary concentrating defects (12-15). Renal medullary carcinoma was reported in patients with SCT (16). It is not certain that SCT could lead to chronic kidney disease (CKD). It was reported that SCT is associated with CKD and albuminuria in African Americans (17). Inversely the association between SCT and CKD could not be shown in other studies (18-19).

This study aims to assess SCT frequency and whether SCT screening is necessary in patients with CKD in areas with high SCT prevalence.

MATERIAL AND METHODS

A total of 164 patients with CKD such as chronic renal failure (CRF), tubulopathy, proteinuria, and hematuria who were followed-up in the Pediatric and Adult Nephrology Departments of Mersin University Faculty of Medicine were enrolled in the study. The study was conducted in line with the WMA Declaration of Helsinki. The Clinical Research Ethics Committee of Mersin University approved the study (2018/247). Information regarding diagnosis, Hemoglobin (Hgb), glomerular filtration rate, urine density, proteinuria, hematuria, family history for SCD was collected from the records retrospectively. HbA2, HbS values were evaluated by Hemoglobin Electrophoresis (Bio-Rad HPLC Variant) (2). SCT was defined as the ratio of Hgb S 30-45%. CRF was defined as estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m^2 calculated by Modified Schwartz in children (Constant k × height in centimeters/serum creatinine in micromoles per liter). The value of k was 0.413. In adults eGFR was calculated using the modification of diet in renal disease (MDRD) equation, based on serum creatinine, age, race and gender. End stage renal failure was defined as eGFR<15 ml/min/1.73m$^{2.}$ Tubulopathy group consisted of patients who had urinary concentration defects with beta 2 microglobulin increment in the urine (>370 mcg/day). The level of beta 2 microglobulin in urine was determined using Immulite 2000 (Siemens Healthcare Diagnostics) by the Chemiluminescence method. Urinary concentration impairment was defined in patients whose urinary density was below 1010 after 12 hourly dehydration. Proteinuria was defined as urinary protein excretion 4-40 mg/m^2/h. Orthostatic proteinuria was excluded in those patients. Patients who had isolated proteinuria with unknown etiology were enrolled in the

study. Hematuria was defined as >5 Red blood cells/hpf in centrifuged urine specimens. Idiopathic persistent microscopic hematuric patients were included in the study.

RESULTS

A total of 164 patients with chronic kidney diseases were enrolled in the study. The mean age of the patients was 33.18±27.33 (1-92) years. Chronic renal failure, hematuria, proteinuria and tubulopathy had in 92 (56.1%), 31 (18.9%), 22 (13.4%) and 19 (11.6%) patients, respectively. Three patients (1.82%) with CRF had Hemoglobin S and their ages were 54, 75 and 76 respectively. The demographic and renal features of these patients were shown in Table 1. Family history for SCA was negative in all of those patients.

Age	Sex	CRF Etiology	RRT	HgS (%)	GFR (ml/min/1.73m^2)	Proteinuria	Hematuria
54	Male	Unknown	+	38.8	8	+	-
75	Male	Unknown	-	37.6	45	+	-
75	Female	Hypertension	-	37.2	25	+	-

Table 1. The Demographic and Renal Features of the Patients with SCT and Chronic Renal Failure

CRF: Chronic renal failure, RRT: Renal replacement therapy, HgS: Hemoglobin S, GFR: Glomerular filtration rate

DISCUSSION

In this study, we aimed to detect the frequency of SCT in the patients with CKD. We detected only three SCT (1.8%) in the 164 CKD patients with CRF, tubulupathy, proteinuria, and hematuria. All of the patients with SCT had CRF. According to this result we could say, that SCT ratio is higher in the patients with CRF (3 of 92 patients; 3.3%) compared to other chronic renal diseases. It was demonstrated that SCT frequency in Mersin was 13.6% (7). However, it might be due to the small sample size.

Red cell sickling causes chronic microvascular disease and reduced medullary blood flow, and local hypoxia in SCD. This leads to prostaglandin release and vasodilation, and increased renal blood flow and increment in GFR causes proteinuria and glomerulosclerosis and CKD (20). FSGS is a well-known glomerulopathy in patients with sickle cell disease (21). Although no study demonstrated nephrotic syndrome in patients with SCT, increased risk of albuminuria was reported in patients with SCT when compared to noncarriers (17). Hematuria is commonly seen in patients with SCT. In about 50% of cases, hematuria due to obstruction secondary sloughed papillae and infection, and papillary necrosis which is generally self-limiting but which can also lead to prolonged to macroscopic hematuria (22). Urinary concentration defect is other renal manifestation of both SCD and SCT patients. Microscopic infarction of renal medulla due to extreme hypoxemia, acidosis and hyperthermia leads to loss of maximal urine concentrating ability which is progressive with age and develops in most adults with SCT (23-24). Urine osmolality can reach values higher than plasma during overnight dehydration (400-800 mOsmol) in people with SCT (24). Increased urinary levels of beta 2 microglobulin and reduced urinary osmolality (median=541mOsm/kg, range=406-722) were detected in patients with SCT in a study (25).

In our study SCT was not detected in patients with hematuria (N=31), proteinuria (N=22) or tubulopathy (N=19). It was an interesting finding that all three patients with SCT had CRF. The presence of SCT

in these patients have had worsened the prognosis, and accelerated the progression of renal disease. We think that this issue should be investigated by further studies.

In conclusion SCT frequency is not increased and SCT screening is not necessary in patients with CKD according to this study. Further studies with larger sample size should be done in Turkish patients with CKD to detect whether SCT is associated with CKD.

Authors declare no conflict of interest.

REFERENCES

1. Shaw C, Sharpe C.C, Could sicle cell trait be a predisposing risk factor for CKD? Nephrol Dial Transplant, 2010: 25; 2403-2405.
2. Ashley-Koch A, Yang Q, Olney RS, Sickle hemoglobin (HbS) allele and sickle cell disease: a HuGE review, Am J Epidemiol 2000: 151; 839–845.
3. Connes P, Hardy-Dessources MD, Hue O, Counterpoint: sickle cell trait should not be considered asymptomatic and as a benign condition during physical activity, J Appl Physiol 2007: 103; 2138–2140.
4. Fabritius H, Millan J, Le Corroller Y, Systematic screening of hemoglobinopathies in blood donors in Guadeloupe (French West Indies), Rev Fr Transfus Immunohematol 1978: 21; 937–950.
5. Dünya'da ve Türkiye'de talasemi ve hemoglobinopatiler. Arcasoy A. (editör). Hemoglobinopati ve Talasemi Önlem-Tanı-Tedavi. 2. Baskı. Antalya: Ulusal Hemoglob inopati Konseyi Sağlık Bakanlığı 2003. p.11-19.
6. Gümrük F, Altay Ç, Orak hücre anemisi, Katkı,1995:16; 327-345.
7. Arpacı A, Aksoy K, Dikmen N. Çukurova'da orak hücre anemisi ve talasemi taraması, XXII. Ulusal Hematoloji Kongresi, İstanbul 1991: 115.
8. Eraslan S. Beta Talaseminin Moleküler Tanısı. Düzen Genetik Hastalıklar Tanı Merkezi, Ankara-Türkiye, 2005.
9. Kılınç Y, Akmanlar N, Kümi M, Köker I, The incidences of hemoglobinopathies and thalassemias in cord blood of newborns from Çukurova Province, Med Bull İstanbul Medical Faculty 1992: 25; 9- 14.
10. Buckalew VM Jr, Someren A, Renal manifestations of sickle cell disease, Arch Intern Med. 1974:133;660–669.
11. Statius van Eps L, Earley L. Strauss and Welt's Diseases of the Kidney. 3rd ed, Boston: Little, Brown & Company, 1979: 1229-1240.
12. Key NS, Derebail VK, Sickle cell trait: novel clinical significance, Hematology Am Soc Hematol Educ Program, 2010: 418-422.
13. Tsaras G, Owusu-Ansah A, Boateng FO, Amoateng-Adjepong Y. Complications associated with sickle cell trait: a brief narrative review, Am J Med. 2009: 122: 507–512.
14. Heller P, Best WR, Nelson RB, Becktel J, Clinical implications of sickle cell trait and glucose-6-phosphate dehydrogenase deficiency in hospitalized black male patients, N Engl J Med. 1979: 300 (18); 1001-1005.

15. Statius van Eps LW, Pinedo-Veels C, de Vries GH, de Koning J, Nature of concentrating defect in sickle cell nephropathy: microradioangiographic studies. Lancet. 1970: 1 (7644); 450-452.
16. Alvarez O, Rodriguez MM, Jordan L, Sarnaik S, Renal medullary carcinoma and sickle cell trait: A systematic review. Pediatr Blood Cancer, 2015: 62(10); 1694-1699.
17. Naik R.P, Derebail V.K, Grams M.E, Franceschini N, Auer P.L, Peloso G.M, Association of Sickle Cell Trait With Chronic Kidney Disease and Albuninuria in African Americans, JAMA, 2014: 312 (20) ; 2115-2125.
18. Mukendi K, Lepira FB, Makulo JR, Sumaili KE, Kayembe PK, Nseka MN, Sickle cell trait is not associated with chronic kidney disease in adult Congolese patients: a clinic-based, cross-sectional study, CVJ Africa, 2015: 26 (3); 125-129.
19. Hicks P.J, Langefeld C.D, Lu L, Bleyer A.J, Divers J, Nachman P.H, Sickle cell trait is not independently associated with susceptibility to end-stage renal disease in African Americans, Kidney Int, 2011: 80 (12);1339-1343.
20. Piccone C, Dell KM. Sickle Cell Nephropathy in Children, Pedaitric Nephrology (7nd ed) Vol.2. Berlin Heidelberg: Springer Verlag, 2016: 1526.
21. Maigne G, Ferlicot S, Galacteros F, Belenfant X, Ulinski T, Niaudet P et al. Glomerular lesions in patients with sickle cell disease, Medicine 2010:89 (1) ;18-27.
22. Eckert DE, Jonutis AJ, Davidson AJ, The incidence and manifestations of urographic papillary abnormalities in patients with S hemoglobinopathies. Radiology, 1974: 113; 59–63.
23. Gupta AK, Kirchner KA, Nicholson R, Adams JG, III, Schechter AN, Noguchi CT, et al, Effects of alpha-thalassemia and sickle polymerization tendency on the urine-concentrating defect of individuals with sickle cell trait, J Clin Invest 1991: 88(6);1963-1968.
24. Statius Van Eps LW, De Jong PE, Sickle Cell Disease, In: Schrier RW, Gottschalk, CW, eds. Disease of the Kidney, 1997; p. 2201-2219.
25. Sesso R. Almeida M.A., Figueiredo M. S, Bordin J.O, Renal dysfunction in patients with sickle cell anemia or sickle cell trait, Braz J Med Biol Res. 1998: 31; 1257-1262.