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Evaluation of Cytomorphological Changes in Urine Samples of Uremic Patients Undergoing Regular Hemodialysis

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Abstract

Background Dialysis is one of the common strategies of renal replacement therapy for patients with chronic renal failure; however it harbors significant cellular changes in various body fluids.

Objective To evaluate the cellular changes in urine samples of patients undergoing dialysis.

Methods Seventy-two fresh midstream, spontaneously voided urine samples, they were included in the study. Early morning samples were excluded, Duration of dialysis was taken into consideration (short term and long term dialysis). Samples were centrifuged at 3000 round per minute for 15 minutes, the supernatants were decanted and the sediments were examined cytomorphologically.

Results The gross appearance of all urine samples was neither purulent nor hemorrhagic. Microscopically there was an excessive shedding of urothelial cells in urine samples of patients undergoing dialysis compared with samples of the control group which showed evidence of normal shedding. There were no significant cytological atypia or malignancy in all urine samples. The excessive exfoliation in the absence of significant inflammation, hemorrhagic, or cytological atypia was compared with control group.

Conclusions The study revealed that some cytological changes do occur in the urothilial cells in patients undergoing dialysis; these changes need further attention to disclose their real causes.

Key words chronic renal failure, hemodialysis, cytomorphology, epithelial exfoliation

Introduction

Chronic renal failure remains a major health problem. Dialysis (hemo- and peritoneal) is regarded one of the most common strategy of renal replacement therapy and the main sole for saving the life [(1)]. Urine cytology has an acceptable sensitivity and specificity. It is easy, cheap, quick, readily accepted by the patients, and can be repeated many times without the need for preparations of the patients for the test [(2,3)]. The most important accomplished cytology of urinary tract is the diagnosis of clinically suspected cases of carcinoma particularly carcinoma in situ [(4)].

Routine screening is performed for the detection and diagnosis of tumors and precancerous state of urinary tract, the incidence of false positive and false negative result is 5% and 15% respectively [(5,6)].

Various types of cells may appear during cytomorphological study of the urine samples including physiological exfoliation, transitional, sequamouse, columnar, traumatic exfoliation, red blood cells and cast [(7)].

Dialysis (mainly peritoneal of any duration) can induce significantly atypical changes in mesothelial cells [(8)].

The abnormal cells can be benign cytological findings, precancerous or neoplastic and dysplastic changes [(9-12)].

Dialyses harbor some cellular changes in various body fluids [(13-15)].

The aim of the study was to analyze the cytomorphplogical changes of exfoliated urothilial cells in urine samples of the patients undergoing dialysis and to determine the relation-ship between the degree and type of cellular changes and the duration of dialysis.

Methods

From April 2005 to August 2005, 72 urine samples were collected from patients with end stage renal failure undergoing dialysis at Al-Kadhimya Teaching Hospital.

Patients with indwelling catheters, previous history of passing renal stone, chronic irritants (I mean like exposure to the chemical materials and drugs). Malignant and benign tumors of urinary tract and those with significant hematuria (16 cases) were excluded from the study.

A spontaneously passed, freshly voided, midstream urine samples (15 ml) in three disposable tubes (5 ml each) were collected from each patient and send for cytological examination. The presence of red blood cells (RBC) was regarded significant when the number of RBC was more than 3-4 in female and 2-3 in male. The number of exfoliated cells was considered low if it was ranged from 0-1, moderate from 2-6 and high if the number was more than 6 cells per HPF.

The patients were divided into two groups; the first group was those with short term dialysis (duration of dialysis of less than one year), the second group were those with long term dialysis (duration of dialysis of more than one year). The mean duration of dialysis was 14.6 months. Of all 68% underwent hemodialysis six hours every week, the remaining (32%) had nine hours per week. Gambro AK96 machines were used. A third group of 20 healthy subjects were included as a control group.

Descriptive statistical analysis studies were applied for each group including mean, median, mode and standard deviation.

Chi-square tests were applied for comparison, p value < 0.005 was regarded significant.

Results:

Seventy two patients on dialysis were subjected to urine cytomorphological examination, 41 were males and 31 were females, they were divided into two groups according to the duration of dialysis

Group I: included patients undergoing dialysis for less than, or equal to one year (n= 33).

Group II: included patients on dialysis for more than one year (n= 39).

Group III: Included control persons (n=20) of matching age and sex.

The age range was 20-65 years with a mean of 49.06 years. The distribution of age groups in the three groups is shown in Table 1. The sex distribution is in Table 2.

The most probable causes of end stage renal disease based on clinical ground are shown in Table 3.

Table 4 shows that the urine color was deep orange in 91.7% in groups I and II, clear yellow color in 65% of the control group.

The exfoliation of urothilial cells in each group was shown in Table 4, there was high exfoliation (> 6 cells/HPF) in groups I and II in comparison to the control group who showed low exfoliation (0-1 cells/HPF).

Both single and cluster cells were found in the same smear in 80.6% in urine samples of group I and II while the arrangements of exfoliated urothilial cells in urine samples of control group were arranged in single pattern (Table 4).

The frequencies of red blood cells (acute and chronic) in urine samples of each group studied are shown in Table 5.

The atypical or malignant cytological features were not found in all groups.

Table 1: Age distribution of the study groups

Age Group(year)	Study Groups					
	Group I	(%)	Group II	(%)	Group III	(%)
20-25	3	(9.1)	6	(15.4)	4	(20)
30-39	5	(15.2)	4	(10.3)	14	(70)
40-49	4	(12.1)	8	(20.5)	2	(10)
50-59	6	(18.2)	8	(20.5)		
60 and above	15	(45.5)	13	(33,3)		
Total	33	(100)	39	(100)	20	(100)
Chi-square test	value		df		*p* value	
	85.873		8		0.000 (highly significant)	

Table 2: The sex distribution of the study groups

Study Groups	SEX		Total (%)
	Male (%)	Female (%)	
Group I	17 (51.5)	16 (48.5)	33 (100)
Group II	24 (61.5)	15 (38.5)	39 (100)
Group III	10 (50)	10 (50)	20 (100)
Total	51(55.4)	41 (44.6)	92 (100)

Chi-sequare test *p* value > 0.005 (not significant)

Table 3: The urine color of the study groups (macroscopical appearance)

Urine color	Group I (%)	Group II (%)	Group III (%)	Total (%)
Deep orange	29 (87.9)	37 (94.4)	2 (10.0)	68 (73.9)
Straw color	3 (9.1)	1 (2.6)	5 (25.0)	9 (9.8)
Yellow	1 (3.0)	1 (2.6)	13 (65.0)	15 (16.3)
Total	33 (100)	39 (100)	20 (100)	92 (100)
Pearson Chi- square test		value	df	*p* value
		58.239	4	000

Table 4: The exfoliation of urothilial cells and their patterns of arrangement in the urine sample smears of both dialyzing and control groups

No. of exfoliated urothilial cells	Group I (%)	Group II (%)	Group III (%)	Total (%)
Low (0-1 cells/HPF)	-	-	20 (100)	20 (21.7)
Moderate (2-6 cells/HPF)	7 (21.2)	5 (12.8)	-	12 (13.0)
High (> 6 cells/HPF)	26 (78.8)	34 (87.2)	-	60 (65.2)
Urothilial cells arrangement				
Single	6 (18.2)	6 (15.4)	20 (100)	32 (34.8)
Cluster	2 (6.1)	-	-	2 (2.2)
Both	25 (75.8)	33 (84.6)	-	58 (63.0)
Total	33 (100)	39 (100)	20 (100)	92 (100)

Table 5: The type (inflammatory or red cells) and the distribution of cells in both dialyzing and control groups

Red blood cells in urine samples	Group I (%)	Group II (%)	Group III (%)	Total (%)
Significant	6 (18.2)	8 (20.5)	-	14 (15.2)
Non	27 (81.8)	31 (79.5)	20 (100)	78 (84.8)
Total	33 (100)	39 (100)	20 (100)	92 (100)
Inflammatory cells in the urine samples				
Lymphocytic	3 (9.1)	1 (26)	-	4 (4.3)
Lymphocytic and neutrophilic	1 (3.0)	1 (26)	-	2 (2.2)
Non	29 (87,9)	37 (94.9)	20 (100)	86 (93.5)
Total	33 (!00)	39 (100)	20 (100)	92 (100)

Discussion

For the most practicing nephrologists and pathologists, the term urinary tract cytology brings to mind almost immediately the diagnosis of urinary tract neoplasm. Obviously many non neoplastic disorders may also be reflected in the urine cytology specimens [17]. Thus the technique of the cytological diagnosis of urinary tract malignancy has been around for well over 150 years and widely published for at least 65 years [18].

Under normal circumstances mid stream freshly voided urine contains relatively scattered urothilial cells and few cells of other types, including polymorph nuclear leukocytes, red cells and macrophages [19], however, urinary cytology preparations are usually not ordered by the clinicians unless having a clinical suggestion of urinary tract disease, an abnormal urine analysis, or both [20]. Thus the sparsely cellular "normal urinary cytology preparation is unusual in

day to day practice, that's why taking the control group of patients from wide age range to confirm the previous knowledge. The current results are nearly similar findings in the series conducted by Yarub et al and Kutaibah et al [17,18].

The number of urothilial cells and nonepithilial cells in a given freshly voided urine sample may vary widely depending not only on the how long the disease process goes on, but also on the manner by which the specimens were collected. Excluded in this study all the specimens which were obtained by catheterization, irrigation, ordinary brushing techniques, which normally yields a cellular smear. In addition to that the specimen preparation may also have some effect on the cell yield and the individual cell characteristics and that is why using an ordinary centrifugation (not cytocentrifuge or membrane filter technique) to overcome excessive normal yield of the urothilial cells [21]. The method of fixation, slide preparation (pre-albumin coated slides method used to prevent cell loss), and staining (routine alcohol fixed papanicolaou stain were used to exclude counting of keratinized sequamous cells especially in female patients which relatively resemble superficial urothilial cells. All these might interfere or change the diagnostic yield in the interpretation of data.

Despite the above mentioned facts, the diagnostic yield is relatively more accurately correlate with the number and volume of the urine sample [22,23].

In comparison with control group, the urine samples of uremic patients undergoing dialysis showed excessive shedding of urothilial cells in the form of clusters. The number of samples (small samples) and the mean duration of hemodialysis (the mean duration of hemodialysis in the current study less than 15 months) and the presence of comorbid disease (anemia and malnutrition) which are highly prevalent among our patients might affect the results.

In conclusion, there was excessive shedding of urothilial cells in the urine samples of patients undergoing dialysis (short and long term) compared with control group.

There was a significant cell cluster arrangement of exfoliated urothilial cells in the urine samples of both groups (short and long term dialysis) compared with control group which were mainly single cells.

There were no significant cellular cytomorphological changes of both groups (short and long term dialysis) and no cell atypia and / or malignant changes in the urine samples of both groups (short term and long term dialysis)

I recommend that every cyto-pathologist should be aware of these changes and more advanced study or studies should done to know the exact pathophysiology and cellular molecular biology in predialysis and in patients undergoing different forms of dialysis.

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